FOGSI Focus Benefits Beyond Contraception

Dr. Nandita Palshetkar
President FOGSI & Editor in Chief

EDITORIAL TEAM

Dr Shobha N Gudi
Chairperson family welfare committee
FOGSI

Dr Ritu Joshi
Dr Atul Ganatra
Dr Basab Mukherjee

FOGSI Focus Benefits Beyond Contraception

Dr Nandita Palshetkar
President

Dr Sudha Prasad
Vice president

Dr Jaydeep Tank
Secretary General

EDITORIAL TEAM

Dr Shobha N Gudi
Chairperson family welfare committee
FOGSI

Dr Ritu Joshi
Dr Atul Ganatra
Dr Basab Mukherjee

FOGSI Focus on Benefits Beyond Contraception

EDITORS

Dr Nandita Palshetkar
MD FCPS FICOG FRCOG
President, FOGSI (2019)
Chairperson, MSR (2017-18)
Vice President, AMOGS (2016-18)
Past President, MOGS (2016-17)

Dr Shobha N Gudi
MD,DNB,FICOG,CIMP.
Prof and HOD,
St Philomenas Hospital, Bengaluru,
Chairperson F.W.C. FOGSI 19-21
President BSOG 2018.

Dr Ritu Joshi
MBBS, MS
Obstetrics & Gynaecology
Consultant gynaecologist ,
Fortis Escorts Jaipur.
Vice president West Zone FOGSI 2014
Chairperson FWC FOGSI 2010 -2012

Dr Atul Ganatra
MD,DGO,FICOG.
Obstetrician Gynecologist
& Gynecological Endoscopist
Dr. R. J. Ganatra's Nursing Home
& Fortis Hospitals, Mumbai
–Vice President (West Zone)
FOGSI 2020-2021
Chairperson MTP Committee
FOGSI (2012-2014)

Dr Basab Mukherjee
MD, FICOG, FRCOG(London)
Consultant Gynaecologist ,
Columbia Asia Hospital, Mumbai.
Vice President Elect FOGSI 2021
Chairperson FWC FOGSI (2013-2015)

Team FOGSI 2019 Office Bearers

President	Dr Nandita Palshetkar
Secretary General	Dr Jaydeep Tank
Vice President (West Zone)	Dr Rajendrasingh Pardeshi
Vice President (West Zone)	Dr Haresh Doshi
Vice President (North Zone)	Dr Sudha Prasad
Vice President (East Zone)	Dr Rajat Mohanty
Vice President (South Zone)	Dr Aswath Kumar
Deputy Secretary General	Dr Madhuri Patel
Treasurer	Dr Suvarna Khadilkar
Joint Treasurer	Dr Parikshit Tank
Joint Secretary	Dr Ameya Purandare
Immediate Past President	Dr Jaideep Malhotra
President Elect	Dr Alpesh Gandhi

Chairpersons of the Committees

Adolescent Health	Dr Girish Mane
Clinical Research	Dr Meena Samant
Endocrinology	Dr Pratik Tambe
Endometriosis	Dr Kuldeep Jain
Endoscopic Surgery	Dr B Ramesh
Ethics and Medicolegal	Dr Geetendra Sharma
Family Welfare	Dr Shobha Gudi
Food Drugs MedicoSx Equipment	Dr Vidya Thobbi
Genetics and Fetal Medicine	Dr Mandakini Pradhan
HIV/AIDS	Dr Mrutyunjay Mohapatra
Imaging Science	Dr Meenu Agarwal
Infertility	Dr Asha Baxi
International Academic Exchange	Dr Varsha Baste
MTP	Dr Bharti Maheshwari
Medical Education	Dr Abha Singh
Medical Disorders in Pregnancy	Dr Komal Chavan
Midlife Management	Dr Rajendra Nagarkatti
Oncology	Dr Bhagyalaxmi Nayak
Perinatology	Dr Vaishali Chavan
Practical Obstetrics	Dr Sanjay Das
Public Awareness	Dr Kalyan Barmade
Quiz	Dr Sebanti Goswami
Safe Motherhood	Dr N Palaniappan
Breast	Dr Sneha Bhuyar
Sexual Medicine	Dr Sudha Tandon
Urogynaecology	Dr Nita Thakre
Young Talent Promotion	Dr Vinita Singh

President's Message

It gives me great pleasure to know that the FOGSI Focus on Benfits beyond contraception is ready for release. The aim of this FOGSI Focus is to highlight the latest evidence based guidelines, approaches to diagnosis and treatment and protocols for practice on this subject.

As busy practitioners, we rarely have time to read and update ourselves with current evidence. We hope this volume will help you to keep abreast of the latest developments in this field and give you some valuable tips and pointers which you can implement in day-to-day practice.

The Presidential theme for my FOGSI year 2019 is "We for Stree – Safer, Stronger, Smarter". During the year, we will attempt to focus on academic, social and community health initiatives aimed at improving the profile of women in our country. I urge every single one of you to unite and stand with us and contribute to a series of initiatives which will refocus our contributions not only toward the health of Indian women, but their social, financial and educational upliftment as well.

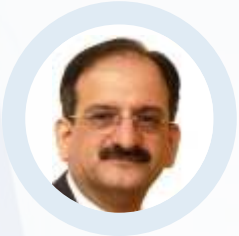
FOGSI is committed to delivering continuing medical education programmes and helping our members to perform to the best of their ability in the areas in which they practice. We also have a raft of initiatives to help women from poor socioeconomic areas receive appropriate care through our social and community healthcare initiatives eg. The FOGSI Saving Mothers initiative. The FOGSI Manyata project also aims to bring a certain minimum standard of care to the women of India via accreditation and training of private nursing homes and healthcare personnel.

I congratulate the editors for their hard work and sincere efforts in helping to write, collate, edit and publish this FOGSI Focus.

Nandita P. Palshetkar

Dr Nandita Palshetkar
MD FCPS FICOG FRCOG

President, FOGSI (2019)
Chairperson, MSR (2017-18)
Vice President, AMOGS (2016-18)
Past President, MOGS (2016-17)



Foreword.
Benefits beyond Contraception

Dr. Nozer Sheriar

Consultant, Obstetrics and Gynecology
Breach Candy, Hinduja Healthcare Surgical and
Holy Family Hospitals, Mumbai
Past Secretary General and Chair, MTP Committee
Federation of Obstetric and Gynecological Societies of India
Past President Mumbai Obstetric and Gynecological Society
Co-Chair, Medical Advisory Panel Family Planning Association of India

'Gonna change my way of thinking, make myself a different set of rules.'
Bob Dylan

I vividly remember the first set of six FOGSI Focus published in 1993. The brainchild of Dr. Usha Krishna the publication was developed to give focused clinical value on selected subjects and has since become a flagship publication of FOGSI for its membership.
Since then the FOGSI Focus has addressed the issue of contraception many times but this Focus on **Benefits beyond Contraception** brings a completely different contemporary perspective to this subject. The team of Nandita Palshetkar, President and Shobha Gudi, Chair, Family Welfare Committee of FOGSI and the Issue Editors Ritu Joshi, Atul Ganatra and Basab Mukherjee need to be commended for curating this insightful compilation.

While the historical antecedents of contraception are engaging, the development of oral contraception is particularly fascinating. John Rock, a devout Catholic with five children and nineteen grandchildren started with a mission to help barren women have babies. His collaboration with Gregory Pincus began with experiments to use hormones to help women conceive. The plan to use progesterone to suppress ovulation and then withdraw it for a rebound effect was probably the first application beyond contraception. Of course using hormones to prevent pregnancy followed exactly the same logic and the rest was history.

The Pill once proved effective at blocking ovulation was immediately approved by the USA FDA in 1957 for the treatment of female disorders and not for contraception. Since thirty American states had laws against birth control, the Pill existed undercover for its early life. So women found a way and there was a sudden epidemic of menstrual irregularity conveniently reported and treated across the country
While each contraceptive method or technique, medication or device acts through distinctive actions, many of these give a host of non-contraceptive applications and benefits. These benefits can accrue from every type and group of available contraception -

Male and female barrier contraception block partner tissue contact and access to the upper genital tract.

Spermicides have an inherent antiseptic effect and can act as bactericides and viricides.

Intrauterine devices act by interposition and physical presence while the progestational intrauterine systems induce endometrial suppression and a myometrialprogestational effect.

Combined hormonal contraception, combined oral contraception, vaginal ring or contraceptive patch as also progestin only pills act through ovarian suppression and with some combined preparations have an additional antiandrogenic and antimineralcorticoid effect.

Injectable progestogens and implants induce ovarian suppression and exert a strong progestational effect.

Female sterilization interrupts and disrupts tubal continuity.

These many modes of action provide many applications for contraceptives to be used beyond contraception. Though most of these applications are off label, their clinical use is backed by solid scientific evidence and recommendations. These actions and applications may be classified as follows -

Protection

Barrier contraceptives provide 50% reduction in sexually transmitted infections by their local antiseptic action that can be preventative for vaginal and cervical infections.

Treatment

Combined hormonal contraceptives have substantial benefits for cycle related conditions, such as irregular menstruation, dysmenorrhea and menorrhagia. Along with and progestogen only contraception they are approved to treat menstrual disturbance including heavy menstrual bleeding and primary dysmenorrhea. The levonorgestrel intrauterine system is acknowledged to be more effective than combined oral contraceptives in reducing menstrual blood loss.

Combined oral contraception suppresses abnormal ovarian function regularizing menstrution in polycystic ovarian syndrome. It is the first line treatment for hyperandrogenism and hirsutism. It has demonstrated benefit for controlling mild to moderate acne, specifically for inflammatory lesions.

Though all combined oral contraception is effective, that with drosperinone is the approved treatment of premenstrual dysphoric disorder, a severe form of premenstrual syndrome. It also reduces mastalgia due to fibrocystic breast disease and long term use results in an overall reduction in benign breast disease.

While combined hormonal contraception and injectable progestins and implants are both used in the treatment of endometriosis and related pain, the progestational intrauterine systems are highly effective in treating adenomyosis.

Prevention

Barrier contraceptives reduce the risk of cervical intraepithelial neoplasia by preventing human papilloma virus infection.

Combined hormonal contraceptives are known to prevent benign ovarian cysts, with the greatest risk reduction for endometriomas. Large, population based studies indicate that their use is also associated with a decreased risk of cervical, ovarian, endometrial and coorectal cancer.

Combined hormonal contraception and progestogen only contraception are both used for endometrial protection and are . beneficial for endometrial hyperplasia and uterine polyps.

Supplementation

Combined oral contraceptives are used in the perimenopause for contraception, treatment of menstrual irregularity and treatment of hypoestrogenic symptoms.

They can also be used for hormone replacement therapy for women aged below 50 years and of premature ovarian failure. They protect against endometrial and ovarian cancer, benefit bone mineral density and alleviate menstrual complaints, hyperandrogenic symptoms and vasomotor disturbance.

Suppression

Combined oral contraception is used for down regulation of the pituitary ovarian axis in assisted reproductive technology protocols.

Adjunctive benefits

The reduction in menstrual blood loss as also amenorrhoea induced by combined and progestogen only hormonal contraception has a positive hematological benefit with the prevention and treatment of anemia.

Combined oral contraception is used for adjustment of menstrual cycle and timing to accommodate personal requirement and work schedules

Combined hormonal contraception in a long cycle or continuous regime benefits women with menstrual migraine without aura by either allowing minimal changes or eliminating hormonal changes all together.

The same techniques of bipolar coagulation, detachment or clipping of the fallopian tube used for laparoscopic female sterilization are used for pre assisted reproduction detachment of hydrosalpinges.

Individual empowerment

The greatest benefit beyond contraception is the life changing autonomy that contraceptive choice offers individual women and girls. It is by doing this more than anything else that modern contraception has rearranged the furniture of human relations as never expected and forever.

Preface

Contraception makes a woman safer, stronger, smarter.

More than one billion people across the world use contraception for birth control, with the single most desire to raise healthier, better educated and more prosperous families.It is obvious in many ways that contraception practices and prescriptions have the potential for changing societies for the better and boosting a nation's economic growth.

There is another aspect to the use of contraceptives for the health of the individual client that FOGSI wishes to highlight, especially for the smart working women, the athletes and the sportspersonalities, the professionals, corporate officials, the self employed and even the student and research scholars. The benefits of using hormonal contraceptives for abnormal uterine bleeding and benign gynecological disorders,for advantages of bone health,relief from symptoms of peri-menopause ,for prevention of cancers as well in managing complex diseases like endometriosis and Polycystic ovarian disease, all need to be re-emphasized . A relief from the aforementioned problems leads to better performance at the work place, less absence and loss of working hours and higher achievements of reaching targets and completing projects.

Through this edition of FOGSI focus , we wish to present the evidence in support of use of hormonal and other contraceptives for situations other than or in addition to the need of contraception. Even the wonderful God given natural LAM(Lactation amenorrhea method)conferring advantages to the mother and infant, and thetremendous potential of the simple barrier methods in significantly reducing the STD/HIV burden are included.

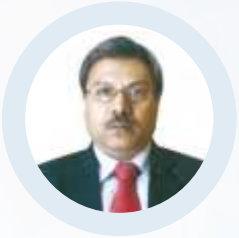
Planning for reproductive health and exercising a choice for the method , is highly conducive to enabling empowerment for women .. In addition, by conferring other health benefits, contraception makes a woman stronger, safer and smarter.

Yours sincerely,

Dr Nandita Palshetkar **Dr Shobha N. Gudi**

TABLE OF CONTENTS

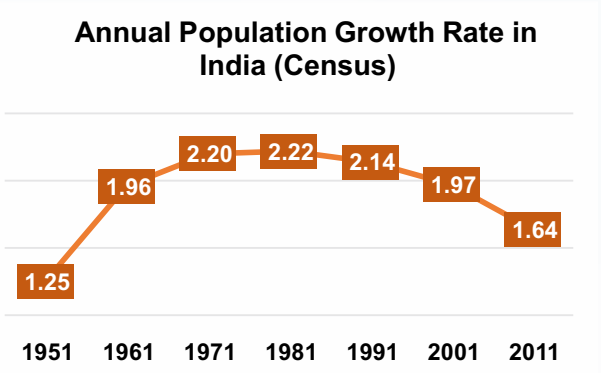
Family Planning for nation's economic growth: Investing to reap the dividends



Dr S. K. Sikdar
MBBS, MD,
Additional Commissioner In-charge: Family Planning
MOHFW, Government of India

1. Population Dynamics in India:

The second largest country and the largest democracy in the world- India is now witnessing a decline in population growth rates. After witnessing the rapid population growth for two decades since 1952 (when the National Family Planning Program was launched) the country witnessed the declining trend with the sharpest ever decline in 2011 (Census). Census also estimates that this decline is more pronounced in the high focus states.



India has considerable state wise variations.
The Report on Population Projection- 2019 by Registrar General of India states that out of the total projected increase in population of 31 crores in India during 2011-36, 50% is likely to occur in the five States of Bihar, Uttar Pradesh Maharashtra, West Bengal and Madhya Pradesh. Nineteen percent of the total population increase in India during the same period is anticipated to occur in Uttar Pradesh alone. The population in these five states together is expected to grow at 1.0 percent per annum during 2011-36.

In 1951 India's population was 60% of that of China. Currently, China and India account for 38
percent of the world's population. According to World population prospects 2019, India is
projected to overtake China by 2027.

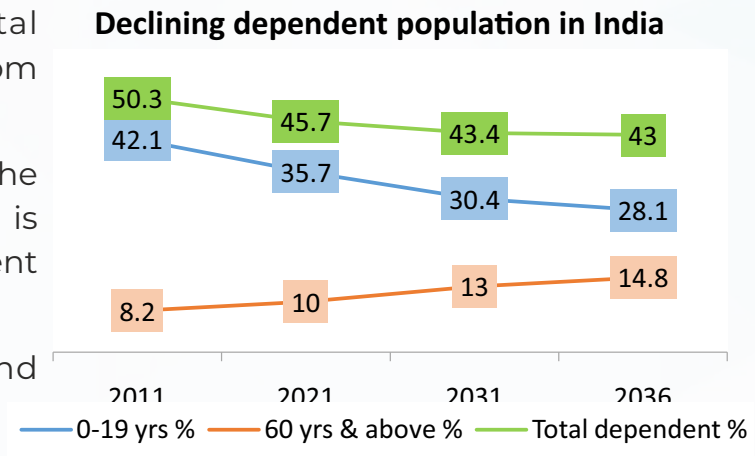
India's population is expected to continue to grow until mid-century (due to population momentum) however the population growth will come to an end: The number of children in
India peaked more than a decade ago and is now falling. (UNDESA projection).

A key driver of this declining trend has been the steady decline in India's total fertility rate (TFR). India's TFR has halved from 4.5 in 1984 to 2.2 as of 2017 (SRS).

1.1 Changing age structure of India's population / Changing demographic profile of India:

The fertility transition in India has accelerated in recent years which is resulting in rapid changesin the age structure of the population. The recently published report on Population Projection2019 by Registrar General of India states that between 2011 and 2036, because of the declining fertility

- the proportion of population aged under 15 years is projected to decline from 30.8 to 19.8 percent;
- the youth population in the age- group 15-24 years is expected to increase from 23.3 crores in 2011 to 25.2 crores in 2021 and then continue to decrease to 22.7 crores in 2036. Its proportion to total population is expected to fall from 19.3 to 14.9 percent.
- the proportion of population in the working age-group 15-59 years is expected to rise from 60.7 percent in 2011 to 65.1 percent in 2036.
- x the older ages (60 years and above) are set to increase considerably (from 8.2 to 14.8 percent). Further with the declining fertility, alongwith the increases in life expectancy, the number of older persons in the population is expected to increase by more than double from 10 crores in 2011 to 23 crores in 2036.



Another important consequence of the declining fertility will be that, at the national level, the population

in the school-going age of 5-14 years is expected to decline from 25.4 crores in 2011 to 20.7 crores in 2036.

The main force driving India's changing age structure are the maturing of past birth cohorts, upward trends in life expectancy due to increasing survival rates at older ages, and falling fertility.

1.2 The Demographic Dividend in India:

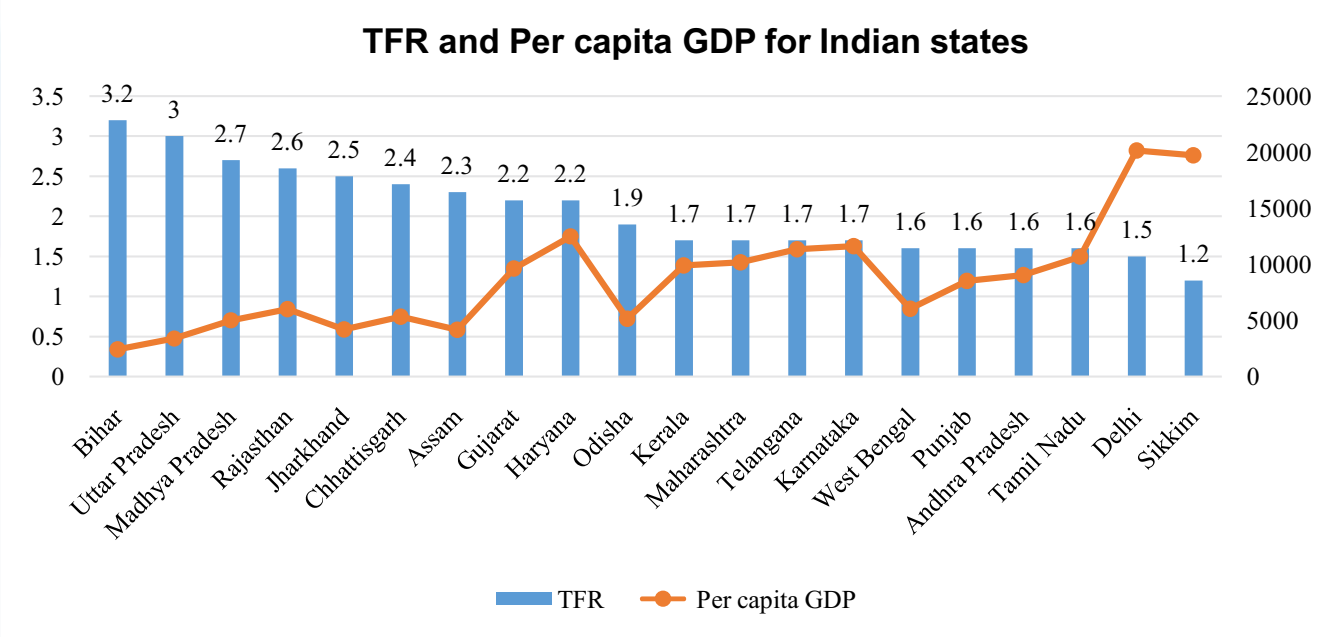
Demographic dividend leads to larger proportion of population in the working age group compared to younger and old age groups. India has the biggest advantage of demographic dividend (proportion of working population out of total population is high), which will be a key driver for future growth. 15 million youngsters will enter the workforce annually for the next five years. A study on demographic dividend in India by United Nations Population Fund (UNFPA) reveals that the window of demographic dividend opportunity in India is available for five decades from 2005-06 to 2055-56, longer than any other country in the world. Also this demographic dividend window is available at different times in different states because of differential behaviour of the population parameters.

2. Demographic changes and Economic Growth:

It is now well established that improving literacy and economic conditions for individuals lowers birth rates, while low fertility in turn plays a positive role in economic growth. Family planning (FP) programmes impact women's health by providing universal access to sexual and reproductive healthcare services and counselling information. With more than 50% of working age population, India will be a potential workforce supplier over the coming decades.

2.1 Impact of Family Planning on economic growth:

Family Planning allows the youth to stay healthy and free of reproductive, sexual and mental health issues and ensures that they stay in school and complete education. It gives them the freedom to enter the job market or start their own enterprise, be more productive at work, increase savings and prioritise spending on things that improve their lives. It also allows the young to start a family at a time when they can offer the best opportunities for their children. India's experience also shows that the states with higher TFR (mostly Northern states) tends to have the lower GDP as compared to states with lower TFR (mostly Southern states)



A strong Family Planning program is thus imperative to economic growth in following ways:

- Diverting resources from spending on children to investing in physical and human infrastructure- Government investment in family planning more than pays for itself. Economist Scott Moreland calculated that each dollar invested in family planning allows a government to forego $2 to $6 dollars of spending on other social services like education and immunization. Those extra money can go toward infrastructure, health and education to help governments harness the demographic dividend.

- Improving women's health- For each additional dollar spent on contraceptive services, the cost of pregnancy-related care drops by US$2.20 (Darroch, et al, 2017).

- Increasing women's workforce which further results in decline in fertility- Family planning not only leads to better health and more education for both women and their children, it also results in higher income and greater household assets for their families (T. Paul Schultz, 2007). Therefore the longer a woman waits to have children, the longer she can participate in the paid labor force, thereby boosting the economic health and prosperity of poor communities.

- Improving education of children

- Improving health: Improved Health of population acts as a driver to economic growth by ensuring, a productive workforce, improving school enrolment ultimately resulting in a more educated workforce, decreasing physical and mental disabilities in children by improving cognitive function and reducing cost of care for geriatrics. And finally, healthy populations attract foreign direct investment.

- Improving political stability- Evidences suggest that countries with a youth bulge have a high risk of social unrest and political violence. This risk will dissipate when the youth bulge shrinks and each adult supports fewer children, which can be achieved through fertility decline (Richard Cincotta, 2008).

- Decreasing family spending and thus lifts families out of poverty-University of Michigan economist Martha Bailey and others found that in the U.S., people born in counties which received funding for family planning programs in the 1960s were 2 to 4 percent less likely to live in poverty in their childhood and as adults.

- Ensuring better implementation of schemes and programmes by factoring in population dynamics.

The benefits of contraception go beyond health, including demographic, economic and environment impacting all 17 sustainable development goals (SDGs). As part of the Sustainable Development Goals (SDGs), "Ensuring universal access to sexual and reproductive health (SRH) services by 2030" was determined to have one of the two highest benefit-cost ratios (Kohler & Behrman, 2014). Investments in the health of girls and women have the potential to speed up a country's demographic transition and to increase the size of the demographic dividend.

FP has been recognized as one of the most cost-effective solutions for achieving gender equality and equity (goal 5) by empowering women with knowledge and agency to control their bodies and reproductive choices by accessing contraceptive methods (E. Starbird et.al 2016). Birth spacing can have great implications on health, for instance, reduction in malnutrition (goal 2) and long-term good health (goal 3) for the mother and the child. Access to contraceptives helps in delaying, spacing and limiting pregnancies; lowers healthcare costs and ensures that more girls complete their education, enter and stay in the workforce, eventually creating gender parity at workplace.

3. Approaches towards lowering fertility- India's experience:

India was the first country in the world to have launched a National Family Planning Programme way back in 1952. One of the goals enunciated in its National Population Policy 2000, was to stabilize the population at a level consistent with the requirement of national economy. The program has since come a long way and currently it has been redesigned to not only attain population stabilization but also to considerably reduce maternal, infant and child mortality and morbidity. The National Health Policy (NHP) 2017 also provides for a policy guidance to shaping health systems in all its dimensions. The NHP sets out indicative, quantitative goals and objectives which includes the achievement of Total Fertility Rate (TFR) of 2.1 by 2025. The National Health Policy recognizes that improved access, education and empowerment would be the basis of successful population stabilization. Hence over the years India's National Family Planning Programme too has evolved with a shift in focus from merely population control to more critical issues of saving the lives and improving the health of mothers and children through use of reversible spacing methods leading to reduction in unwanted, closely spaced and mistimed pregnancies and thus avoiding pregnancies with higher risks and chances of unsafe abortions.

India has experienced a substantial decline in the infant mortality rate, from over 165 deaths per thousand live births in the 1950s to around 33 today. India's child (i.e., under age 5) mortality rate has fallen from 138 deaths per thousand in the early 1980s to 37 today. The fertility rate has declined sharply from approximately 6 children per woman in the 1950s to 2.2 children per woman today. The percentage of girls married below the age of 18 years has substantially declined from 47% (NFHS 3) to 27% (NFHS 4) over the last decade and the teenage fertility has also dropped by half from 16% (NFHS III) to 7.9% (NFHS IV).

Considering the fact that India's demographic window of opportunity is now open, India has several opportunities to increase its chances of utilizing this period effectively. Making wider and deeper investments in health is an important step towards the same. India has considerable potential to promote higher income through programmatic and financial commitments to health. Under National Health policy 2017 India has committed to increase the health spending by 2.5% GDP.

Another important step in this regards is accelerating the fertility decline and better reproductive health to its citizens. This can be achieved through:

- Expansion of family planning services as per clients' need.
- Promote infant and child survival
- Improving girls' education

3.1 Expansion of family planning services as per clients' need:

National Family Planning program has evolved over time from targeted approach to reproductive choices. Despite the concentrated efforts, still 13 percent of currently married women have an unmet need for contraception (6 percent for spacing births and 7 percent for limiting births). Studies show that if the current unmet need for family planning could be fulfilled over the next 5 years, we can avert 35,000 maternal deaths, 1.2 million infant death,

save more than Rs. 4450 crores and save Rs. 6500 crores, if safe abortion services are coupled with increased family planning services. The current focus of the program is towards meeting the unmet need of contraceptives and increasing the use of modern contraceptive use which are directly linked to reducing maternal and child mortality across the nation. The modus operandi is to enable both men and women to make responsible choices and thus help in averting unintended and mistimed pregnancies, achieve desired family size and promote the health of the mother and child.

Over the years, the program has been expanded to reach every nook and corner of the country and has penetrated into PHCs and SCs in rural areas, Urban Family Welfare Centers in the urban areas. With the recent new initiatives being undertaken to expand contraceptive choices and high fertility approach (Mission Parivar Vikas),the Government is ensuring the improved access to contraceptive choices. Lately there has been an enhanced focus to ensure commodity security through a web based, app based and SMS based system- Family Planning Logistics and Management Information System.

India is also laying an emphasis on addressing the unmet need of contraception in post pregnancy period and has set a global best practice in provision of post-partum Family Planning services through public health facilities.

3.2 Promote infant and child survival:

Evidences suggest that Vaccines against childhood disease are one potent way to realize an improvement in child survival, which leads to more than proportionate fertility reductions. Such an approach might include expanding coverage of established and inexpensive vaccinations and include introducing a new schedule of vaccinations thereby addressing several leading causes of child death in India. Childhood vaccines also have the virtue of promoting better school attendance, better cognitive function, and better adult health, all of which tend to make vaccinated children more productive, and therefore higher-earning, adults. India stands to benefit greatly from initiatives to increase vaccination coverage; its coverage rates are currently well below world averages. India's Universal Immunization Programme (UIP) is one of the largest public health programmes targeting close of 2.67 crore newborns and 2.9 crore pregnant women annually. Under UIP, immunization is provided free of cost against 12 vaccine preventable diseases:

- Nationally against 10 diseases - Diphtheria, Pertussis, Tetanus, Polio, Measles, Rubella, Rotavirus diarrhoea, severe form of Childhood Tuberculosis, Hepatitis B and Meningitis & Pneumonia caused by Hemophilus Influenza type B

- Sub-nationally against 2 diseases - Pneumococcal Pneumonia and Japanese Encephalitis

3.3 Improving Girls' education:

Girls' education can serve as both an indicator of development and an instrument for promoting fertility decline. Educated mothers tend to have fewer children, as education raises the cost of having children by improving the work opportunities that most women are forced to forgo by having children. Education also empowers women to express their views on lifestyle and fertility decisions. The Government is now ensuring inclusive growth for all through Aspirational Districts Program where Health & Nutrition and Education forms an important pillar under the core areas of focus.

In conclusion, demographics matter to the pace and process of economic growth and development. Today, the demographic dividend is in India's favour and Family Planning can and should be used to leverage it. Longer lives and smaller families lead to more working-age people supporting fewer dependents. This reduces costs and increases the country's wealth, economic growth and productivity of the people. Ultimately, these result in reduction in poverty and inequalities. Thus Family Planning is the single most intervention that will lead to the achievement of the SDGs through a multiplier effect.

Socio-economic benefits of contraception at the microcosm level of individual families

Author Dr. Jyoti Vajpayee MD (Ob/gyn)

MD (OBG).
Publichealthspecialist, Consultant Bill and
Melinda Gates foundation.Board member PSI

Key facts

- **214 million women of reproductive age in developing countries who want to avoid pregnancy are not using a modern contraceptive method.**
- **Some family planning methods, such as condoms, help prevent the transmission of HIV and other sexually transmitted infections.**
- **Family planning / contraception reduces the need for abortion, especially unsafe abortion.**
- **Family planning reinforces people's rights to determine the number and spacing of their children.**
- **By preventing unintended pregnancy, family planning /contraception prevents deaths of mothers and children.**

Benefits of contraception

- Promotion of family planning and ensuring access to preferred contraceptive methods for women and couples is essential to securing the well-being and autonomy of women, while supporting the health and development of communities.

- Preventing pregnancy-related health risks in women
- A woman's ability to choose if and when to become pregnant has a direct impact on her health and well-being. Family planning allows spacing of pregnancies and can delay pregnancies in young women at increased risk of health problems and death from early childbearing. It prevents unintended pregnancies, including those of older women who face increased risks related to pregnancy. Family planning enables women who wish to limit the size of their families to do so. Evidence suggests that women who have more than 4 children are at increased risk of maternal mortality.

- By reducing rates of unintended pregnancies, family planning also reduces the need for unsafe abortion.

- Reducing infant mortality
  Family planning can prevent closely spaced and ill-timed pregnancies and births, which contribute to some of the world's highest infant mortality rates. Infants of mothers who die as a result of giving birth also have a greater risk of death and poor health.

-

- Helping to prevent HIV/AIDs
  Family planning reduces the risk of unintended pregnancies among women living with HIV, resulting in fewer infected babies and orphans. In addition, male and female condoms provide dual protection against unintended pregnancies and against STIs including HIV.
- Empowering people and enhancing education
  Family planning enables people to make informed choices about their sexual and reproductive health. Family planning represents an opportunity for women to pursue additional education and participate in public life, including paid employment in non-family organizations. Additionally, having smaller families allows parents to invest more in each child. Children with fewer siblings tend to stay in school longer than those with many siblings.
- Reducing adolescent pregnancies
  Pregnant adolescents are more likely to have preterm or low birth-weight babies. Babies born to adolescents have higher rates of neonatal mortality. Many adolescent girls who become pregnant have to leave school. This has long-term implications for them as individuals, their families and communities.
- Slowing population growth
  Family planning is key to slowing unsustainable population growth and the resulting negative impacts on the economy, environment, and national and regional development efforts.
- Mental Health, Unintended Pregnancy and Reproductive Outcomes
  Women with depression and anxiety experience an elevated risk of unintended pregnancy, and those pregnancies may be more likely to end in induced abortion, compared to women without depression and anxiety. Depression and anxiety are precursors to a host of negative perinatal and postpartum outcomes, including maternal and infant morbidity, obstetrical complications, preterm labour, stillbirth, low birth weight, and antepartum and postpartum depression, especially when pregnancies are unintended. Poor, underinsured, undereducated, and minority women disproportionately suffer mental health morbidity, low rates of detection and treatment and adverse reproductive outcomes, including unintended pregnancy.

Overview

Family planning is one of the 10 great public health achievements of the 20th century. The availability of family planning services allows individuals to achieve desired birth spacing and family size, and contributes to improved health outcomes for infants, children, women, and families.

Family planning services include:

- Contraceptive services
- Pregnancy testing and counselling
- Pregnancy achieving services including preconception health services
- Basic infertility services
- Sexually transmitted disease services

- Broader reproductive health services, including patient education and counselling
- Breast and pelvic examinations
- Breast and cervical cancer screening
- Sexually transmitted infection (STI) and human immunodeficiency virus (HIV) prevention education, counseling, testing, and referral

Abstinence from sexual activity is the only 100% effective way to avoid unintended pregnancy. For individuals who are sexually active, correct and consistent contraceptive use is highly effective at preventing unintended pregnancy. The most effective methods to prevent unintended pregnancy include long-acting reversible contraceptives such as intrauterine devices (IUDs) and contraceptive implants, followed by other hormonal contraceptives including oral contraceptives (pills), the patch, the ring, and the Depo-Provera shot (DMPA). Condoms protect against both unintended pregnancy and STIs, and their use should be encouraged. Both men and women should be counselled about using condoms at every act of sexual intercourse when not in a long-term, mutually monogamous sexual relationship.

Why Is Family Planning/Contraception Important?

For many women, a family planning clinic is their entry point into the health care system and one they consider their usual source of care.In 2015, publicly funded family planning services helped prevent 1.9 million unintended pregnancies, including 440,000 teen pregnancies. In 2010, every public dollar spent on family planning saved the federal and state governments $7.09

Unintended pregnancies include pregnancies that are reported by women as being mistimed or unwanted. Almost half (45%) of the 6.1 million annual pregnancies in the United States are unintended. Unintended pregnancies are associated with many negative health and economic consequences.The public cost of births resulting from unintended pregnancies was estimated at $21 billion in 2010 (this figure includes costs for prenatal care, labour and delivery, post-partum care, and 1 year of infant care.
For women, negative outcomes associated with unintended pregnancy can include:

- Delays in initiating prenatal care
- Reduced likelihood of breastfeeding
- Increased risk of maternal depression
- Increased risk of physical violence during pregnancy

Births resulting from unintended pregnancies can have negative consequences including birth defects and low birth weight.Children from unintended pregnancies are more likely to experience poor mental and physical health during childhood, and have lower educational attainment and more behavioural issues in their teen years.

The negative consequences associated with unintended pregnancies are greater for teen parents and their children. Eighty-two percent of pregnancies to mothers ages 15 to 19 are unintended.Twenty percent of all unintended pregnancies occur among teens.

Teen mothers:

- Are less likely to graduate from high school or attain a GED by the time they reach age 30
- Earn an average of approximately $3,500 less per year, when compared with those who delay childbearing until their 20s
- Receive nearly twice as much federal aid for nearly twice as long

Similarly, early fatherhood is associated with lower educational attainment and lower income.The average annual cost of teen childbearing to U.S. taxpayers is estimated at $9.1 billion, or $1,430 for each teen mother per year.Moreover, children of teen parents are more likely to have lower cognitive attainment and exhibit more behaviour problems.Sons of teen mothers are more likely to be incarcerated, and daughters are more likely to become adolescent mothers.

The ability to decide when, how many or whether to have children is not only a basic human right; it is also the key to economic empowerment, especially for poor women. But in too many developing countries, this right is being undermined by a lack of access to safe, modern forms of contraception.The decision to start a family is one of the most important choices a person can make. It is also a fundamental human right; only individual adults should have the power to decide whether, when, or how often to conceive. And yet, for millions of people around the world, this right remains unrealized.More than 200 million women in developing countries who want to delay or avoid pregnancy are not using modern contraception. Women who are poor, less educated, or live in rural areas can face significant economic, cultural, and institutional barriers to birth control, and often turn to dangerous forms of pregnancy prevention out of desperation. If women had universal access to voluntary family-planning information and services, maternal deaths could be reduced by as much as three-quarters and infant deaths by as much as a fifth. But family planning does more than save lives; it also saves money. For every dollar invested in reproductive health services, $2.20 is saved in pregnancy-related health-care costs. Moreover, the longer a woman waits to have children, the longer she can participate in the paid labor force, thereby boosting the economic health and prosperity of poor communities.Some governments have already recognized these benefits and are allocating funds accordingly. In Thailand, for example, the Ministry of Health has increased its family-planning budget on the grounds that the added spending now will reduce health-care costs later.The Thai authorities' assessment is correct; when developing countries make investments that empower young people to start a family only when they are ready, birth rates fall and the share of the working-age population increases relative to the dependent population. These so-called “demographic dividends” are forecast to be particularly high for countries in Sub-Saharan Africa, where roughly a third of the population is between the ages of 10 and 24.

Investment in human capital, when accompanied by sound economic policies and robust labour markets, produces significant gains for developing economies. Fully funding the family-planning needs of poor countries would lift millions out of poverty, improve rates of educational attainment, and help close the gender pay gap in the

Global South. Developed countries could solve the global family-planning funding shortfall for a mere 20 cents per person per year, a bargain given the projected returns for individuals, families, and economies. In addition to increased spending, new policies, laws, and implementation of existing regulations will be needed to help protect women and to empower young couples. To improve access to contraceptive methods and to protect the rights of women and girls, a family planning summit in July 2012 launched the Family Planning 2020 (FP2020) Initiative, aiming to reach another 120 million women in the 69 poorest countries with modern contraceptives by 2020 12,13. As of the end of 2017, about 40 countries had made political commitments to this initiative (see http://www.familyplanning2020.org/ for a full and up-to-date list).

A demographic dividend of the FP2020 Initiative and the SDG reproductive health target: A case study result from India and Nigeria

Background: The demographic dividend, defined as the economic growth potential resulting from favourable shifts in population age structure following rapid fertility decline, has been widely employed to advocate improving access to family planning. The current framework focuses on the long-term potential, while the short-term benefits may also help persuade policy makers to invest in family planning.

Methods: We estimate the short- and medium-term economic benefits from two major family planning goals: the Family Planning 2020 (FP2020)'s goal of adding 120 million modern contraceptive users by 2020; Sustainable Development Goals (SDG) 3.7 of ensuring universal access to family planning by 2030. We apply the cohort component method to World Population Prospects and National Transfer Accounts data. India and Nigeria, respectively the most populous Asian and African country under the FP2020 initiative, are used as case studies.

Results: Meeting the FP2020 target implies that on average, the number of children that need to be supported by every 100 working-age people would decrease by 8 persons in India and 11 persons in Nigeria in 2020; the associated reduction remains at 8 persons in India, but increases to 14 persons in Nigeria by 2030 under the SDG 3.7. In India meeting the FP2020 target would yield a saving of US$18.2 billion (PPP) in consumption expenditures for children and youth in the year 2020 alone, and that increased to US$89.7 billion by 2030. In Nigeria the consumption saved would be US$2.5 billion in 2020 and $12.9 billion by 2030.

The tremendous economic benefits from meeting the FP2020 and SDG family planning targets demonstrate the cost-effectiveness of investment in promoting access to contraceptive methods. The gap already apparent between the observed and targeted trajectories indicates tremendous missing opportunities. Accelerated progress is needed to achieve the FP2020 and SDG goals and so reap the demographic dividend.

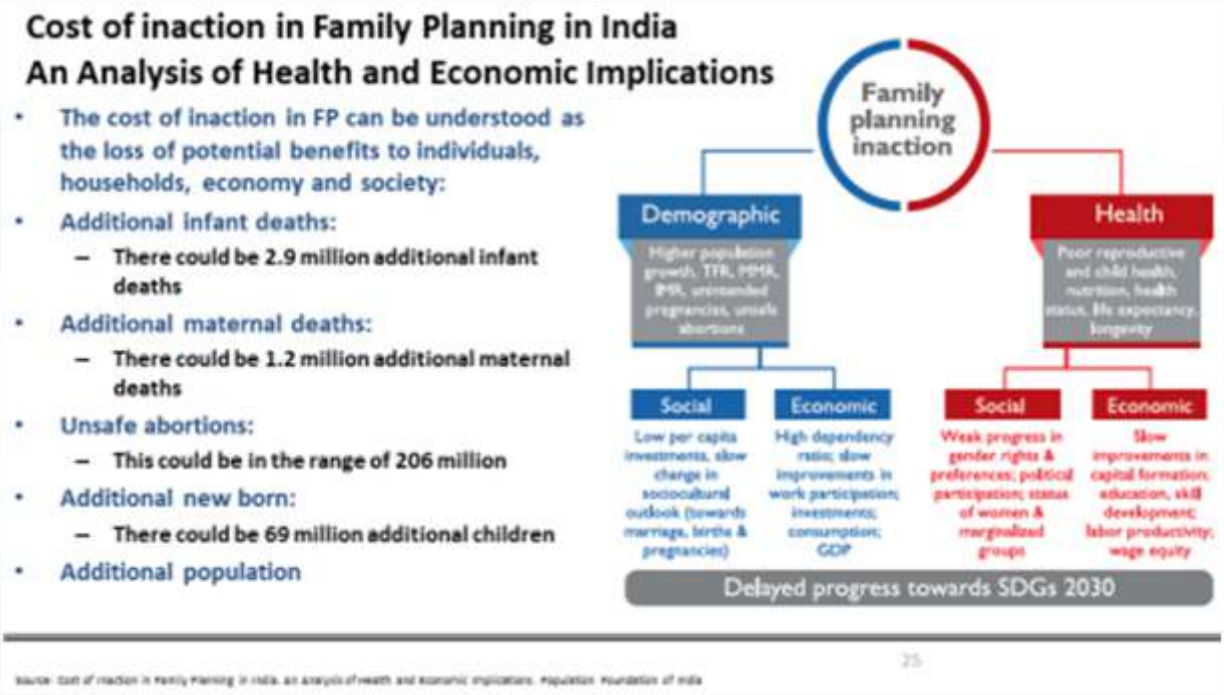
Access to family planning is a critical component of reproductive rights. Family planning also provides multi-faceted benefits to women and their families. It is unique among medical interventions in its breadth of health, developmental and economic benefits, such as reducing maternal and child mortality, empowering women and girls, and enhancing environmental sustainability. The Lancet series on family planning in 2012 documented clearly the extensive gains resulting from family planning. For instance, Ahmed and colleagues estimated that in 2008 contraceptive use in 172 countries averted 272,040 maternal deaths, and that satisfying unmet need for contraceptive methods could prevent another 104,000 deaths per year 2. Cleland et al. made nearly identical estimates using a different methodology 3. Additionally, Canning and Schultz evaluated the economic consequences of family planning, including increases in female labor force participation and proportion of women in paid employment 4.

However, after reaching a global peak following the 1994 International Conference on Population and Development (ICPD) in Cairo, both financial support and political commitment for family planning have been insufficient, and they even declined in the decade prior to 2012. On the other hand, the need for family planning increased due to population growth. With falling funding and growing population, the gap widens at both ends. Consequently, progress to increase access to contraception in developing countries has been slow. Women in sub-Saharan Africa, for example, continue having an average of more than five children 6. Improvement of family planning related indicators in low- and middle-income countries has lagged behind that of indicators in other development sectors, such as education, child survival and infectious disease control. Contraceptive prevalence has increased by only 0.1% points annually during the first decade of the 21 century. The reduction of maternal mortality fell short of its 2015 Millennium Development Goal (MDG) 8.
Two major arguments have been made to promote investments in reproductive health: human rights and economic development. The first considers reproductive health to be a fundamental human right that should be delivered for its intrinsic value. The second argues its instrumental value, particularly for stimulating economic growth and accelerating poverty reduction. A rapid reduction in fertility rate implies fewer births, and consequently a decline in dependency ratio (number of young and old dependents to working-age population).

Specific strategies to address reproductive health needs of adolescents and youth:

While it is well recognized that adolescents and youth have distinctive needs, access to reproductivehealth services by adolescents and youth is mired in challenges of access to services; attitudinal barriers among providers and restrictive social norms. Greater investments and early interventions in their education, health including reproductive and sexual health needs and skill development activities will enhance their contribution to economic output and growth. To meet India's commitments to the SDGs and FP2020 and considering the huge demographic dividend, specific

health strategies especially for adolescents and youth that address their health needs and priorities is critical. This strategy should underscore a voluntary, rights and choice-based approach for addressing their sexual and reproductive health concerns. Specific focus on increasing access to information and reproductive health services, delaying their age at marriage, first pregnancy and empowering them to take informed decisions on spacing between children is the only way to address population momentum which contributes to 70 per cent of the population growth.



The Economic Effects of Contraceptive Access: A Review of the Evidence and Conclusion

Research shows the ways that access to contraception affected women's economic outcomes in the following ways:

1. Reducing Mortality:

Access to contraception has shown sharp declines in maternal mortality (by 3/4ths) and infant mortality(by 1/5th). Infant and under-five mortalities are correlated with the prevalence of risky births. Risky births are those that are too closely timed or occur in older women who have had many births.

2. Educational Attainment

- Young women's access to contraception improved higher education rates.
- Women both enrolled in and graduated from college in great numbers due to contraceptive access.

3. Labour Force Participation

- Access to contraception allowed women to delay childbirth and increase their human capital investment in education and their careers.
- Contraception access contributed to a substantial increase in the proportion of women in the workforce and the number of hours worked by women.

4. Career Outcomes

- In the 1970s, women began making up higher proportions of individuals with careers in professional fields, such as medicine and law.

Among college-educated women, some of this increase can be attributed to access to the contraception.

5. Earnings

- Access to contraception translated into higher wages for women, as women were able to pursue more education before entering the labour force.

6. Poverty

- Having access to contraception by age 20 reduced the probability that a woman lived in poverty.
- Contraceptive access likely impacted women's expectations for their future (or their sense of empowerment more broadly defined), which may have contributed to a reduction in poverty.

7. Effects on the Next Generation

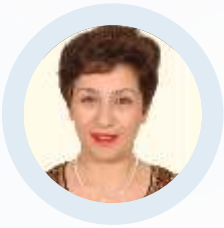
- As legalization of contraception allowed more highly educated women to delay childbearing, the resulting cohort of births was more likely to live in poverty in the short term (as fewer births were born to non-poor women).
- Legal changes to contraceptive access resulted in fertility delays rather than reductions for more highly educated women. As births were retimed, longer-run effects show more children were born into households with more highly educated mothers, and children were less likely to live in poverty.
- In contrast, access to federally funded family planning programs resulted in fewer children in both the short and long run.
- Economic effects of family planning programs on the next generation extended to their adulthood, with a substantial reduction in the number living in poverty as adults.

8. Reduction in total out-of-pocket expenditure on delivery care and child hospitalisation.

- Currently, Indian households experience high level of financial hardships while seeking hospitalisation and delivery care. In 2014, about 14 per cent cases of delivery care and about 20 per cent cases of child hospitalisation experienced catastrophic OOPE.

The cost of inaction in family planning and lack of access to contraceptives can beunderstood as the loss of potential benefits toindividuals, households, economy and society dueto specific programme or policy inaction. Familyplanning inaction can have an adverse impact onthe social and economic development of India,particularly in the demographically backward states.Many of these implications are apparent in the formof poor economic and health development in thesestates.

INCULCATING SAFE SEX PRACTICES IN ADOLESCENTS



Dr. Roza Olyai
Vice President, FOGSI 2014
Chairperson, FOGSI Adolescent
Health Committee 2010-12

Prof. Dr. S. Sampathkumari
Prof (OG), I O G, Madras Medical College, Chennai
Chairperson, FOGSI Adolescent
Health Committee 2016-19

Unprotected sexual intercourse can cause unwanted pregnancies, sexually transmitted infections, risk of abortions and other long term consequences on the health of the individual like pelvic pain, infertilityand vaginal discharge compromising the future adults.

Why adolescents?

Adolescents are a high risk group for they have a natural tendency for curiosity, risk taking behaviour and peer pressure. This along with their inadequate knowledge puts them at risk of complications arising from unprotected sexual intercourse. 50% adolescents are sexually active but only 22% are aware of safe sex practices. Majority of patients with STI now fall in 15-24 age group. This explains the burning need to inculcate safe sex practices among our adolescents to protect and promote adolescent health.

Why Sex education?

Many are of the opinion that sex education increases their chances of sexual activity. On the contrary a well informed adolescent with knowledge of safe sex practices is better off than an ignorant curious adolescent. It is imperative to say that parents, teachers, health educators play a vital role in imparting this sex education. But it is important that we respect the autonomy of the adolescents and avoid a patronizing preachy advice. Provide them with information, and allow them to make their own wise choices.Withholding information only makes them indulge in risky behaviour due to lack of knowledge and thereby put themselves and their partners at risk of sexually transmitted infections[1].

Role of a Healthcare provider:

It is important to be non judgemental. Adolescents are not likely to walk into a health centre for information or contraception if they are going to be judges or embarrassed. Have a welcoming attitude. Provide a separate outpatient clinic to allow adolescents to come and have a consult. Maintain confidentiality unless it threatens the health of the adolescent. Educate them about safe sex practices and types of suitable contraception and details about where they can avail those contraceptives.

Awareness of Contraception:
Contraception avoids unintended pregnancies thereby reducing the burden on healthcare and financial needs to cover the complications. This is why oral contraceptive pills – Mala N and condoms – Nirodh are provided free of cost by the government. But as per Fraser guidelines, if an adolescent is able to comprehend the information given, that sexual activity is likely to proceed with or without contraception, and withholding contraception is only going to affect the health of the adolescent, it can be considered adolescent is mentally capable of taking a decision for themselves and can be provided with contraception without parental consent.

Emergency contraception:
Also called as interceptives, these help to avoid complications following unprotected sexual intercourse. However there exists need for informing the adolescent that this is not a regular contraception and in the event they are likely to be sexually active, they need to follow another reliable method.

Safe sex:
This aims to decrease exchange of bodily fluids which is the main causative factor for sexually transmitted infections. Body fluids are saliva, urine, blood, semen, vaginal secretions. And all types of sex ranging from oral, vaginal to anal can increase chances of STIs.

NACO has advised ABC approach in promoting safe sex practices among adolescents2,

A- Abstinence, delay the first sexual activity
B- Being faithful, involving with single partner in a monogamous relationship
C- Condom, correct and complete use to protect against HIV, STI, unwanted pregnancy

In order to practice safe sex,

1. Talk to your partner and know about them, their risk of STI.
2. Think twice instead of rushing into the act.
3. Admit if you have an STI, so that your partner can take measures to protect themselves.
4. Avoid multiple sexual partners.
5. Use barrier methods – condoms: to protect against STI and also unwanted pregnancies.
6. Use proper lubricants when needed, Saliva as a lubricant only increases the risk of STI. Water based lubricants avoid sores and cuts while oil based lubricants used with condoms weaken the latex and lower the efficacy.
7. Do not have sex if there are open wounds – sores, cut, new tattoo, new piercings. Allow time for healing.
8. Kissing is also not safe as there is risk of herpes transmission.
9. Avoid alcohol and substance abuse.

10. Douching after intercourse only increases risk of pushing infection farther inside. It offers no protection against STI or pregnancy.
11. Vaccinate yourself against HPV, HBV.
12. Get yourself tested for STI in sexual health clinics.
13. Improving literacy rate- It is found that educated adolescents understand the concept and need for safe sex better and use the condoms properly3

Risk stratification:

Low risk: Kissing, cuddling, masturbation, sexual intercourse with barrier contraceptives

High risk: sexual intercourse without condoms, reusing condoms, Withdrawing before ejaculation instead of barrier methods as pre ejaculatory fluid is equally infectious and can lead to pregnancy, broken condoms, anal intercourse, oral sex

Risk factors: polygamous relationship, alcohol or recreational drug use during intercourse, sex under pressure, hiding history of STI for fear of being judged4

Warning signs:

More than knowledge of safe sex it is important to educate the adolescent regarding when the need to contact for help.

1. Break or leak or slipping of condom during sex
2. Sores, ulcers, lesions in penis, vagina, anal area or around mouth.
3. History of unprotected sexual intercourse
4. History of sexual assault
5. Possibility of pregnancy

How to disseminate information?

- Organise plays, talks at schools and colleges.
- Have a counsellor who can address the issues sensitively5.
- Organize health camps.
- Parents are the best source of information for an adolescent. However parents find it uncomfortable and are unaware of how to proceed. Parents should adopt a friendly nature and educate kids when they are of appropriate age. Talk calmly, listen and clear their doubts honestly, inform them about birth control, safe sex, date rape, STIs. Allow the kid to converse freely about anything from a younger age so that they have the confidence to discuss about their sexual life. Do not make the kid feel pressured to talk. Have a careful watch while respecting their need for privacy and autonomy. Forcing them only alienates you, thereby making them resort to other modes of information from their peer group.
- Direct them to websites and information leaflets so they can read and understand by themselves6.

Frequently Asked Questions

- What can damage condoms? Oil-based lubricants, Vaseline
- What are the different brands of condoms available in India? Nirodh (free), Deluxe
- Nirodh, Kamasutra, Fiesta, Kohinoor, and many others
- How much do they cost? Rs. 2 - Rs. 15 normally. Imported condoms usually cost more than Rs. 10 Contd.
- Are condoms marketed socially? Yes, there are social marketing organizations (SMO) that market condoms, they sell condoms at a price lower than market rate
- Are free condoms of poor quality? No every batch of condoms are tested the same way whether supplied freely or marketed
- Can an HIV infected person have sex using a condom? Yes
- Are there condoms for women? Yes! Called Femidom, it is costly and is marketed in India
- Are there condoms for women? Yes! Called Femidom, it is costly and is marketed in India

Case Scenario

Case 1: Miss X ,19 years comes to you with a complaint of vaginal discharge that she has had for the last two weeks. She mentions that it is continuous and causes a foul odour. Recently she had sexual contact with her boyfriend who also complained of a burning sensation while passing urine. In order to determine whether the vaginal discharge is normal or not, what questions will you ask her? If is it likely to be an STI, what actions would you suggest? How do you prepare this young patient for consultation by her doctor?

Case 2: After attending a group education session on STI and HIV in the community, a youth walks up to you and informs you that his friend is suffering from a genital ulcer and wants to know what to do. You begin to explore his knowledge about STI. The youth admits that he himself has the ulcer, which he noticed a few days ago. What will you do? How do you facilitate the treatment and what other action will you recommend?

Conclusion:

Increased awareness of safe sex practices, increased availability of condoms, interactive health care staff can go a long away in improving the sexual health of adolescents.

References:

1. Maheshwari SU, Kalaivani S; Patterns of sexual bahavious in adolescents and young adults attending STD clinic in a tertiary care centre in South India; Indian J Sex Trans Disease; 2017; 38; 171-175
2. NACO;http://www.naco.gov.in/NACO/Quick_Links/Youth/Information_On_Safe_Sex/youthand HIV/AIDS
3. Sudha RT, Vijay DT, Lakshmi V; Awareness, attitudes, and beliefs of general public towards HIV/ AIDS in Hyderabad; Indian J Med Sci; 2005; 59; 307-16
4. Australian STI Management guidelines, 2016
5. Dana Clifton MD,Jane Trinh, Duke University Hospital; Improving safe sex practices in adolescents and young adults; Academic pediatrics; 2016; 16(6); 16-17
6. Teens Health; http://kidshealth.org/en/teens/sexual-health/#catstds
7. Training Manual for Counsellors at STI/RTI Clinics; http://www.naco.gov.in/sites/default/files/Counselor%20facilitator%20guide.pdf

Benefits of LAM (LACTATIONAL AMENORRHEA METHOD)

The Ideal Support Method In Post Partum Phase

Dr. ReenaWani
(MD, FRCOG, FICOG, DNBE, FCPS, DGO, DFP)
Professor & Head of Dept, Obstetrics & Gynecology
HBTMC&Dr R N Cooper Hospital, Juhu.
Chairperson Perinatology Committee FOGSI 2015-2017

Dr Rashmi Jalvee
(MS, DGO, DNB)
Asst Prof, HBTMC & Dr R N Cooper Hospital

Introduction

Margaret Sanger, American nurse,educator and birth control activist had said "When motherhood becomes the fruit of a deep yearning, not the result of ignorance or accident, its children will become the foundation of a new race."

LAM has been a method of natural family planning which has protected millions of women worldwide from unwanted pregnancies and bestowed the multiple benefits of exclusive breastfeeding to their newborns.

Puerperium is the period following childbirth during which the body tissues,particularly the pelvic organs, revert to the pre-pregnancy levels by the process of involution. Puerpera is a woman in puerperium who needs help and support in many ways.

Aims of Puerperal Care:

Restoring maternal health and preventing illness.
Maintaining infant health and preventing illness.
Establishing and promoting lactation.
Health promotion by educating the woman about her child's and her own future health.
Initiation of immunization program for infant.
Discussion of family planning options and offering contraceptive advice.

Physiology: [1]

Return of ovulation and menstruation usually does not occur within puerperal period. Important determinants are exclusive breast feeding, frequency and duration of infant suckling (see table below):

Timing	No lactation	If lactation established
♦ Menstruation	6-12 weeks	36 weeks(average)
♦Earliest ovulation	4 weeks	12 weeks
♦Average time for ovulation	8-10 weeks	17 weeks (variable)

Changes in Breasts:

- Colostrum secretion (starts antenatally) continues for 2-3 days. It is a yellowish fluid, rich in nutritious and immunologic factors for the neonate, and women must be encouraged to feed as early as possible.
- Breast engorgement occurs by day 3 or 4, when the suppressive effects of high estrogen and progesterone of pregnancy wear off and prolactin acts to increase milk production.
- If suckling is established, milk production is continued and secretion of adequate quantities of milk occurs.

2 components of the physiology of lactation:

a) Milk production and secretion:

- Estrogen, progesterone and lactogen (HPL) cause growth and development of duct andalveolar systems of breast in pregnancy. After parturition, the inhibition of estrogen and progesterone on prolactin secretion is removed and prolactin acts on the glands to promote milk production and secretion into ducts.

b) Milk ejection:

- milk from glandular portion of the breast enters subareolar milk sinuses (15-20) by contraction of myoepithelial cells.
- suckling stimulates the “let down” reflex or milk ejection response, or draft reflex.
- oxytocin release via this reflex stimulates ejection of milk from the nipple, and also helps in uterine involution.

Usage in India:

According to the National Family Health Survey 42, modern contraceptive use by currently married women has remained unchanged, at just under 50%, between 2005-06 and 2015-16. Female sterilization is the most popular contraceptive method with more than 36% of couples in the reproductive ageopting for it. Natural family planning methods like LAM, withdrawal, rhythm method are probably protecting more women than we knw by statistics!!

User Advantage of LAM :

A) Benefits to Mother:

- *Contraceptive protection*

  The Lactational Amenorrhea Method is a short-term family planning method based on the natural effect of breastfeeding on fertility. The lactational amenorrhea method requires 3 conditions. All 3 must be met:
- her menstrual period has not returned since delivery
- baby is fully or nearly fully breastfed and is fed often, day and night (no interval of >4–6 hours between breastfeeds)

  Fully breastfeeding means exclusive breastfeeding (the infant receives no other liquid or food, not even water, in addition to breast milk) and almost-exclusive breastfeeding (the infant receives vitamins, water, juice, or other nutrients once in a while)
- baby is less than six months old.

Mechanism of action:

LAM works primarily by preventing ovulation.

Frequent breastfeeding temporarilydisrupts the GnRH (gonadotropin releasinghormone) rhythm and suppresses the hypothalamic–pituitary–ovarian axis. This

results in a reduction of the LH (luteinizing hormone) produced and anovulation. The risk of pregnancy in thefirst six months for a breastfeeding mother who meets the LAM criteria is 2%.3

Women breastfeeding for longerthan 6 months post-partum should initiate other modernmethods of contraception to avoid unplanned pregnancyirrespective of breastfeeding style or menstrual status.

- Non - contraceptiveBenefits:
  - promotes bonding between mother and child
  - It is economical
  - It is entirely natural
  - Facilitates involution of uterus due to action of oxytocin
  - Longer duration of breastfeeding protects against breast and ovarian carcinoma.

    Ever breastfeeding was associated with 22%reduction of breast carcinoma risk compared with never breastfeeding.Mothers who ever breastfed their children had a 30% reduction in the risk of ovarian carcinoma, when compared with women who never breastfed4
  - Breastfeeding helps promote weight loss in the postpartum period.

B) Benefits to Newborn:

According to World Health Organization (WHO), optimal breastfeeding includes early initiation of breast feeding, exclusive breast feeding for 6 months, frequent feeding, continuous breast feeding for 2 years and increase frequency of feeding during illness. 5 Breastfeeding gives children the healthiest start in life and is one of the simplest, smartest and most cost-effective ways of ensuring that all children survive and thrive.

- Breast milk provides ideal nutrition for babies.Breastfeeding helps to prevent malnutrition in all its forms in babies.
- The predominant antibody in breast milk, secretory IgA (sIgA), confersimmune-protection by inhibiting adherence to or penetration of the gastrointestinal (GI) tract by pathogens and by phagocytosis or cytotoxicity of pathogens.
- Depending on prior maternal exposure to pathogens, the acquired secretory antibodies, such as IgM and IgGprovide the infant with environment-specific immune-protection.
- Breastmilk combats infectious diseases, decreases incidenceand severity of diarrhoea, lowers respiratory infections, acute otitis media, prevents dental caries andmalocclusion.
- Breast milk contains hormones, neuropeptides and growth factors that affect growth, development and self-regulation of food intake in the infant.
- Studies indicate that breastfed babies have higher intelligence scores and are less likely to develop problems with behavior and learning as they grow older.6

World Breastfeeding Week:

Worlds breastfeeding week (WBW) is celebrated every year from 1st to 7th August all over the globe to encourage breastfeeding and improve health of babies around the world. Objectives of the World Breastfeeding Week:

- Encouraging parents to breastfeed.
- Raising awareness about the importance of breastfeeding and damage caused by complementary feeding.
- Providing proven scientific material about the importance of breastfeeding.
- Supporting breastfeeding at workplaces.

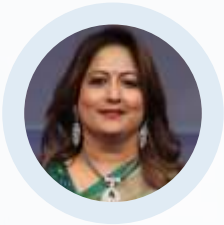
The WBW2019 slogan “Empower Parents, Enable Breastfeeding”was chosen to be inclusive of all types of parents in today's world. It focused on supporting both parentsto be empowered in order to realize their breastfeeding goals.Breastfeeding is in the mother's domain and when fathers, partners, families, workplace and communities support her, breastfeeding improves.

Role of providers:

To improve patient success with LAM, the importance of counselling cannot be under played. We must understand the many factors that determine LAM compliance, including characteristics and habits of individual users, a woman's experience with previous contraceptive methods, real and perceived fears about adverse effects such as menstrual irregularities and packaging features that can impede or facilitate proper usage.

References:

1. WaniReena. Ch 10, The Normal Puerperium. In: Essential Obstetrics 2nd edition. Bhalani Book Depot, 2010.
2. NHFS 4 (National Family Health Survey) 2015-16, Ministry of Health and Family Welfare, Government of India.
3. Speroff L, Mishell DR. The postpartum visit: it's time for a change in order to optimally initiate contraception. Contraception. 2008;78(2):90-8.
4. Ranadip Chowdhury,1 BireshwarSinha, et al. Breastfeeding and maternal health outcomes: A systematic review and meta-analysis. ActaPaediatr. 2015 Dec; 104 (Suppl 467): 96–113.
5. World Health Organization. 10 facts on breastfeeding. WHO Updated August 2017. https://www.who.int/features/factfiles/breastfeeding/en/.
6. Kramer MS, Aboud F, Mironova E, et al. Breastfeeding and child cognitive development: New evidence from a large randomized trial. Arch Gen Psychiatry. 2008 May;65(5):578-84.



Tackling PCOS with Hormonal Contraceptives

Dr Nandita Palshetkar
MD FCPS FICOG FRCOG
President, FOGSI (2019)
Chairperson, MSR (2017-18)
Vice President, AMOGS (2016-18)
Past President, MOGS (2016-17)

Dr Shobha N Gudi
MD, DNB, FICOG, CIMP.
Prof and HOD,
St Philomenas Hospital, Bengaluru,
Chairperson F.W.C. FOGSI 19-21
President BSOG 2018.

The past decade in medicine has seen the emergence of several non communicable diseases .The prevalence of Diabetes, Hypertension, thyroid disorders , cardiac disease, cancers and psychiatric illness has increased. We all know that one such illness of the reproductive and endocrine system is polycystic ovarian syndrome. PCOS is a complex, hetero- genous , metabolic problem , a life style disorder affecting almost 5 to 10% of our women of reproductive age group.

Adolescent girls and women who are affected will show variable clinical features of hyperandrogenism (hirsutism and/or acne), anovulation with resultant oligomenorrhea and other menstrual irregularities, and infertility. The classical polycystic appearance of ovaries on ultrasound is present in 70% of women. The diagnosis of PCOS requires the presence of two out of the three characteristics of polycystic ovaries, clinical or biochemical hyper-androgenismand anovulation.

Managing PCOS :

The primary approach to management is life style modification. A well regulated exercise plan with good diet modification with consistent weight reduction in women with high BMI goes a long way in improving the endocrinal milieu and enhances the response to hormonal therapy (1).

It is well acknowledged that Combined oral contraceptive (COC) pills are the first-line medical therapy for the long-term management of PCOS.COCs are a combination of ethinyl estradiol and progestin. Women with PCOS using COC consistently will have regular menses, reduction of androgen excess, with effective contraception and protection from endometrial cancer, thebenefits outweighing the risks.

How do COCsact ?

OCs contain low doses of estrogens and progestins (Table 1). These hormones inhibit the synthesis and secretion of GnRH at the level of the hypothalamus. Estrogens inhibit the selection and development of a dominant follicle by suppression of FSH. Progestins inhibit ovulation via suppression of LH surge. Progestins also make the cervix hostile to sperm penetration by increasing the viscosity of cervical mucus and prevent implantation through an alteration of endometrial lining (4).

Are there any concerns for COC use?

The potential adverse cardiovascular and metabolic effects of OCs have been well acknowledged. The risks are higher in older, obese women, in smokers, in women with diabetes, hypertension and dyslipidemia. The evidence so far indicates an increased relative risk of venous thrombosis associated with OCs varying among different formulations. In young nonsmoking women , risk of arterial thrombosis is not significantly increased with OC use. The morbidly obese women with PCOS with severe insulin resistance might have increased risk of diabetes which is not surprising. Each PCOS patient's cardiometabolic risk profile at baseline and during follow-up

should be determined and a tailored approach to prescribing oral contraception to be adopted. This individualized risk stratification includes age, smoking, obesity, any degree of glucose intolerance including prediabetes and diabetes, hypertension, dyslipidemia, thrombophilia, and personal or family history of a venous thromboembolic event. To prevent long term health consequences of this chronic disorder, any therapy started will have to continue for several months to years, and consistent follow up to identify any new manifestation of risk factor as well compliance to treatment and life style is mandatory. (2).

What are types of COCs available?

Table 1.

Currently Available Low-Dose (≤35 μg of EE) Combined OC Pills According to Type of Progestin and EE Dose

Progestin Type	Progestin Dose, mg	EE Dose, μg
First generation		
Norethindrone	1	20
Norethindrone	1.5	30
Second generation		
Norgestrel	0.3	30
Levonorgestrel	0.1	20
Levonorgestrel	0.15/0.5	30
Third generation		
Gestodene	0.75	30
Desogestrel	0.15	20/30
Antiandrogenic		
Drospirenone	3	20/30
Cyproterone acetate	2	35

Most of the currently available OCs containethinyl estradiol (EE) as the synthetic estrogenic compound. Pills containing less than 50 µg of EE are called Òlow-doseÓ OCs. Virtually all low-dose OCs contain ²35 µg EE, and the dose of synthetic progestin ranges between 0.1 and 3 mg. The amount of EE over the years has significantly reduced to 20–35 µg to increase efficacy, safety, and tolerability . EE has stronger effects than natural estradiol on hepatic metabolism, including synthesis of SHBG, lipoproteins, angiotensinogen, and some estrogen-dependent clotting factors (8). The latest COCs (7, 9), contain natural estrogens like 17 -estradiol, estradiol valerate, and estetrol which overcome these metabolic effects. (3).

The OCs are traditionally classified as generations, which refers to the timing of the introduction of the Progestinmolecule,as shown in Table 1. Synthetic progestins used in first- and second-generation OCs are chemically related to T (19-nortestosterone derivatives). These progestinshave variable chemical structures, potency, pharmacokinetics, different affinities for androgen receptor with corresponding degrees of androgenic side effects of oily skin, acne,hirsutism etc. On the other hand, the third-generation progestinsdesogestrel, norgestimate, and gestodene show higher affinity for progesterone receptors and therefore less androgenicity (3).

The new progestins derived from progesterone or spironolactone like drospirenone, trimegestone, nestorone, cyproterone acetate, and nomegestrolhave no androgenic side effects, are designed to bind specifically to the progesterone receptor and to have no estrogenic or glucocorticoid actions .Dienogest, another new progestin, though structurally related to Testosterone, is antiandrogenic and has no estrogenic or glucocorticoid activity .The progestin with maximum antiandrogenic activity, is cyproterone acetate , has almost twice the antiandrogenic potency of dienogest and drospirenone. (4).

Metabolic effects of estrogen in OCs are modulated by the type of the progestin included . The more androgenic progestins are able to counteract the stimulatory effects of estrogen on liver proteins and coagulation factors, but less androgenic or antiandrogenicprogestins have limited counteraction on the effects of estrogen. Thus, OCs containing third-generation progestins as well as drospirenone and cyproterone acetate have reduced metabolic side effects compared to OCs containing more androgenic progestins (5).

Different generation of oral contraceptive pills

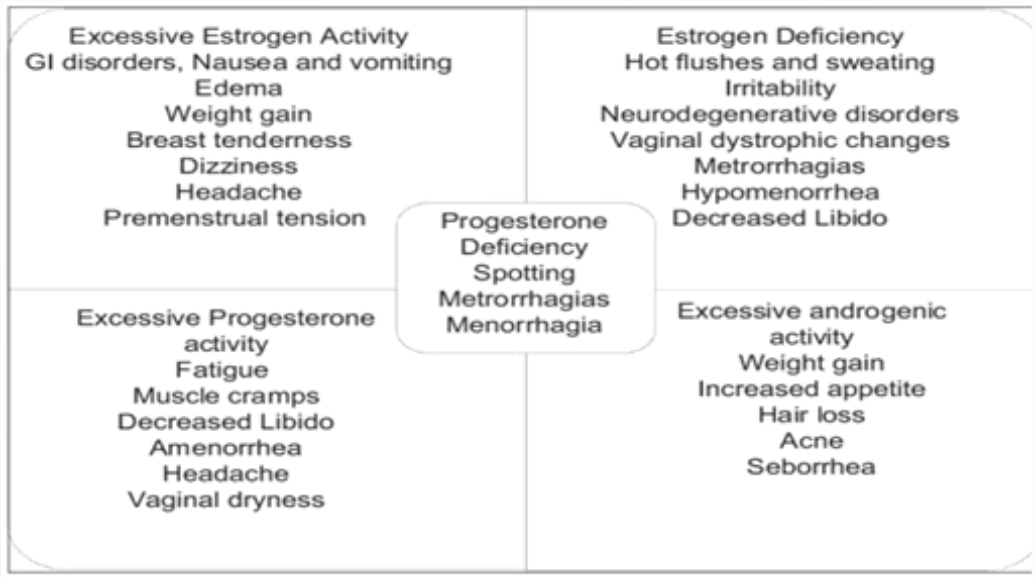
Year	Progression	Estrogen component	Dose (mcg)	Progesterone component	Dose (mg)	Activity of progestins		
						Estrogen	Progesterone	Androgenic
1960-1963	First-generation oral contraceptives	Mestranol (ethinyl estradiol - 3 methyl ether)	75	Norethynodrel	5	++	++	++
			50	Norethisterone acetate/norethindrone	4			
1970s	Second-generation progestin		100	Norethindrone Norgestrel, Levonorgestrel	2	-	++++	++++
	Emergency contraceptive pill	Ethinyl estradiol	100	Norgestrel	1			
	Progesterone only pill	-	-	Norethindrone	0.35			
1980s	Low estrogen doses	Ethinyl estradiol	35	Norethindrone	1			
	First Bi-phased and tri-phased pills	Ethinyl estradiol	35	Norethindrone	0.5/0.75/1			
	Third-generation progestins	Ethinyl estradiol	20-35	Norgestimate, gestodene, desogestrel	0.15	-	+++	++
1989	Lower estrogen	Ethinyl estradiol	20	Levonorgestrel	0.1			
1997	Fourth-generation progestin	Ethinyl estradiol	30	Drospirenone	3	-	+/-	Antiandrogenic
2000-2010	Regimens with reduced hormone-free interval, new progestins			Dienogest				

The main reason for success of treatment with COCs in PCOS is the noncontraceptive benefit ofcycle control, a sense of well being,decreased dysmenorrhea, menorrhagia, and anemia, improvements in acne and hirsutism, and decreased risk of osteoporosis and ectopic pregnancy . Long-term OC use is also associated with decreased risk of ovarian and endometrial cancer (6).

Side effects of OCs

Some side effects of COCs like nausea, mastalgia, headache, and mood swings leads to poor compliance .The positive counseling that most of these side effects are self limiting and reduce after few cycles will prevent discontinuation. The concern about weight gain from conflicting studies has been put to rest by a recent Cochrane review of the 49 available randomized trials which did not find any evidence for long term OC use as a cause for weight gain (7).

Side effects of oral contraceptive pills depending on dose and drug



What are the contraindication for the use of COCs ?

According to the WHO guideline (14,15), absolute and relative contraindications to the use of low-dose OCs are shown in Table 2. These are applicable for low dose COCs, contraceptive patch and contraceptive ring.

Table 2.

Absolute contraindications (ie, unacceptable health risk)
<6 weeks postpartum if breastfeeding
Smoker over the age of 35 y (=15 cigarettes per day)
Hypertension (systolic =160 mm Hg or diastolic =100 mm Hg)
History of deep venous thrombosis/pulmonary embolism
Current deep venous thrombosis/pulmonary embolism
Major surgery with prolonged immobilization
Known thrombogenic mutations (eg, Factor V Leiden, prothrombin mutation, protein S, protein C, and antithrombindeficiencies) [a]
Current case and history of ischemic heart disease
Stroke (history of cerebrovascular accident)
Complicated valvular heart disease
Systemic lupus erythematosus with positive APLA
Migraine headache with focal neurological symptoms
Current breast cancer
Diabetes with nephropathy/retinopathy/neuropathy
Other vascular disease or diabetes of >20 -y duration
Active viral hepatitis
Severe cirrhosis
Liver tumors
Relative contraindications (risks outweighbenefits,MEC -3 for contraception)
Smoker over the age of 35 y (<15 cigarettes per day)

Is screening recommended? : Apart from detailed history and clinical examination, routine screening for above is not recommended because of the rarity of the conditions and the high cost of the screening.
How do COCs help in managing PCOS ?

When fertility is not a concern, COCs remain the first-line treatment for women with PCOS . (5). The improvement in clinical manifestations of hyperandrogenism and return of regular menstrual cycles makes it a very effective therapy. The progestin component suppresses the LHsecretion to decrease ovarian androgen production. The estrogenic fraction increases the levels of SHBG, with decrease in circulating free T levels and its bioavailability. The acne and hirsuitism improve because of the progestin competing for 5 -reductase and the androgen receptors. OCs also slightly reduce adrenal androgen production (9). In general, at least 6 months of treatment with OCs is necessary to detect differences in hirsutism or acne of women with PCOS (10).
Both ESHRE/ASRM-sponsored PCOS Consensus Group recommendations (5) and The Endocrine Society's clinical practice guidelines (11) suggest OCs as first-line management for amelioration of clinical and biochemical androgen excess and menstrual irregularity. They also emphasize that there is no definitive evidence for any difference in efficacy of various OCs . In accordance, OCs are the most commonly prescribed medications for the long-term management of the syndrome. However, concerns remain regarding safety profile and potential risk of thrombosis and metabolic disease (6).

Major concerns with COC use :
The risk of venous thromboembolism(VTE) with COC use is smaller than the risk associated with pregnancy . The VTE rates in women of reproductive age are 0.5–1 in the general population, 6–10, in pregnancy and 50 in the puerperal period, per 10 000 women-years,.(12). The risk of VTE per OC preparation and other acquired or genetic risk factors risk factors, such as obesity, smoking, advanced age, immobility, and hereditary thrombophilia in addition to the inherent risk of metabolic syndrome of PCOS .PCOS appears to be associated with a prothrombotic state, reflected by a decreased global fibrinolytic capacity and increased activity of plasminogen activator inhibitor type 1, a potent inhibitor of fibrinolysis (13). The risk of VTE is increased 2- to 6-fold in OC users compared to nonusers . The risk is highest during the first 3 months of use and returns to that of nonusers within weeks of discontinuation . With reference to COCs, VTE risk depends on the dose of EE and the type of progestin . A lowering of estrogen dose to 30 or 20 µg and the use of second generation as compared to third generation progestinsmight lead to lowering of risk but needs greater research.
There is very low absolute risk of arterial thrombosis in women of reproductive age, with the number of additional arterial thrombotic events attributable to OC use was one or two per 10 000 women per year . The risk is associated with increased age, smoking, and hypertension. Younger nonsmoking women do not appear to possess any thrombotic risk due to OC use. There is even an interesting study from a healthy population suggesingt that OC use during reproductive years might be protective against CVD later in life .

Low-dose OC use for up to 1 year does not have a significant adverse impact on insulin sensitivity or glucose tolerance in most of the patients withPCOS .The risk of diabetes development depends on individual patient characteristics such as BMI, age, ethnicity, and family history of diabetes. The impact of OCs on insulin sensitivity and glucose tolerance status with longer term use in PCOS needs to be evaluated.

Other hormonal contraceptives for PCOS :
There is a paucity of data regarding the use of hormonal contraceptives other than OCs in PCOS. Extrapolating from the general population, one could use a contraceptive patch (weekly application) or contraceptive ring (monthly insertion) in women with PCOS who are unable to take OCs. PCOS patients with a contraindication to estrogen or who do not have androgen excess and are in need of contraception might be candidates for progestin-only contraceptives including long-acting injectables (depot medroxyprogesterone), etonogestrel-containing implant, or levonorgestrel-containing intrauterine system. These methods provide effective protection against endometrial hyperplasia. Decreased bone mineral density is an adverse effect with the use of depot medroxyprogesterone .

Commonest clinical scenario :
A patient with PCOS ,young and overweight, a nonsmoker below 35 years of age with no personal or family history of VTE, diabetes, or hypertension, treatment with an OC is the best available option because she presents with the main complaints of hirsutism and oligomenorrhea and is not considering pregnancy. OC use in this patient is also important for protection from endometrial carcinoma. In case of dyslipidemia (low HDL and increased triglycerides) an individualized approach in this patient may dictate prescription of third or newer generation OC with neutral or antiandrogenic properties over a second-generation OC.

How to start an OC in a patient with PCOS?
Before prescribing any kind of OC, a careful history of past and present medical conditions, any drug use, family history, focused physical examination, and laboratory assessments are required (Table 3). and during follow-up with regular intervals.

Table 3.
Comprehensive Assessment Before Prescription of an OC in PCOS

Medical history
Age
Past and present medical conditions
Any drug use
Migraine

CVD risk factors (smoking, hypertension, obesity, diabetes, dyslipidemia)
Thrombophilia (any known disorder of thrombophilia, personal or family history of previous VTE)
Physical exam
Blood pressure measurement
BMI
Waist circumference
Laboratory tests
75-g 2-h standard OGTT
Lipid profile

Specifically, information regarding migraine and CVD risk factors (smoking, hypertension, obesity, glucose intolerance, dyslipidemia, thrombophilia, previous VTE) is important. Occasionally, a patient with PCOS and multiple risk factors may need to avoid OC use. Blood pressure measurement, BMI, and a pregnancy test are required before a first prescription of OCs, whereas breast examination, pelvic and genital examination, and cervical cytology screening are not routinely recommended because they do not contribute substantially to the safety of OCs. In patients with PCOS, cardiometabolic risk assessment needs to be performed, including a 75-g standard 2-hour OGTT and lipid profile at baseline User preference and individul concerns should be addressed. The patient needs to be informed that OC use does not seem to be associated with weight gain in most women; however, some PCOS patients might gain weight, and clinical assessment of adiposity at regular intervals would be required during follow-up. At the first prescription, all patients should be informed that long-term OC use is safe for the majority but can be associated with minor side effects and with rare but serious harms. Patients should also be informed that there is a small increase in the risk of blood clots with OC use and that there are symptoms that would prompt immediate medical attention, such as warning signs of VTE (leg swelling or pain), visual disturbances, sensory or motor impairment, chest pain, and new headache.

A thrombophilia screen is not recommended routinely before prescribing an OC, and a negative screen may not exclude all types of thrombophilia. Women with a family history of VTE in a first-degree relative <45 years of age may indicate an increased likelihood of hereditary thrombophilia. In PCOS patients with a personal history of thrombophilia, progesterone-only pills would be an option. Contraceptive pills containing progestin only (referred to as the mini-pill) do not have a significant impact on coagulation or fibrinolysis and do not significantly alter carbohydrate or lipid metabolism (14).
OCs are ideally started on the first day of the cycle and up to fifth day. They can be started at any other time if it is certain that the patient is not pregnant. To follow the schedule written on the packaging correctly, an alternative strategy might be to begin on the first Sunday after bleeding.
After 3 months, a revisit needs to be scheduled for assessment of blood pressure and any other problems. OCs should be continued if the patient is comfortable with the drug. An annual visit is required to control for further compliance, side effects, and evaluation of glucose tolerance and lipids.

When young girls are given very low dose formulations, it may result in decrease in BMD, unlike the effect in perimenopausal women where they may help in preserving bone mass.
Drug interactions can be a concern.When a woman is on COC, she requires lower doses of benzodiazepines and higher doses of paracetamol .When on antibiotics or ARV drugs, additional method of contraception recommended. In epileptic women on lamotigrine , the dose of lamotigrine needs to be doubled and then lowered during pill free days (15).
Combined hormonal contraceptives apart from topical treatment has demonstrated to reduce acne.Standard topical treatment for mild acne includes use of gentle cleansers, topical benzoyl peroxide or salicylic acid and hypoallergenic moisturizers. Patients with moderate to severe acne also benefit from routine cleansing, topical antibiotics, retinoic acid, and azelaic acid. Girls with acne involving. Chest or and back may benefit from systemic antibiotics and isotretinoin.

Conclusions
The long termmanagement of PCOS has OCs as a key component, addressing the hyperandrogenic skin manifestations, menstrual irregularities, effective contraception, and protection of endometrium against effects of unopposed estrogen. Although guidelines do not suggest one OC formulation over another in terms of effectiveness, low-dose OCs containing neutral or antiandrogenicprogestins may be the choice in the treatment of PCOS regarding the androgen excess and the metabolic disturbances associated with the disorder. The potential adverse cardiovascular and metabolic effects of OCs have raised some concerns,but the benefits of oral contraception outweigh the risks of long term use in the vast majority of women with PCOS. OC use is associated with an increased RR

of venous thrombosis, whereas absolute risk is very small. (16)Young, nonsmoking patients with PCOS have no risk of arterial thrombosis attributable to OCs. Nevertheless, OC use might increase the risk of diabetes, particularly in obese patients with severe insulin resistance. Future studies evaluating the long-term effects and safety of OCs in the treatment of PCOS are needed. These studies should adequately consider clinical heterogeneity of the syndrome and variation in the efficacy and safety of different combinations. Meanwhile, the WHO guidelines for the contraindications to OC use should be exercised in women with PCOS, and the precise individualized treatment targets and risk stratification depending on patient characteristics should be determined.

References :

1.Approach to the Patient: Contraception in Women With Polycystic Ovary Syndrome
Bulent O. Yildiz
The Journal of Clinical Endocrinology & Metabolism, Volume 100, Issue 3, 1 March 2015, Pages 794–802, https://doi.org/10.1210/jc.2014-3196

2.Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group, Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome, Fertil Steril.2004;81:19-25

3.Consensus on women's health aspects of polycystic ovary syndrome (PCOS): the Amsterdam ESHRE/ASRM-Sponsored 3rd PCOS Consensus Workshop Group, Fertil Steril.2012;97:28-38.e25

4.YildizBO.Oral contraceptives in polycystic ovary syndrome: risk-benefit assessment. SeminReprod Med.2008;26:111-120.

5.Christin-MaitreS, History of oral contraceptive drugs and their use worldwide, Best Pract Res ClinEndocrinol Metab.2013;27:3-12

6.Sitruk-WareR,NathA Characteristics and metabolic effects of estrogen and progestins contained in oral contraceptive pills, Best Pract Res ClinEndocrinol Metab.2013;27:13-24

7.AydinK,CinarN,AksoyDY, BozdagG,Yildiz BO Body composition in lean women with polycystic ovary syndrome: effect of ethinyl estradiol and drospirenone combination.Contraception.2013;87:358-362

13.GalloMF,LopezLM,GrimesDA,SchulzKF, HelmerhorstFM, Combination contraceptives: effects on weight, Cochrane Database Syst Rev.2014;I: CD003987

14.World Health Organization.Medical eligibility criteria for contraceptive use
2009.http://whqlibdoc.who.int/publications/2010/9789241563888_eng.pdf

15.Centers for Disease Control and Prevention.US medical eligibility criteria for contraceptive use, 2010. Morbidity and Mortality Weekly Report. Recommendations and Reports.2010;59RR)04:1-6.

16. De BastosM, StegemanBH, RosendaalFR, et al. Combined oral contraceptives: venous thrombosis.Cochrane Database Syst Rev.2014;3: CD010813

Hormonal Contraceptives for Optimal Management of AUB

Dr Basab Mukherjee
MD, FICOG, FRCOG(London)
Consultant Gynaecologist ,
Columbia Asia Hospital, Mumbai.
Vice President Elect FOGSI 2021
Chairperson FWC FOGSI (2013-2015)

Dr Charu Mittal
MD, DNB (Obs & Gyn)
Consultant Gynecologist, Gwalior, MP
Ex-Assistant Professor, Medical College,
Baroda, Gujarat

Introduction

The reported prevalence of Abnormal Uterine Bleeding (AUB) in India is around 17.9%. 1It can affect women at any point in their lifetime especially most likely during the reproductive years. AUB can be observed as a disturbance in the duration of bleeding, frequency of bleeding, regularity of menses, volume of menstrual loss or any combination of the above.

Clinical approach

A clinician needs to carefully assess each patient of AUBfor their detailed history of symptoms to enable an accurate diagnosis and management. Her desire for current or future fertility should be elicited during this routine history-taking to facilitate an informed decision making by these women seeking treatment.

Table 1.Suggested "normal" limits for menstrual parameters for uterine bleeding

Clinical dimensions of menstruation and menstrual cycle	Descriptive term	Normal limits (5^{th}-95^{th}percentiles)
Frequency of menses, days	Frequent Normal Infrequent	<24 24-38 >38
Regularity of menses: cycle-to-cycle variation over 12 months, days	Absent Regular Irregular	No bleeding Variation ± 2-20 Variation >20
Duration of flow, days	Prolonged Normal Shortened	>8.0 4.5-8.0 <4.5
Volume of monthly blood loss, mL	Heavy Normal Light	>80 20-80 <20

The above mentioned asessment of the parameters of normal menstrual bleeding, establishes a mechanism for defining the various symptoms that comprise AUB. Eliminated are terms such as menorrhagia, oligomenorrhea, metrorrhagia and dysfunctional uterine bleeding.

Etiology of AUB

The etiology of AUB must be categorized as per the currently recommended FIGO classification (anatomical disorders ie PALM - polyps, adenomyosis, leiomyoma, malignancy) and the non-anatomical disorders (COEIN - coagulopathies, ovulatory dysfunction, endometrial, iatrogenic, not otherwise classified) followed by appropriate management. 2

Table 2: PALM-COEIN classification for the etiologies of abnormal uterine bleeding proposed by the International Federation of Gynaecology and Obstetrics (FIGO)2

AUB causes	Subclass	Characteristics	
Structural causes	Polyps **(AUB-P)**	ØPresent in endometrial and endocervical canal ØCategorized as absent or present	
	Adenoma **(AUB-A)**	ØThe genesis is controversial but minimal criterion is identification on ultrasound testing.	
	Leiomyoma **(AUB-L)**	0: Submucosal types, do not impact endometrial cavity Others: 1: < 50% intramural 2: ≥50% intramural 3: totally extracavitary but lean on the endometrium, 100% intramural 4: intramural leiomyomas that are entirely within the myometrium 5: subserosal and atleast 50% intramural	6: subserosal and < 50% intramural 7: subserosal and attached to serosa by stalk 8: do not involve the myometrium include cervical lesions, lesions that exist in the round or broad ligaments without direct attachment to the uterus, and parasitic lesions
	Malignancy & hyperplasia **(AUB-M)**	ØMay occur because of ovulatory disorder ØSub-classification according to the WHO or FIGO system.	
Non-structural causes	Coagulopathy **(AUB-C)**	ØCoagulopathy represents both inherited and acquired ØMost common is inherited von Willebrand disease	
	Ovulatory dysfunction **(AUB-O)**	ØCan lead to amenorrhea or heavy menstrual bleeding	
	Endometrial **(AUB-E)**	ØLikely to occur when other abnormalities are excluded in the presence of normal ovulatory function.	
	Iatrogenic **(AUB-I)**	ØBreakthrough bleeding during use of single or combined gonadal steroid therapy, intrauterine systems, or devices, systemic agents that interfere with dopamine metabolism, or anticoagulant drugs.	
	Not classified **(AUB-N)**	ØRare or ill-defined conditions: Chronic endometritis, arteriovenous malformations, and myometrial hypertrophy.	

Treatment options for AUB

Choice of treatment for AUB depends on overall acuity of presentation, the patient's clinical stability, suspected etiology of the bleeding, desire for future fertility, and any underlying medical problems. The two main objectives while managing acute AUB are: 1) to control the presenting episode of heavy bleeding and 2) to reduce menstrual blood loss in subsequent cycles. Medical therapy is considered the preferred initial treatment. Decisions should be based on the history of any pre-existing or currently detected medical disordersand contraindications to therapies. Surgical therapy is usually directed to specific causes like polyps, symptomatic fibroids, atypical hyperplasia, malignancy and patients not responding to medical therapy.

Hormonal Contraceptives for AUB
Oral preparations
Combined oral contraceptive pills: conventional monthly cyclical use / extended regimen use

Conventional COCs: Ethinyl Estradiol (20/30/35mcg)+ Synthetic progestin S(Levonorgestrel 0.15/0.3mg/ Desogestrel 0.15mg / Cyproterone Acetate 2mg / Drospironone 3mg) available as 21 / 24 +4 / 21 + 7 pill packs.For acute abnormal uterine bleeding, hormonal methods are first-line in medical management. In acute phase of HMB (Heavy Menstrual Bleeding) thrice daily dose of conventional COC is effective in arresting bleeding within 48-72 hours. This can be gradually tapered down to twice daily dosage and then maintained with once daily dosage to complete one month cycle. One study compared participants who underwent therapy with OCs administered three times daily for 1 week with those who underwent therapy with medroxyprogesterone acetate administered three times daily for 1 week for the treatment of acute AUB. The study found that bleeding stopped in 88% of women who took OCs and 76% of women who took medroxyprogesterone acetate within a median time of 3 days.3The major side effect can be intolerance due to nausea and vomiting. The COCP produces an estimated reduction in blood loss of 50% and has the additional benefit of regulation of bleeding.4

The risks of the COCP are mainly due to its estrogen content and include increased risk of thromboembolism, stroke, cardiovascular disease or breast cancer. Therefore, it is contraindicated in women with a BMI >35, smokers over 35 years, women with hypertension, vascular disease, liver dysfunction, migraine with aura, current/recent breast cancer, those with a personal or strong family history of venous thromboembolism or with a known thrombogenic mutation. The COCP also has a detrimental effect on breast milk production and is contraindicated in breastfeeding women. In the absence of risk factors, women can use the COCP until menopause if desired. They need to be counseled that taking other medicines, such as antibiotics and anti-epileptic medicines, can make the hormonal pills less effective.5

Estradiol Valerate (in a dose of 3mg/2mg/1mg sequentially)+ Dienogest 2mg/3mg sequentially): Another treatment option is a novel combination, quadriphasic oral contraceptive product containing estradiol valerate (E2V) and dienogest (DNG). As with other combination oral contraceptives, E2V/DNG works primarily by preventing ovulation. However, in contrast with other combination oral contraceptives, it is the progestin component of E2V/DNG that is responsible for endometrial stabilization. In this quadriphasic dosing regimen, DNG is increased during week 2 of the cycle while E2V is decreased on day 3 and again on day 25. Use of E2V/DNG for six months led to significant reductions in heavy menstrual bleeding with an average 65% reduction in mean blood loss. The product received US Food and Drug Administration approval for prevention of pregnancy in 2010 and for the treatment of heavy menstrual bleeding in 2012.6

Extended Regimen COC:SEASONALE (levonorgestrel and ethinyl estradiol tablets) is an extended-cycle combination oral contraceptive consisting of 84 pink active tablets, each containing 0.15 mg of levonorgestrel, and 0.03 mg of ethinyl estradiol and 7 white inert tablets (without hormones). This regimen results in only four withdrawal bleeds per year which may be acceptable after counseling to many women who are suffering from AUB.

Progesterone only pills / Minipill: Desogestrel 75mcg, available as 28 pill pack, to be taken daily without a break. In contrast to the combined pill, the progesterone only pill (POP) is associated with irregular and unpredictable blood loss. Therefore, it is not usually recommended as a treatment for HMB. However, if no other options are acceptable or safe for a woman to use, a trial of a POP may be appropriate. As these pills do not contain estrogen, they are a safer alternative to the COCP. Some POPs induce amenorrhea in up to 20% of users, for example, desogestrel containing POPs, and are effective treatments for a small proportion of women.7
Injectable preparation

Depot medroyprogesterone acetate (DMPA) Intramuscular or subcutaneous injection of high dose progestogens (e.g., depot medroxyprogesterone acetate [DMPA]) can induce amenorrhea in up to 50% of users. This method of administration offers women an alternative to tablets or intrauterine devices. Injections are usually given every 12 weeks/ 3 months to maintain progestogen exposure. Adequate counseling of the patient should be done about the possibility of irregular spotting or bleeding in the initial few months of starting treatment. Prolonged use is not recommended due to chances of reduced bone mineral density. Side effects can limit compliance and include weight gain, greasy skin and hair, acne and bloating.8

Locally acting hormonal contraceptives
LNG IUS(Levonorgestrel-releasing intrauterine system)
This popular intrauterine system (IUS) contains an androgenic progestogen, levonorgestrel (LNG). LNG is slowly released from the IUS (about 20mcg per day) to act on the local endometrial environment, preventing proliferation. It may also impact on the frequency of ovulation. The LNG-IUS can decrease menstrual loss by up to 96% after 1 year of useand is licensed in the UK for treatment of HMB for 5 years. The LNG-IUS is also associated with additional benefit of reduction of dysmenorrhea. As its actions are local, progestogenic side effects are limited, for example, bloating, breast tenderness, mood changes.Extra care must be taken during insertion in women with distortion of their endometrial cavity due to leiomyoma/fibroids or congenital abnormalities. In these cases, it may be safer to use an alternative hormonal treatment or to insert the IUS under hysteroscopic guidance.

Women should be counseled about potential complications of LNG-IUS use including:9, 10

- Unscheduled bleeding: this occurs in the majority of women during the first 3–6 months of use. Women should be advised that they may experience daily spotting but that this usually settles after 6 months. Perseverance for a minimum of 6 months is required for benefits to be appreciated and for unscheduled, usually light, bleeding to subside.
- Infection: women have an increased risk of infection for the first 3 weeks after insertion.
- Expulsion of IUS: up to one in five LNG-IUS devices can be expelled from the uterine cavity after insertion, with the greatest risk of this during the first 6 weeks post-insertion. The rate of expulsion is higher in nulliparous women.
- Perforation: a rare but serious complication of LNG-IUS insertion is uterine perforation, occurring in 1:1000 cases. Distortion of the endometrial cavity, uterine infection or being less than 4 weeks postpartum will increase the risk of perforation substantially.

NUVA Ring

A study by Jain et al indicated that in women with AUB, the NuvaRing, which releases a daily dose of 15 µg ethinyl estradiol and 120 µg etonogestrel, can control heavy menstrual bleeding as effectively as a combined oral contraceptive pill containing 30 µg ethinyl estradiol and 150 µg levonorgestrel. The study included 60 women, who used either the NuvaRing or the combined oral contraceptive pill for 3 consecutive months. Both forms of contraception significantly reduced blood loss in each menstrual cycle, with no significant difference between them on the pictorial blood loss assessment chart.11

Evidence-based Guidelines 12

AUB-A (Adenomyosis)

In women with AUB-A, desirous of preserving fertility but unwilling for immediate conception, progestogens especially LNG-IUS is recommended as first-line therapy (Grade A; Level 1).

Combined oral contraceptives, danazol, NSAIDs, and progestogens can be offered for symptomatic relief where LNG-IUS and GnRH agonists cannot be indicated (Grade B; Level 4).

AUB-L (Leiomyoma)

Treatment for AUB-L should be individualized because many variables such as age, parity, symptoms, fertility desires may affect the treatment preference. Various options can be generalized as follows:

Women with intramural or subserosal myomas (grade2-6), desirous of preserving fertility, can be managed with tranexamic acid or combined oral contraceptives (COCs) or NSAIDs as second-line therapy (Grade A; Level 2).

Women with intramural or subserosal myomas (grade2-6) and desirous of preserving fertility can be medically managed with LNG-IUS if other medical treatment fails and patient is not trying to conceive for at least 1 year. (Grade A; Level 1)

In women above 40 years of age, not desirous of continued fertility, hysterectomy is the definitive treatment; however medical management including LNG-IUS may be tried in small fibroids (<4cms diameter before undergoing definitive surgery (Grade B Level 3)

AUB-M (Malignancy and Endometrial Hyperplasia)

In AUB-M with endometrial hyperplasia without atypia, LNG-IUS can be considered as first-line therapy; oral progestins can be used if LNG-IUS is contraindicated or if patient is unwilling for LNG-IUS(Grade A; Level 1).

AUB-C (Coagulopathy)

In patients with AUB-C, non-hormonal treatment with tranexamic acid as primary option and hormonal treatment with COCs/LNG-IUS as secondary option are recommended in consultation with a haematologist(Grade A; Level 2)

AUB-O (Ovulatory Dysfunction)

In women not desiring conception presently, COCs can be used as first-line therapy for 6-12 months (Grade A; Level 1)

If COCs are contraindicated or patient is unwilling for COCs, LNG-IUS is recommended if she wishes to use it for atleast 1 year (Grade A; Level 1).

It is suggested to assess response after 1 year of medical management and judge to continue/discontinue existing therapy (Grade B; Level 4).

In adolescents with AUB-O, both hormonal and non-hormonal therapies can be prescribed, (Grade A; Level 4).

AUB-E (Endometrial)

Management of AUB-E can be similar to the management of AUB-O (Grade A; Level 4).

AUB-I (Iatrogenic causes)

Whenever possible, medications causing AUB should be changed to other alternatives, if no alternatives are available, LNG-IUS is recommended (Grade A; Level 1).

AUB-N (Not defined)

In patients with idiopathic AUB and desire effective contraception, LNG-IUS is recommended as first-line therapy to reduce menstrual bleeding (Grade A; Level 1).

In patients with AUB-N desirous of continued fertility, in whom, LNG-IUS are contraindicated, use of COCs are recommended as second line therapy (Grade A; Level 1).

Tailoring the treatment to patient's choice addressing her specific needs

Patients must be informed of the efficacy of the different treatment options for heavy menstrual bleeding. Given these options, clinicians need to provide guidance according to the length of treatment desired by the patient. Daily, short-term, or long-term options are available. Patients without contraindications who prefer a daily regimen may benefit most from combination oral contraceptives.Patients who do not want a daily oral regimen and are not planning to conceive in the next year may be better suited for insertion of an LNG-IUD. Those who prefer a monthly two-week course may be best suited to cyclic progestin. Patients who desire a very short course (five days or less) may consider an NSAID.

Table 3. Summary of available treatment options for abnormal uterine bleeding based on PALM-COEIN etiology12

Etiology	Treatment
Polyp	Hysteroscopic surgical removal Multiple polyps or polypoidal endometrium and fertility is not desired–LNG-IUS can be combined with surgical removal
Adenomyosis	LNG-IUS, if LNG IUS is not accepted–GnRH agonists with add back therapy; if it fails OCP, NSAIDs, progestogens
Leiomyoma	Intramural or sub-serosal myomas (grade 2-6) Tranexamic acid or COCs or NSAIDs, LNG-IUS, if treatment fails myomectomy depending on location In women >40 years of age, fertility is not desired, for small fibroids (< 4-5 cm)–medical management followed by hysterectomy Short-term management (up to 6 months)–GnRH agonists with add back therapy followed by myomectomy Long-term management–LNG-IUS Newer medical options: ulipristal acetate or low dose mifepristone Sub mucosal myoma (grade 0-1)hysteroscopic (< 4 cm) or abdominal(open or laparoscopic for > 4 cm)
Malignancy	Atypical endometrial hyperplasia–surgical treatment Continued fertility not desired–hysterectomy Hyperplasia without atypia LNG-IUS followed by oral progestins or PRMs
COEIN	LNG-IUS or tranexamic acid, NSAIDs, followed by COCs or cyclic oral progestins Medical or surgical treatment failed or contraindicated: GnRH agonists with add-back hormone therapy When steroidal and other options unsuitable: Centchroman

PALM: Polyp, Adenoma, Leiomyoma, Malignancy and hyperplasia; LNG-IUS: Levonorgestrel intrauterine system; NSAIDs: Non-steroidal anti-inflammatory drugs; COCs: Combined oral contraceptives; OCP: Oral contraceptive pill; PRMs: Progesterone receptor modulators; GnRH: Gonadotropin Releasing Hormone

Conclusion

Theclinician's role is to evaluate the woman for proper diagnosis of the cause of her AUB and provide adequate information about various treatment options, thus guiding the woman to choose the treatment most appropriate for her. Written information can be additionally helpful and patient information leaflets can be provided. Their concerns and queries should be appropriately addressed to remove any fear or anxiety due to myths related to hormonal treatment. Treatment success can be ultimately determined by overall improvement in the woman's quality of life.

References

1. Sharma A, Dogra Y. Trends of AUB in tertiary centre of Shimla hills. J Midlife Health. 2013;4:67-8.
2. Munro MG, Critchley HO, Broder MS, Fraser IS. FIGO classification system (PALM-COEIN) for causes of abnormal uterine bleeding in non-gravid women of reproductive age. Int. J. Gynaecol. Obstet. 2011;113(1):3–13.
3. Munro MG, Mainor N, Basu R, Brisinger M, Barreda L. Oral medroxyprogesterone acetate and combination oral contraceptives for acute uterine bleeding: a randomized controlled trial. Obstet Gynecol 2006;108:924–9. Management of Acute Abnormal Uterine Bleeding in Nonpregnant Reproductive-Aged Women. ACOG Committee Opinion. Number 557, April 2013. Reaffirmed 2019.
4. Fraser IS, Kovacs GT. The efficacy of non-contraceptive uses for hormonal contraceptives. Med. J. Aust. 2003;178(12):621–623.
5. FSRH. UK Medical Eligibility Criteria for Contraceptive Use. www.fsrh.org/pdfs/UKME2009.pdf
6. Rafie S, Borgelt L, Koepf ER, Temple-Cooper M, Lehman KJ. Novel oral contraceptive for heavy menstrual bleeding: estradiol valerate and dienogest. Int J Women's Health 2013;5:313-321.
7. Benagiano G, Primiero FM. Seventy-five microgram desogestrel minipill, a new perspective in estrogen-free contraception. Ann. NY Acad. Sci. 2003;997:163–173
8. Said S, Omar K, Koetsawang S, et al. A multicentered Phase III comparative clinical trial of depot-medroxyprogesterone acetate given three-monthly at doses of 100 mg or 150 mg: II. The comparison of bleeding patterns. World Health Organization. Task force on long-acting systemic agents for fertility regulation special programme of research, development and research training in human reproduction. Contraception. 1987;35(6):591–610.
9. Andersson K, Odlind V, Rybo G. Levonorgestrel-releasing and copper-releasing (Nova T) IUDs during five years of use: a randomized comparative trial. Contraception. 1994;49(1):56–72.
10. Sheng J, Zhang WY, Zhang JP, Lu D. The LNG-IUS study on adenomyosis: a 3-year follow-up study on the efficacy and side effects of the use of levonorgestrel intrauterine system for the treatment of dysmenorrhea associated with adenomyosis. Contraception. 2009;79(3):189–193
11. Jain S, Vaid NB, Narang Y, Suneja A, Guleria K. A Randomised Controlled Trial Comparing the Efficacy and Side-Effects of Intravaginal Ring (Nuvaring(®)) With Combined Oral Hormonal Preparation in Dysfunctional Uterine Bleeding. J Clin Diagn Res. 2016 Mar. 10 (3):QC21-4)
    Management of Abnormal Uterine Bleeding in Reproductive Period. Evidence-based Good Clinical Practice Recommendations for Indian women. A Gynae Endocrine Society of India (GESI) initiative in collaboration with Endocrine Committee of Association of Obstetricians and Gynaecologists of Delhi 2016. https://www.fogsi.org › wp-content › uploads › 2016/02 › gcpr-on-aub

Contraceptives for Management of Endometriosis

Atul Ganatra
MD,DGO,FICOG.
Obstetrician Gynecologist
& Gynecological Endoscopist
Dr. R. J. Ganatra's Nursing Home
& Fortis Hospitals, Mumbai
–Vice President (West Zone)
FOGSI 2020-2021
Chairperson MTP Committee
FOGSI (2012-2014)

Ameya Purandare
MD, DNB, FCPS, DGO, DFP, MNAMS, FICMCH,
FICOG, Fellowship in Gyn Endoscopy(Ger)
Consultant Obstetrician & Gynaecologist
at Purandare Hospital.
Joint Secretary, FOGSI 2019
Chairperson, Food Drugs Medical Surgical
Equipment Committee, FOGSI 2015-17

Ritu Hinduja
MD,MRM (UK), DRM (Germany)
Consultant Reproductive
Medicine Nova IVF Fertility
Andheri ,Mumbai

Endometriosis is a benign gynecological condition, which is estimated to affect 10% of women in the general population and appears to be increasing in incidence, explained in part by changing reproductive patterns.[1]

The quality of life in women with endometriosis is often greatly impaired, with a positive correlation between the intensity of pelvic pain and presence of anxiety symptoms, with increasing physical limitations associated with increased pain intensity.[2]

Prescribing contraception for women with endometriosis, suspected or diagnosed is aimed at reducing their degree of pain, emotional profile, and the effects on their quality of life should influence the choice of method.

Another goal of contraceptive choice should be directed toward prophylaxis of endometriosis progression and, following laparoscopic treatment of endometriosis, minimizing the risk of recurrence and impairment of fertility.[3]

Contraceptive choices

Ideally, since endometriosis is an estrogen-dependent disease, use of progestogen-only methods of contraception is generally preferable, especially when these methods are long- acting (long-acting reversible contraception). These include oral desogestrel, more recently oral dienogest, intramuscular depot medroxyprogesterone acetate (DMPA), the subdermal etonogestrel (ENG) implant, and the levonorgestrel (LNG)- releasing intrauterine system (IUS). A small proof of concept study of a progestin-releasing subdermal implant indicated that progestogen implants were likely to have a beneficial effect on symptoms of endometriosis.[4] This is likely to apply to all LNG implants. The implant and LNG IUS have the advantage of a long duration of action and the lowest pregnancy rates of all the available contraceptive methods, with a rapid return of fertility on discontinuation. All progestogen-only contraceptive methods cause variable and unpredictable changes in bleeding patterns, and as they do not suppress ovulation, are associated with a small increase in functional follicular cysts. These may transiently affect pain and bleeding. Women considering these methods require careful counseling in order to make an informed choice.

Factors that need to be considered in contraceptive choices for women with endometriosis.

- Effective contraception
- Endometriosis symptom control
  Desire for future pregnancy (women wanting children should be encouraged to attempt pregnancy as soon as possible)
- Prevention of progression of endometriosis
- Fertility control plus post-surgical prevention of recurrence
- Effect on physical, mental, and social well-being
- Personal preferences

Progestogen-releasing IUS

The main mode of action of the LNG IUS is at a uterine level, with endometrial atrophy and an inflammatory response maximal at 3 months and maintained for the life of the device.[5,6] It also increases cervical mucus viscosity, impeding sperm penetration, and releases glycodelin A within the uterine glands, inhibiting fertilization and implantation. There is some inhibition of ovulation in the first 12 months, but most cycles are ovulatory. Since serum estradiol levels are generally within the normal range, it is not entirely clear why the LNG IUS should offer a symptomatic advantage for women with endometriosis. It has been postulated that the atrophic changes induced in the endometrium may similarly occur in the ectopic endometriotic lesions.[7] A number of other mechanisms for the effectiveness of the LNG IUS in controlling pain have been postulated, including a reduction in local angiogenesis, reduction in uterine innervation, reduction in pelvic vascular "congestion", and an increase in apoptosis in lesions.[8] Undoubtedly, the very thin endometrium and minimal bleeding in established LNG IUS users will minimize any ongoing retrograde menstruation.

Most women using the LNG IUS experience irregular bleeding. Spotting and frequent or prolonged bleeding may initially be experienced by up to 35% of contraceptive LNG IUS users in the first 3–5 months of use. By 9 months, 50% experience infrequent, light bleeding, and amenorrhea occurs in a further 15%. At 5 years, 23% of women are amenorrheic and 77% experience infrequent bleeding, a useful effect for women with the heavy menstrual bleeding sometimes associated with endometriosis. There are no trials to show that endometriosis subjects have similar experience. Counseling women about these bleeding disturbances prior to IUS use is important.

Hormonal side effects such as mood changes, acne, breast tenderness, and headaches may occur in about 3%–5% of users initially but diminish over time.[9] Since many women with endometriosis may wish to delay pregnancy or have completed their families, the LNG IUS, with a lifespan up to 5 years, which can also alleviate pelvic pain and heavy bleeding, is an ideal method with rapid return of fertility on removal if required.[10]

Subdermal progestogen implants

Two subdermal implants, a single ENG rod, with a 3-year lifespan, and an LNG two-rod system with a 5-year lifespan, are currently in use.. The ENG implant prevents the luteinizing hormone surge so that ovarian follicular development usually occurs with- out ovulation. The LNG implant disrupts follicular growth and the ovulatory process, causing a variety of changes that range from anovulation to insufficient luteal function.11Both implants increase the viscosity of cervical mucus and produce an endometrium that is thin but not atrophic. Both are highly effective methods, with a pregnancy rate of 0.01%–0.1%

per year in typical use.[12] The woman rapidly returns to her normal fertility when the implants are removed. Because the implants contain no estrogen, the most common side effects are changes in menstrual bleeding patterns,[13]which sometimes lead to requests for removal.[14]Most other common side effects are similar to those experienced by women who use other hormonal contraceptives. The finding of ovarian cysts or enlarged ovarian follicles during the 1st year of use of ENG and LNG implants is common and transient, and should not be interpreted as pathological,15but in women with endometriosis it may be difficult to distinguish between functional and endometriotic cysts unless a good quality transvaginal ultrasound examination is performed.

Although there are only limited data, implants appear to be effective in decreasing the pain associated with endometriosis. Walch et al16found that by 6 months of use of the ENG implant the average decrease in pain was 68%. A Thai study of the ENG implant in 50 women with endometriosis found that the visual analog scale score for pain reduced from 7.08±2.09 to 0.84±1.67 at the 12th week of treatment. Regular menstruation, amenorrhea, spotting, and breakthrough bleeding were reported by 42%, 28%, 26%, and 4% of women, respectively. Eighty percent of women were satisfied or very satisfied with the implant while 10% were uncertain. All continued implant use at the end of the study.[18]

Depot medroxyprogesterone acetate

DMPA is available either as an intramuscular injection (150 mg once every 3 months) or a subcutaneous injection (106 mg) which can be self-administered. With a failure rate of 0.5% and a mode of action primarily by suppression of ovulation with ancillary effects on the endometrium and cervical mucus, it is an effective contraceptive for women with endometriosis. It also appears to have an effect on pain scores, with an estimated 53%–90% decrease in pain[18] and an 80% improvement in dyspareunia during treatment. The subcutaneous injection appears to be equally as effective as the intramuscular injection, both as a contraceptive and in pain relief.[19],[20] However, a Cochrane review of 13 studies concluded that there was only limited evidence to support the use of progestogens, including DMPA, for the relief of endometriosis-related pain.[21]

DMPA should not be recommended for women who plan to attempt pregnancy within the next 2 years as DMPA can result in a delay in the return of fertility for up to 18 months. As with all progestogen-only contraception methods, DMPA causes menstrual irregularities, with 50% of women exhibiting amenorrhea by 12 months of use.

Oral progestogen-only methods

Of the four main oral progestogen-only methods, ie, LNG 30 µg, norethisterone 350 µg, desogestrel 75 µg, and dienogest 2 mg, the latter two are preferable since they inhibit ovulation in 97% of cycles and produce significantly lower estradiol levels.[22] There are no data specific to pain associated with endometriosis in women without prior surgical intervention; however, by 3–4 months of starting the desogestrel progestogen-only pill, dysmenorrhea in 93% of 406 women resolved or considerably improved and analgesic use dropped from 70% at baseline to 8%.[23]

Dienogest is a progestogen-only hormone preparation for the treatment of endometriosis. It works by suppressing oestradiol production and preventing the growth of the endometrium.Dienogest can be started on any day of the menstrual cycle. It should be taken every day without interruption.Dienogest reduces the pain associated with endometriosis and is comparable to gonadotropin-releasing hormone agonists. Usually a dose of 2mg per day.

Combined estrogen/progestogen contraceptives

Combinations of estrogens and progestogens for contraception can be delivered orally, transdermally as a skin patch, or intravaginally as a ring. All are equally efficacious as contraceptives, and the route of administration depends on the personal preference of the individual woman.

In recent years, the choice of oral estrogen/progestogen combinations has increased with the advent of several new progestogens, including dienogest, drospirenone, and nomegestrol acetate, and recently the use of estradiol-17 instead of ethinyl estradiol. Oral preparations of ethinyl estradiol in combination with different progestogens have been used extensively for many years for the management of dysmenorrhea associated with endometriosis. A number of studies usingCOCs with different progestogens, eg, desogestrel,[24] gestodene,[25] norethisterone,[26] drospirenone,[27]LNG suggest that all COCs are effective in ameliorating dysmenorrhea in the majority of women with endometriosis. As there are no comparative studies to suggest that one COC may be more effective than others, the initial use of any low- dose monophasic COC is appropriate.

COCs provide effective contraception, and some studies have shown that they can reduce the size of endometriomas.[26],[27] This positive effect appears to be due to the downregulation of cell proliferation and an increase in the rate of apoptosis in eutopic endometrium and cyst lining.[28]However, a Cochrane review found that comparative studies between COCs and other treatments for pelvic pain were inadequate to fully evaluate the role of COCs.[29]Nevertheless, COCs provide a low-cost, effective, and acceptable method of contraception that can ameliorate dysmenorrhea, and are of benefit to many women. Continuous rather than cyclical administration of a COC may be more efficacious for control of dysmenorrhea because it is associated with less frequent menstrual bleed- ing.[24],[30] However, careful counseling is required to ensure unpredictable bleeding is acceptable.

There has been debate in the literature regarding the role that COCs may play in the development of endometriosis.31A meta-analysis of 18 studies found the relative risk of development of endometriosis was 1.19 in ever users of COCs, 0.63 in current users, and 1.21 in past users.[24] To clarify this, Chapron et al[31] carried out a cross-sectional study of women without visible endometriosis at surgery compared with women with surgically diagnosed endometriosis, and found that women who had previously used COCs for the management of severe dysmenorrhea were more likely to be diagnosed with endometriosis at a later date, a finding confirmed by Vercellini et al.[32]Although there is no clear scientific proof, it suggests that there is a protective effect against progression of endometriosis by COCs, and past use of COCs for severe dysmenorrhea may act as a marker for endometriosis and contributing to a delay in recognition of the disease, for up to 7 years after onset of symptoms .

There has been only one report of the comparative use of the contraceptive vaginal ring and transdermal patch in women with endometriosis. The women started on continuous treatment with both methods, but almost 50% in each group reverted to cyclic use because of irregular bleeding. Pain symptoms were reduced with both methods, but the ring was more effective in controlling symptoms in women with deep rectovaginal lesions. The women using the contraceptive vaginal ring method were more satisfied with the treatment than women using the patch.[24]

Method	Estrogen containing	Pain relief	Highly effective contraception	Long-acting	Cycle control	Blood loss	Effect on BMD	Possible functional ovarian cysts
Progestogen only pill	No	Yes	Yes, but compliance problematic	No	Variable	Variable	No	Yes
Subdermal implant	No	Yes	Yes	Yes 3 years	Variable	Variable	No	Yes
LNG IUS	No	Yes	Yes	Yes 5 years	Variable	Reduced	No	Yes
DMPA	No	Yes	Yes	3 monthly	Amenorrhea common	Reduced	Yes but reversible	Rare
COC* continuous	Yes	Yes	Yes, but compliance problematic	No daily use	Variable	Reduced	No	No
COC* cyclic	Yes	Variable	Compliance problematic in adolescents	No daily use	Good	Reduced	No	No
CVR	Yes	Probable	Yes	No monthly	Good	Reduced	No	No
Transdermal patch	Yes	Probable	Yes	No weekly	Good	Reduced	No	No

Note: *Preferably an estradiol-containing COC.
Abbreviations: BMD, bone mineral density; COC, combined oral contraceptive; CVR, contraceptive vaginal ring; DMPA, depot medroxyprogesterone acetate; LNG, levonorgestrel; IUS, intrauterine system.

Table 1: Comparison of various contraceptives that can be used in the management of endometriosis

Contraception after surgical treatment for endometriosis

Following surgical management of endometriosis, effective contraception is important for those women who have completed their families or desire to postpone pregnancy. The contraceptive method chosen should also carry the benefit of preventing recurrence of pelvic pain, endometriomas, or other

significantly greater patient satisfaction. A Cochrane review concluded that there was limited but consistent evidence that postoperative use of the LNG IUS reduced the recurrence of dysmenorrhea in women with endometriosis38DMPA also appears to have a beneficial effect on control of pain following conservative surgery for endometriosis. It provides low-cost, effective contraception but has the disadvantage of an unpredictable delay of some months in the return of fertility after cessation for those women who still desire a pregnancy.[39]

Contraception for adolescentswith suspected or diagnosed endometriosis Endometriosis has been shown to occur in adolescents as young as 10 years, and can be a major cause of chronic pelvic pain and dysmenorrhea, which are greatly disruptive to lifestyle.[40]In fact, symptoms of endometriosis often begin in adolescence for many women later diagnosed with the disease. Adolescents have been shown to frequently have a 10-year delay from the onset of symptoms to the diagnosis being made. Hence, there is a real need for physicians to have a high degree of suspicion of underlying endometriosis in adolescents with moder- ate to severe dysmenorrhea or other chronic pelvic pain, especially if a family history is present. The aim of using hormonal methods of contraception in young women with endometriosis should be to provide effective fertility control and at the same time alleviate associated pain and progression of the disease.

Continuous administration of COCs is usually the method recommended for adolescents with dysmenorrhea likely due to endometriosis. However, adolescents may have problems adhering to daily oral medication and may find any associated irregular bleeding difficult to manage. Long-acting and reversible progestogen contraceptives are appropriate and highly effective methods of contraception, which require no action on the part of the user after insertion, and have been demonstrated to provide substantial alleviation of pain. Since endometriosis is an estrogen-dependent disease, long-acting reversible contraceptives are preferable to COCs for long- term management in adolescents. The American College of Obstetricians and Gynecologists Committee on Adolescent Health Care, Long-Acting Reversible Contraception Working Group, in their latest opinion, have stated that long-acting reversible contraceptives should be considered as first-line contraceptives for adolescents.41

DMPA has been widely used by adolescents and shown to be highly effective for both contraception and pain control. However, concerns have been raised about the long-term effects of bone loss on peak bone mass associated with use of DMPA in young adolescents. A study of long-term DMPA in young women aged 12–18 years found that although bone mineral density (BMD) declined during use, long-term loss did not continue, and most bone was fairly rapidly replaced following discontinuation. Harel et alfound that bone mineral density returned to baseline levels within 60 weeks of discontinuation of DMPA.

DMPA has been associated with weight gain, which is of particular concern to many young women. Young DMPA users have been shown to gain more weight than COC users, especially if they are overweight at the start of treatment.[42,43]
In the USA, adolescents have shown an interest in using the subcutaneous form of DMPA, and at least a third were found to be capable of self-administration after brief education and minimal assistance.[44] There are no specific data on the long-term effects of DMPA use in young women with endometriosis.

Although there are no data on the use of the ENG implant alone in young women with endometriosis, it is a useful method of contraception, and offers the additional benefit of a reduction in pelvic pain.

Conclusion

The contraceptive choice in women with endometriosis must fulfill two main objectives, ie, offer highly effective fertility control and provide reliable pain relief for prolonged periods, with fairly rapid reversal if a pregnancy is desired. Ideally, the method should also prevent progression of the disease or recurrence after surgical management. In choice of a method, many additional factors may need to be taken into account, including the side effect profile, the ongoing cost, and the preference of the woman, who should always be made aware of the benefits and risks to enable her to make an informed decision.

References

1) Viganò P1, Parazzini F, Somigliana E, Vercellini P. Endometriosis: epidemiology and aetiological factors. Best Pract Res ClinObstetGynaecol. 2004;18:177–200
2) Sepulcria RP, Amaral VF. Depressive symptoms, anxiety, and quality of life in women with pelvic endometriosis. Eur J ObstetGynecolReprod Biol. 2009;142:53–56.
3) Vercellini P, Barbara G, Somigliana E, Bianchi S, Abbiati A, Fedele L. Comparison of contraceptive ring and patch for the treatment of symptomatic endometriosis. FertilSteril. 2010;93:2150–2161
4) Ylanen K, Laatikainen T, Lähteenmäki P, Moo-Young AJ. Subdermal progestin implant (Nesterone) in the treatment of endometriosis: clini- cal response to various doses. Acta ObstetGynecol Scand. 2003;82: 167–172
5) Ortiz ME, Croxatto HB. Copper-T intrauterine device and levonorgestrel intrauterine system: biological bases of their mechanism of action. Contraception. 2007;75:S16–S30.
6) Lähteenmäki P, Bardin CW, Eloma K, et al. Selection and performance of the levonorgestrel-releasing intrauterine system. Acta ObstetGynecol Scand. 1997;164:69–74.
7) Hidalgo M1, Bahamondes L, Perrotti M, Diaz J, Dantas-Monteiro C, Petta C. Bleeding patterns and clinical performance of the levonorg- estrel-releasing intrauterine system (Mirena) up to two years. Contraception. 2002;65:129–132.

8) Maruo T, Laoag-Fernandez JB, Pakarinen P, Murakoshi H, Spitz IM, Johansson E. Effects of the levonorgestrel-releasing intrauterine sys- tem on proliferation and apoptosis in the endometrium. Hum Reprod. 2001;16:2103–2108.
9) Luukkainen T, Pakarinen P, Toivonen J. Progestin-releasing intrauterine systems. SeminReprod Med. 2001;19:355–363.
10) Bahamondes L, Petta CA, Fernandes A, Monteiro I. Use of the levonorgestrel-releasing intrauterine system in women with endometriosis, chronic pelvic pain and dysmenorrhea. Contraception. 2007;75 Suppl6:S134–S139.
11) Croxatto HB, Mäkäräinen L. The pharmacodynamics and efficacy of Implanon. An overview of the data. Contraception. 1998;58: 91S–97S.
12) Meirik O, Fraser IS, d'Arcangues C; WHO Consultation on Implantable Contraceptives for Women. Implantable contraceptives for women. Hum Reprod Update. 2003;9:49–59.
13) Mansour D, Korver T, Marintcheva-Petrova M, Fraser IS. The effects of Implanon on menstrual bleeding patterns. Eur J Contracept Reprod Health Care. 2008;13 Suppl 1:13–28.
14) Weisberg E, Fraser I. Australian women's experience with Implanon. Aust Fam Physician. 2005;34:694–696.
15) Hidalgo MM, Lisondo C, Juliato CT, Espejo-Arce X, Monteiro I, Baha- mondes L. Ovarian cysts in users of Implanon® and Jadelle® subdermal contraceptive implants. Contraception. 2006;73:532–536.
16) Walch K, Unfrieda G, Hubera J, et al. Implanon® versus medroxypro- gesterone acetate: effects on pain scores in patients with symptomatic endometriosis – a pilot study. Contraception. 2009;79:29–34.
17) Ponpuckdee J, Taneepanichskul S. The effects of Implanon in the symptomatic treatment of endometriosis. J Med Assoc Thai. 2005;88 Suppl2:S7–S10.
18) Crosignani PG, Luciano A, Ray A, Bergqvist A. Subcutaneous depot medroxyprogesterone acetate versus leuprolide acetate in the treatment of endometriosis-associated pain. Hum Reprod. 2006;21: 248–256.
19) Simon MA, Shulman LP. Subcutaneous versus intramuscular depot methoxyprogesterone acetate: a comparative review. Womens Health (LondEngl). 2006;2:191–197.
20) Schlaff WD, Carson SA, Luciano A, Ross D, Bergqvist A. Subcutaneous injection of depot medroxyprogesterone acetate compared with leupro- lide acetate in the treatment of endometriosis-associated pain. FertilSteril. 2006;85:314–325.
21) Brown J, Kives S, Akhtar M. Progestagens and anti-progestagens for pain associated with endometriosis. Cochrane Database Syst Rev. 2012;3:CD002122.
22) Rice CF, Killick SR, Dieben T, CoelinghBennink H. A comparison of the inhibition of ovulation achieved by desogestrel 75 µg and levonorg- estrel 30 µg daily. Hum Reprod. 1999;14:982–995.
23) Ahrendt HJ, Karckt U, Pichl T, Mueller T, Ernst U. The effects of an oestrogen-free, desogestrel-containing oral contraceptive in women with cyclical symptoms: results from two studies on oestrogen-related symptoms and dysmenorrhoea. Eur J Contracept Reprod Health Care. 2007;12:354–361.
24) Vercellini P, Frontino G, De Giorgi O, Pietropaolo G, Pasin R, Crosignani PG. Continuous use of an oral contraceptive for endometriosis- associated recurrent dysmenorrhea that does not respond to a cyclic pill regimen. FertilSteril. 2003;80:560–563.
25) Ferrari S, Persico P, Di Puppo F, et al. Continuous low-dose oral contraceptive in the treatment of colorectal endometriosis evaluated by rectal endoscopic ultrasonography. Acta ObstetGynecol Scand. 2012;91:699–703.
26) Harada T, Momoeda M, Taketani Y, Hoshiai H, Terakawa N. Low-dose oral contraceptive pill for dysmenorrhea associated with endometriosis: a placebo-controlled, double-blind, randomized trial. FertilSteril. 2008;90:1583–1588.
27) Mabrouk M, Solfrini S, Frascà C, et al. A new oral contraceptive regi- men for endometriosis management: preliminary experience with 24/4- day drospirenone/ethinylestradiol 3 mg/20 mcg. Gynecol Endocrinol. 2012;28:451–454.
28) Meresman GF, Augé L, Barañao RI, Lombardi E, Tesone M, Sueldo C. Oral contraceptives suppress cell proliferation and enhance apoptosis of eutopic endometrial tissue from patients with endometriosis. FertilSteril. 2002;77:1141–1147.
29) Davis L, Kennedy SS, Moore J, Prentice A. Modern combined oral contraceptives for pain associated with endometriosis. Cochrane Database Syst Rev. 2007;3:CD001019.
30) Guzick DS, Huang LS, Broadman BA, Nealon M, Hornstein MD. Randomized trial of leuprolide versus continuous oral contraceptives in the treatment of endometriosis-associated pelvic pain. FertilSteril. 2011;95:1568–1573.

31) Chapron C, Souza C, Borghese B, et al. Oral contraceptives and endometriosis: the past use of oral contraceptives for treating severe primary dysmenorrhea is associated with endometriosis, especially deep infiltrating endometriosis. Hum Reprod. 2011;26:2028–2035.
32) Vercellini P, Somigliana E, Viganò P, De Matteis S, Barbara G, Fedele L. Post-operative endometriosis recurrence: a plea for prevention based on pathogenetic, epidemiological and clinical evidence. Reprod Biomed Online. 2010;21:259–265.
33) Vlahos N, Vlachos A, Triantafyllidou O, Vitoratos N, Creatsas G. Continuous versus cyclic use of oral contraceptives after surgery for symptomatic endometriosis: a prospective cohort study. FertilSteril. 2013;100:1337–1342.
34) Seracchioli R, Mabrouk M, Frascà C, et al. Long-term cyclic and continuous oral contraceptive therapy and endometrioma recurrence: a randomized controlled trial. FertilSteril. 2010;93:52–56.
35) Vercellini P, Somigliana E, Daguati R, Vigano P, Meroni F, Crosignani PG. Postoperative oral contraceptive exposure and risk of endometrioma recurrence. Am J Obstet Gynecol. 2008;198:504. e1–e5.
36) Vercellini P, De Matteis S, Somigliana E, Buggio L, Frattaruolo MP, Fedele L. Long-term adjuvant therapy for the prevention of postopera- tive endometrioma recurrence: a systematic review and meta-analysis. Acta ObstetGynecol Scand. 2013;92:8–16.
37) Tanmahasamut P, Rattanachaiyanont M, Angsuwathana S, Techatraisak K, Indhavivadhana S, Leerasiri P. Postoperative levonorgestrel-releasing intrauterine system for pelvic endometriosis-related pain: a randomized controlled trial. Obstet Gynecol. 2012;119: 519–526.
38) Abou-Setta AM, Houston B, Al-Inany HG, Farquhar C. Levonorgestrel- releasing intrauterine device (LNG-IUD) for symptomatic endo- metriosis following surgery. Cochrane Database Syst Rev. 2013;1: CD005072.
39) Zhou J, Lei ZW, Lü JQ, et al. [Conservative surgery combined with depot medroxyprogesterone acetate in treatment of moderate or severe endometriosis]. Zhonghua Fu Chan KeZaZhi. 2005;40:5–8. Chinese.
40) Goldstein DP, deCholnoky C, Leventhal JM, Emans SJ. New insights into the old problem of chronic pelvic pain. J Pediatr Surg. 1979;14:675–680.
41) American College of Obstetricians and Gynecologists Adolescent Health Care Committee Opinion. Adolescents and long-acting revers- ible contraception: implants and intrauterine devices. October 16, 2012. Available from: http://www.acog.org/About-ACOG/ACOG- Departments/Adolescent-Health-Care/Adolescents-and-Long-Acting- Reversible-Contraception/ Accessed April 12, 2015.
42) Risser WL, Geftera LR, Barratt MS, Risser JMH. Weight change in adolescents who used hormonal contraception. J Adolesc Health. 1999;24:433–436.
43) Mangan SA, Larsen PG, Hudson S. Overweight teens at increased risk for weight gain while using depot medroxyprogesterone acetate. J PediatrAdolesc Gynecol. 2002;15:79–82.
44) Williams RL, Hensel DJ, Fortenberry JD. Self-administration of sub- cutaneous depot medroxyprogesterone acetate by adolescent women. Contraception. 2013;88:401–407.

Managing the Perimenopause transition with Contraception and HRT

Sheela V Mane
MD, FICOG,FICMCH.
DNB Professor, KCG Hospital and consultant,
Anugraha nursing Home, Bengaluru.
Vice president South Zone FOGSI 2014
Chairperson Safe Motherhood committee FOGSI (2008-2011)

Jyothika A Desai
MD,DGO,PGDMLE, FICOG.
Consultant Gynecologist Desai Nursing Home.
South zone quiz co-ordinatorFOGSI(2012-21)
President BSOG, 2013.

Perimenopause is the transition to menopause. This is an important period as it provides a window of opportunity for life style modifications and pharmacotherapy to improve perimenopausal health.

The Reproductive aging workshop (STRAW) 1 hasclassified this period as

- Early perimenopause – Stage -2 is a period of variable length. During this stage the menstrual cycle is altered but regular, the antral follicle count is low and the levels of FSH are high, (>10miu/l) while the levels of AMH and inhibin are low. However there are usually no menopausal symptoms. This stage usually begins at around 40 years of age.
- Late Perimenopause - Stage -1 is of one to three years duration when there are periods of amenorrhea interspersed with menstruation. The FSH levels are >25miu/l and there may be vasomotor and/or other symptoms of menopause.
- Early Post menopause – Stage +1a is the first 12 months after the final menstrual period,which has the same symptomatology as late perimenopause.

The age at menopause varies in different ethnic subgroups. Recently genome wide studies have identified manysingle nucleotide polymorphisms (SNP) which may be associated with age at menopause (AOM) and may thus be applied to predict the age of menopause. 2

Perimenopausal patients present with vasomotor, psychological, and urological symptoms as well as disturbances of their bleeding pattern. Pregnancy risk is not always something they are aware of and consequently can sometimes be overlooked.3 Genuine early or premature menopause is a risk factor for osteoporosis, heart disease, and dementia; these patients need to understand the benefits of HRT until at least the age of 50 years.4

During perimenopause there is a decline in pulsatile secretion of gonadotropin releasing hormone from the hypothalamus thus disrupting gonadotropin secretion from the pituitary. This leads to anovulation and initially a deficiency of progesterone followed by gradual decline in estrogen levels.

Estrogen being a natural antioxidant, maintains health during reproductive years. Its deficiency results in a host of non- communicable diseases like cardiovascular disease, hypertension, obesity, diabetes and even mental health disorders like anxiety and depression. Life Style modifications will certainly improve symptoms of menopause. Regular exercise is very important as it maintains body weight, improves coronary circulation, delays the onset of diabetes and prevents sarcopenia and osteopenia. Practice of Yoga improves balance, delays frailty and improves circulation to many vital internal organs. Kegels exercises improve the tone of the pelvic floor and prevent pelvic floor dysfunction and prolapse.

A diet rich in vegetables fruits and fibre is recommended. Low intake of salt, sugar and red meat is beneficial. Supplements of vitamin B12, D and Calcium are required during this period. Role of anti-oxidants, resveratrol andmelatonin is currently empirical and needs to be evaluated in placebo controlled trials.

Contraception in the perimenopause: 40+ has sometimes been compared with the teenage, as the maximum number of divorces occur during this time, with a renewed interest in sexual relationships. Also, the onset of the menopausal symptoms makes couples lax about contraception, with increased induced miscarriages too at this age. A woman can be regarded as safe from pregnancy risk a year after her FMP, if she is>50 years, or 2 years after her FMP if she is <50 years. This is useful only if she is using a non-hormonal method of contraception, as with hormonal methods she cannot be sure if her amenorrhoea was natural or method induced. Current recommendationsare for women using combined methods or the Depo-Proverainjection to change to an alternative method at age 50 years, but the other methods of contraception do not have any upper age restriction.5

Does a woman on contraceptives need to know whether she has attained menopause? Follicle stimulating hormone (FSH) levels are useful in women wishing to cease progestogen-only contraception (POC) (but not estrogen-containing products). Two FSH levels ≥30 iu/l, 6 weeks apart show that a woman is post-menopausal and she then needs to wait at least for1 year before safely stopping contraception.3 FSH levels are also indicated when a woman stops menstruating before 40 years, to help us manage Primary Ovarian Insufficiency. When a woman is still bleeding, though irregularly, it does not make sense to evaluate FSH as it can lull one into a false sense of safety from pregnancy risk. MHT should always be guided by symptoms and not by the FSH level alone.

There are certain guiding principles in treating the Menopausal woman which can be applied to the Perimenopause as well. MHT is not indicated for Primary prevention of Osteoporosis, Cardiovascular accidents or Alzheimer's syndrome.

Next, in the commonest indications like Vasomotor Symptoms and GSM (Genitourinary Syndrome of Menopause), the most effective hormone is Estrogen, either systemically in the former, or locally in the latter, for a period not exceeding 5 years, provided there is no uterus. Otherwise, Progesterone supplementation, either orally as MPA, Micronized Progesterone or Dydrogesterone or as an intrauterine delivery system, like LNG-IUS, has to be provided to prevent endometrial hyperplasia which can result from only ERT.

Use of menopausal hormone therapy (MHT) has decreased approximately 80 percent since the initial publication of the WHI results in 20026. Though we have data showing the safety of MHT in younger postmenopausal women, very few Physicians prescribe MHT today.
Pharmacotherapy does improve the quality of life of many women in the perimenopausal age group. MHT improves menopausal symptoms, but can cause bleeding problems and does not offer contraception. Let us have a look at the available management options and their indications.
Estrogen: Estrogens can be administered orally, transdermal, percutaneously, intramuscularly, intranasal, subcutaneously, or locally (vaginally) with doses and timing tailored to each patient. It can be given

alone as ERT, or combined with Progesterone.Whatever the route, the effect on symptom relief and Bone density are the same. However, the metabolic effects differ.

Oral Route- briefly, oral estrogens increase Triglycerides, increase SHBG with resulting lower Testosterone levels, (may decrease libido, however, studies have not proven this), with increased risks of VTE and Thrombo-embolism.
Dose: Earlier the principle of one size fits all was practiced and doses of CEEof 0.625mgs or its equivalent in 17 B Estradiol of 1mg, used to be the starting dose. But now, because this high starting dose can be associated with more side effects, a lower dose of CEE of 0.3mgs or 17 B Estradiol of 0.5mg is used as the starting one and the dose gradually titrated to higher doses depending on the response.

Combined Oral Contraceptives: COC is a safe, effective alternative to HRT in healthy, non-smoking, perimenopausal women and offers additional benefits, including: control over bleeding, contraception, and protection against ovarian and uterine cancers.3

The older 21 day version with a 7 day Pill Free Interval is not ideal in the perimenopause, as longer bleeds, mood swings, headaches, exacerbation of vasomotor symptoms in the PFI are often seen. More favored regimens are those with a shorter PFI, or even extended three month regimens. COC however, unlike LNG-IUS or MHT, is contraindicated in certain women: smokers >35 years, those with hypertension, focal migraine (transdermal HRT recommended), and

complicated diabetes.7In this age group, low dose COC, containing only 20 ugms of Ethinyl Estradiol is preferred, as this is definitely higher than the conventional MHT and controls symptoms well. COCs are better avoided in obese Perimenopausal women.

Transdermal Route– The transdermal administration is preferred when there is intolerance to oral treatment, abnormal LFT, hypertriglyceridemia, Diabetes mellitus, and a risk of thromboembolic disease. This route bypasses the first-pass effect seen with the oral route and provides better bioavailability facilitating a long-term balance of estrogen in the body along with a morephysiological ratio of estradiol and estrone.6 Transdermal estrogen is also preferred for women with migraine headaches with auras.

Contraindications — Contraindications to MHT include a history of breast cancer, CHD, a previous venous thromboembolic event or stroke, active liver disease, unexplained vaginal bleeding, high-risk endometrial cancer, or transient ischemic attack.7

Oral estrogens should be avoided in women with active gallbladder disease, hypertriglyceridemia, or known thrombophilia such as factor V Leiden (without a personal history of venous thromboembolism).

Progesterone

Oral: Micronized Progesterone is the favoured one today, as it does not have the effects on CVS and on the breast which were seen in the WHI Trial with MPA. 200 mgs daily for 12 days or 100 mgs daily continuously is preferred. When oral Progesterone is not tolerated because of bloating etc, LNG-IUS is the answer.

IUS-LNG-IUS is licensed for contraception, heavy menstrual bleeding (HMB), and as the progestogen element of MHT. Amenorrhoea or decreased bleeding is achieved in 65% of LNG-IUS users in the first year of use. LNG-IUS has been shown to be more effective in reversing anaemia than COC and its increasing use in the treatment of heavy menstrual bleeding has led to a significant decrease in hysterectomies.8

LNG-IUS plus ERT provide the only form of continuous combined (potentially bleed-free) MHT licensed in perimenopausal women. There is some confusion about when to remove a LNG-IUS in the perimenopausal age group. If inserted before the age of 45 years, then, it should be removed after 5 years. If after the age of 45years, FSRH (Faculty OF Sexual and Reproductive Healthcare) recommends an extended use. Be that as it may, at every return visit, two things have to be asked for- a. the return of HMB and the need for contraception.5,8

Duration: For most symptoms, short term MHT- either for 5 years or once the age of 60 is reached is the goal. With this duration, most of the vasomotor symptoms are relieved. However some women may suffer from vasomotor symptoms for 7 to 11 years. Then, it is safer to start on a non-hormonal method before restarting estrogen.

When do we stop MHT? 40 50% of women with vasomotor symptoms stop it in 1year, but 65 -75% stop it after 2 years 42 It is important that it is not stopped suddenly, but should be tapered gradually over sometime, to avoid recurrence of symptoms- one pill per week is decreased. Similarly, with Progesterone.

Androgens: Initially thought that there is a relative decrease of Testosterone and with that, decreased libido, androgens were supplemented, but studies have not shown any increase in libido.

Tibolone: is a synthetic molecule which on degradation produces metabolites which have estrogenic, androgenic and progestational effects. It is a great mood and libido elevator, probably by lowering SHBG. Tibolone seems to be effective on estrogen-withdrawal symptoms such as hot flushes, sweating, insomnia, headache, and vaginal dryness, with results generally comparable to the effects exerted by estrogen-based treatments, and the additional property of a progestogenic activity on the endometrium.9

Non- Hormonal Therapy: May be good as short term therapy but their long term use on Estrogen deprivation has not been proved.

Anti-depressants: Paroxetine, Venlafaxine and Des-Venlafaxine may reduce hot flushes. 100 mgs of Venlafaxine produced a significant reduction ofhot flushes and night sweats after 4 – 12 weeks of therapy.10Mood lability/depression – MHT, alone or in combination with an antidepressant such as a selective serotonin reuptake inhibitor (SSRI), is effective for women who experience mood lability or depression during the menopausal transition. 10In one trial of ET for perimenopausal depression, 50 perimenopausal women with major depression, dysthymia, or minor depressive disorders received transdermal estradiol (0.1 mg) or placebo for 12 weeks. Remission of depression occurred in 68 percent of patients compared with only 20 percent receiving placebo11. The Kronos Early Estrogen Prevention Study (KEEPS), a trial of MHT in younger menopausal women ages 45 to 54 years who underwent extensive mood evaluations, reported that four years of oral estrogen appeared to improve mood as women receiving oral conjugated

estrogen combined with micronized progesterone had lower depression and anxiety scores than those receiving either transdermal estradiol with micronizedprogesterone or placebo12
Gabapentintoo can be tried for hot flashes if estrogens are contraindicated or not effective

SERMS:Bazedoxifene (BZA) is a new SERM that reduces bone mass loss in postmenopausal women and reduces the risk of vertebral and non-vertebral (in the high-risk group) fractures without stimulating breast tissue or endometrium.13 It can be used for treatment or prevention of osteoporosis in postmenopausal women. It does not stimulate the mammary gland or the endometrium. When used at a dose of 20 or 40 mg per day, it protects the endometrium during systematic estrogen treatment (tissue selective estrogen complexes [TSECs]).14

Phytoestrogens: are derived from plants, non-steroidal in nature, having estrogenic effects on Menopausal symptoms.15
They are usually divided into three groups:
Isoflavones (daidzein, genistein, biochanin A, formononetin,glycitein)
Lignans (secoisolariciresinol-diglucosid, matairesinol)

Coumestans
Consumption of Soya, which is a rich source of Isoflavones, reduces the risk of breast cancer, but this is dependent on the time when it was started. Perhaps South Asian women who consume a lot of Soya, have a lower incidence of menopausal symptoms and Breast cancer when compared to the European and North American women.16,17

Most phytoestrogens are found in red clover, alfalfa and their germinated seeds, cohosh, red grapevine, cereals, rice, strawberries, garlic and dates.18
CRE: is an extract made from the root of the Black Cohosh. It contains enzymes which have an anti-oxidizing and anti-inflammatory effect. The efficacy of CRE in the treatment of the vegetative climacteric syndrome has been proved by a meta-analysis of nine clinical randomized double-blind studies with the reduction of problems by 26% against placebo.19

It does not change the Estrogen profile in the blood and works through its action on reducing serotonin reuptake in the brain. That is the reason why, it can be safely given in breast cancer survivors with menopausal symptoms.

Pollen Extract: 160 mg (twice daily) of pollen extract was able to reduce significantly menopausal symptoms such as vasomotor symptoms, fatigue, irritability, depression, or vaginal dryness in a prospective study.20

GSM: Skin atrophy as a result of estrogen deficiency is the cause of GSM, with its attendant chronic vaginitis, Dyspareunia and pruritus vulvae. Estriolcan be started at 0.5mg daily for 2-3 weeks, by which time there is relief, followed by 0.5 mg one to two times a week. Estradiol vaginal tablets may be started as 0.01mg daily for 10 to 14days, followed by one tablet twice a week.21

Apart from Estrogens, Ospemifeme is also used in GSM. It has a positive effect on the parabasal cells, increasing them by 30-40%, increases the count of the superficial cells by 10-20%, thereby reducing the Ph of the vagina, vaginal dryness and dyspareunia. It has no effect on blood parameters except for a positive effect on lipid profile.

Special Consideration
Women with Breast cancer: may have earlier menopause because of Chemotherapy and severe vasomotor symptoms due to Tamoxifen. Still, ET is not recommended in such women. Other methods of tackling menopausal symptoms and preventing Osteoporosis should be tried. (HABITS trial)

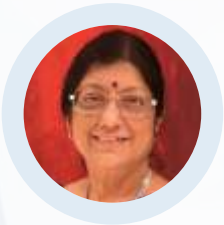
Women with Endometrial Cancer: Women with low risk and menopausal symptoms can be given MHT, also to prevent the long term effects of Estrogen deficiency. In high risk cases, definitely contraindicated. Hon- hormonal treatment preferred.

Conclusion: It is important that women in the age group of 45-55years need to have the following issues addressed- Vasomotor symptoms, fear of pregnancy and irregular, heavy bleeding. LNG-IUS with ERT addresses all these issues with satisfaction.

References

1. Soules MR, Parrott E, Santoro N & Woods N Stages of reproductive aging workshop (STRAW) Journal of Womens Health & gender Based medicine 2004 vol 10 no 9
2. Bae H, Lunetta k, Murabito J, Anderson S, Schupf N, Perls T &Sebastiani P et al Genetic associations with age of menopause in familial longevity. Menopause 26(10):1204-12
3. Jenny Brotherston, Contraception meets HRT: seeking optimal management of the perimenopause; Br J Gen Pract. 2015 Sep
4. Shah D, Nagarajan N. Premature menopause — meeting the needs. Post Reproductive Health. 2014;20(2):62–68.
5. FSRH Clinical Effectiveness Unit Contraception for women aged over 40 years. Clinical Guidance. 2010
6. Tomas Fait; Menopause hormone therapy: latest developments and clinical practice, Drugs Context. 2019; 8: 212551
7. Stuenkel et al;Treatment of the Symptoms of the Menopause- An Endocrine Society Clinical Practice Guideline, Journal of Clinical Endocrin Metabolism,2015
8. Sprague B L et al; Managing menopausal Symptoms and associated clinical issues in Breast Cancer survivors, Journal of Clinical Endocrin Metabolism, 2017
9. FSRH Clinical Effectiveness Unit Combined hormonal contraception. Clinical Guidance 2011 (update 2012)
10. Andrea Riccardo Genazanni et al, Beneficial effect of Tibolone on mood, cognition, well-being, and sexuality in menopausal women, Neuropsychiatr Dis Treat. 2006 Sep
11. Soares C N et al; Efficacy of Estrogen in depressive disorders in perimenopausal women- A Double Blind Random Placebo Controlled Trial;Arch General Psychiatry, 2001
12. Gleason C E et al; Effects of Hormone Therapy on cognition and mood in recently postmenopausal women, Findings from the RCT KEEPS –Cognition and Affective study, PLoS Medicine, 2015
13. Joffe H, Guthrie KA, La croix AZ, et al. Low-dose estrogen and the serotonin-norepinephrine reuptake inhibitor venlafaxine for vasomotor symptoms. JAMA Intern Med. 2014;
14. Archer DF, Pinkerton JV, Utian WH, et al. Bazedoxifene, a SERM: effects on the endometrium, ovarium and breast from a randomized controlled trial in osteoporotic postmenopausal women. Menopause. 2009
15. Pinkerton JV, Komm BS, Mirkin S. Tissue selective estrogen complex combination with Bazedoxifene/conjugated estrogens as a model. Climacteric. 2013
16. Lethaby A, Marjoribanks J, Kronenberg F, et al. Phytoestrogens for menopausal vasomotor symptoms. Cochrane Database Syst Rev. 2013;12:
17. Gold EB, Leung K, Crawford SL, et al. Phytoestrogen and fiber intakes in relation to incident vasomotor symptoms: results from the Study of Women's Health Across the Nation. Menopause. 2013;20(3):305–314
18. Fritz H, Seely D, Flower G, et al. Soy, red clover and Isoflavones and breast cancer: a systematic review. PLoS One. 2013
19. Beer AM, Osmers R, Schnitker J, et al. Efficacy of black cohosh (Cimicifugaracemosa) medicines for treatment of menopausal symptoms – comments on major statements of the Cochrane Collaboration report 2012 “black cohosh (Cimicifuga spp.) for menopausal symptoms (review)” Gynecol Endocrinol. 2013
20. Fait T, Sailer M, Regidor PA. Prospective observational study to evaluate the efficacy and safety of the pollen extract in the management of women with menopausal symptoms. Gynecol Endocrinol. 2018;34
21. The NAMS, 2017 Hormone Therapy Position Statement. Menopause. 2017
22. Nappi RE, Panay N, Bruyniks N, et al. “The clinical relevance of the effect of ospemifene on symptoms of vulvar and vaginal atrophy”. Climacteric. 2015

Contraceptives for reducing The STD burden



Sudha Prasad
MD, FICMCH. Infertility and ART specialist.
IVF AND INFERTILITY CLINIC, LNJPH,
Former head and IVF co-ordinator,
Dept. of OBG,MAMC, New Delhi.
Vice president FOGSI North zone 2019

Saswati Sanyal Choudhury
MD FICOG FICMCH FIAOG
Associate professor Gauhati medical college.
Chairperson M. E. C., FOGSI (2013-2015)

In many aspects reproductive health where the responsibility is shared between both partners, the burden for a mixed biological and social reasons falls in women especially with burden of sexually transmitted infections with resulting infertility. Females are more likely to be affected but less likely to seeks care, more difficult to diagnose but more vulnerable to social discrimination and disastrous consequences. The most effective method available for protection of STIsis condom controlled by male.

In 1950 barrier method of contraception was most popular and main method of contraception. After 60s with invention of oral pills its use was less. But after the HIV & AIDS came into picture barriers again became important for prevention of sexually transmitted infection

Barrier method is a method where there is a barrier in between ovum and sperm. The most common barrier method is male condom. Other barriers include cervical cap, vaginal diaphragm and female condom. Condoms not only keeps sperm out of vagina preventing pregnancy it also keeps infection from semen and external male genitalia to come in contact with vagina and also vaginal infections to spread to other partners

There are 4 types of barrier contraception

1. Condom – male and female
2. Occlusive caps- vaginal diaphragm, cervical caps, vault cap, vimule cap
3. Vaginal sponge- nonooxynol-9
4. Spermicide- nonooxynol-9 , chemical suppositories, foam tablets; aerosol creams

Male condoms is the only known contraceptive proven to prevent STI including HIV and AIDS. If used consistently and correctly condom useprevents 80% to 95% of transmission of HIV infection. Other infections which is preventable by using condoms are those STIs which spread by discharge like gonorrhea, syphilis, trichomoniasis and chlamydia. It also protects against STIs which spread by skin to skin contacts such as herpes and human papilloma virus. It protects against transmission of HIV via heterosexual intercourse and acquiring other STIs like gonorrhea, chalamydia Herpes syphilis. The presence of STI increases the chance HIV transmission. If condom is used in HIV positive patients it will protect against acquiring other strains forHIV

Female condoms are sheaths that fit inside vagina made of thin transparent polyurethane. It has 2 rings at two ends, one end is open and the ring there helps to keep the condom in holds it in position and ring in the closed upper end is fitted under symphysis. It is lubricated with silicone based lubricant on both sides. It is 17 cm long, with an open outer end of 70 mm diameter with a ring attached to prevent it advancing beyond the vulva and 60 cm diameter inner ring at the inner closed end aiding retention in vagina. It is inserted after squeezing inner ring like diaphragm and whole device forms a well lubricated secondary vagina. It keeps the sperm away from coming in contact with vagina thereby preventing pregnancy. It also keeps infection in semen or male genital infections like syphilis,herpes, chlamydia, lymphogranulomavenerum etc. away from coming in contact with vagina and thereby preventing its spread. Same way it prevents vaginal infections like chlamydia,

trichomoniasis etc. to spread to male partners. It also prevents hepatitis B virus, HPV cytomegalovirus and HIV infections. Failure rate of female condom with typical use is 21/hundred women year and perfect use 5 per 100 women year. Moreover it keeps privacy and is under women's control.(1). Advantages of female condom are self-use, under women's control, one universal size, no prerequisites like male condom (erection before use), no effect in male satisfaction, can be used during menstruation and post- partum periods or presence of any local soreness and less likely to rupture during use than male condoms.

Spermicides that contains nono oxynol-9 do not provide protection against STI. Frequent use of it may increase risk of HIV infection as using it several times may cause vaginal irritation and small ulceration in vagina and external genitalia through which HIV virus infection chances becomes more

Diaphragms

Soft latex plastic cup that covers cervix with a flexible ring which keeps the device in place. It is usually applied along with spermicidal jelly in the cap. It probably helps to protect against certain STIs like chlamydia, gonorrhea and trichomoniasis, but not candidiasis

Cervical cap

A soft deep latex, rubber or plastic cap which fits in the cervix and covers it. It is also used with spermicidal jelly or foam. It is kept for 6 hours after ejaculation but not more than 48 hours.

OCP

There is a small risk of vaginitis and vulvovaginitis especially due to candida species. It may possibly increase the chance of other STI like chlamydia and trichomoniasis

Intra uterine device

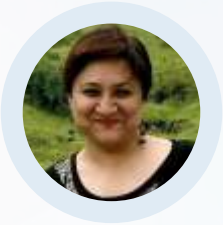
There is increased risk of all sexually transmitted infection with intrauterine device It should not be used in AIDS patients who are not on treatment.(WHO Category 3 relative contraindication). Pelvic inflammatory disease may occur if IUCD is introduced who is having chlamydial or gonorrhea at the time of insertion. Although there is 6 fold increase of PID in the 20 days after the insertion but without exposure to STI overall risk is low.

Pre-requisite of IUCD insertion are exclusion of high risk cases for STIs like age<25 years, change in sexual partners, more than one partner in last year should undergo tests for Chlamydia trachomatis ideally if the report is not available then a course of antibiotics to cover chlamydia is a good clinical practice. Current PID, symptomatic and asymptomatic Chlamydial infection or purulent cervicitis or gonorrhea falls under category 4 as there is unacceptable health risk and should not be used
Abstinence especially at the time of active disease is of utmost importance for the spread of the disease and reinfection.
HIV and contraception
Safer sex is encouraged with use of condoms along with hormonal method to avoid pregnancy and if the patient is not on HAART then all methods of contraception can be used. If patient is on ritonavir –boosted protease inhibitors then adverse action can happen with combined hormonal contraception and progesterone only pills. DMPA implants and LNG IUS and IUCD can be used by HIV positive patients on HAART without increased failure rate. If emergency contraception is needed by them then emergency IUCD is preferable, if at all progesterone only EC is used dose should be doubled or 3mg stat dose

References

1. Contraception and family Planning in Basics of Gynaecology for examinees editors Mukherji J, Ganguly GP, Seal SL Academic publishers 1st edition 446-449
2. Melanie Mann. ' Infection and Sexual death' in a book on Obstetrics and gynaecology in evidence- based text for MRCOG edited by Luesley DM, Baker PN 2ND edition Hodder and Arnold 735-52

Preventive Role of Hormonal Contraception in Benign diseases



Dr. Ritu Joshi
MBBS, MS - Obstetrics &Gynaecology
Consultant gynaecologist ,Fortis Escorts Jaipur.
Vice president West Zone FOGSI 2014
Chairperson FWC FOGSI 2010 -2012

Dr Anupama Bahadur
DNB, MNAMS, FICOG, FIMSA
Additional Professor, Dept of Obstetrics
& Gynecology, AIIMS, Rishikesh (Uttarakhand).

Introduction:

Since 1960, with the advent of oral hormonal contraceptives (OCs) as combined estrogen/ progestogen formulation, these drugs have undergone a steady transformation in utilized progestogens. The progestogen component has different patterns of supplementary effects in addition to its basic effects. Due to these partial actions of progestogen, they have been proved to be useful in incorporating various non-contraceptive benefits of these hormonal contraceptives into the list of indications creating a wide range of beneficial effects besides the primary aims. Also, some changes have been implemented in estrogen component. Initially when OCs were introduced, its prime components were mestranol and ethinyl estradiol. Gradually, intake of mestranol was abandoned because of its conversion to ethinylestradiol in the body. After about 50 years, nowadays, hormonal contraceptives are being developed by either estradiol valerate or micronized estradiol as estrogen component. These have been associated with lowering effect on thromboembolic risk.

Hormonal contraception, besides their primary indication of use,are increasingly being used for non-contraceptive benefits as well. Mechanisms of hormonal contraceptives holds the key to understand non-hormonal benefits. In addition to suppression of ovulation, oral contraceptives inhibit endometrial expression of enzymes such as cyclo-oxygenase, aromatase, estrogen and progesterone. An active metabolite of progesterone, allopregnanolone, stimulates GABA receptors which help in controlling mood changes. The effect is at par with that of serotonin re-uptake inhibitors. OCPs show favorable cost/benefit ratio in addition to high therapeutic value in different medical indications. These have also been shown to have high level of toleration for these drugs compared to other indicated medications.

This article discusses in detail the non-contraceptive uses of hormonal contraceptive pills. Non-contraceptive health benefits are recently being recognized as an important aspect of overall impact of oral hormonal contraceptives [1].

Indications of use:

Table 1 shows the most common non-contraceptive indications for use of hormonal contraceptives.

Table 1. Non contraceptive clinical entities for use of hormonal contraception
1. Menstrual bleeding disorders
2. Dysmenorrhoea
3. Signs of androgen excess
4. Premenstrual syndrome (PMS)
5. Ovarian cyst
6. Endometriosis/adenomysosis
7. Fibroid
8. Pelvic inflammatory disease
9. Others

Menstrual bleeding disorders:

Common menstrual disorders like polymenorrhoea, menorrhagia, etc., which lead to anemia, hence affecting quality of life of patients, have been found to be alleviated by hormonal contraceptives. Oral hormonal contraceptives help in improving anemia and reduce pain, though it is not FDA approved for the same. [2] However, it is the most common off-label indication for use of hormonal contraception in treatment of menstrual disorders. Hormonal contraceptives inhibitcyclo-oxygenase 2 enzyme in the endometrium. 50% reduction has been seen in menstrual blood loss with use of combined hormonal contraceptive pills. [1]

Dysmenorrhea:

Dysmenorrheais one of the most important symptom affecting the quality of life of patient to a considerable level. Dysmenorrhea is related to release of prostaglandins, increasing myometrial contractility. Combined hormonal contraceptive pills improve primary dysmenorrhea in 70-80% women by reducing prostaglandin production. [1]

Symptoms of androgen excess:

Combined hormonal contraceptive use may suppress ovarian production of androgen and increase sex hormone binding globulin, ultimately decreasing the biologically active form of androgens. [3] This effect of combined hormonal contraception is beneficial in reducing signs of androgen excess like seborrhea,

acne, hirsutism, alopecia. Certain progesterone preparation including drospirenone, cyproterone acetate have anti-androgenic properties. Of these cyproterone acetate has been found to have the highest anti-androgenic activity. [4] Apart from improving the hyperandrogenic symptoms, it also effectively reduces size of ovaries and number of follicles, improving the clinical presentation of PCOS (polycystic ovarian syndrome)[5].

Hypoestrogenic States:
OCs have been used as a method of hormone replacement therapy in women with hypothalamic amenorrhea. These patients include women with Turner's Syndrome, adolescents having eating disorders, exercise-induced amenorrhea and even women with premature ovarian failure. Since most studies done have not included these patients, therefore, it is not certain if women with these forms of hypoestrogenic amenorrhea benefits from OCs in terms of preservation of bone density. However, OCs are being widely used for this purpose.[6] Clinical manifestations of menopause and ovarian failure include menstrual irregularities, vaginal dryness, vasomotor instability and loss of bone mass. In perimenopausal period,OC has been used for its various distinct advantages: prevention of pregnancy, regulation of uterine bleeding in a predictable way, alleviation of symptoms of vasomotor instability and vaginal dryness and improves bone mineral density considerably. Estrogen replacement in the form of OCs have also been beneficial in young patients with post- radiation or post-chemotherapy amenorrhea or bilateral oophorectomy.

Premenstrual syndrome (PMS) or Premenstrual Dysphoric Disorder (PMDD):
PMS have been shown to affect women of any reproductive age-group. Women suffering from PMS often relate that symptoms worsen progressively with time.Women in their later reproductive years, have increased contact with health care providers for nonpregnancy-related concerns. This may account for predominance of older women seeking help for PMS. Symptoms of premenstrual syndrome decrease after menopause, during pregnancy and lactation. FDA has approved the use of combined hormonal contraceptives especially drug containing anti-mineralocorticoid activity in treatment of premenstrual syndrome. [7]

It has been suggested that the possible etiology of PMS is water retention. Many women are particularly troubled by bloating and edema. A newer preparation of OC containing a novel progestogen (fourth generation progesterone)having additional diuretic effects (drospirenone) has been found to be effective in women PMDD in studies comparing them with normal women.OCs are likely to relieve physical symptoms associated with PMS but its effectiveness in alleviating the emotional symptoms remain controversial.

Ovarian cyst:

Suppression of hypothalamic-pituitary-ovarian axis by combined hormonal contraceptives, confers protection against both follicular and corpus luteum cysts. The degree of functional ovarian cyst suppression depends on the formulations used. The effect is more powerful with usage of hormonal contraceptive with higher dosage (Ethinyl estradiol dose of 50 mcg). However, the use of combined hormonal contraceptives may have no benefit over treatment of functional ovarian cyst and may just have a preventive role.

Endometriosis / Adenomyosis:

The Royal College of Obstetrics and Gynecologists recommends combined hormonal contraception as a drug of choice for treating symptomatic endometriosis. It helps in reducing pain and size of the lesion. It is also beneficial post-surgery to avoid recurrence of endometriomas. In adenomyosis, it is helpful in reducing dysmenorrhea, heavy bleeding and improves patient's quality of life. Continuous use of hormonal contraception for 30 days has shown to significantly increase endometrial apoptosis (both epithelial and stromal components) compared to those not on treatment. Certain steroid hormones regulate this apoptosis of endometrium which is controlled by expression of various regulatory genes. Proto-oncogene B cell lymphoma/leukemia-2 (Bcl-2) inhibits apoptosis by blocking the receptors, whereas Bax protein antagonizes its survival activity. Endometrial apoptosis is seen to be significantly increased upon 30 days exposure to monophasic OC, determining values similar to those observed in endometrium from control women without endometriosis. Administration of OC in fact, reverses abnormally increased expressionof Bcl-2 in patients with endometriosis and also induces a marked increase in expression of Bax protein. Furthermore, OC exposure significantly reduces endometrial cell proliferation in patients with endometriosis. There has been found to be another functional mechanism linking intake ofOCs and endometriosis.Aromatase expression is found to be increased in women with endometriosis[8]. OCs reduce local aromatase expression in women with endometriosis, providing a rationale for beneficial effect of OCs in affected women [9]. A recent Cochrane Collaboration published in 2000 [10]concluded that, there is no evidence of a difference in outcomes between OCs and GnRH agonists in endometriosis owing to limited data. Further studies are requiredto establish role of OCs in managing symptoms associated with endometriosis.

Myoma:

The Oxford Family Planning Association found a decreased risk of uterine fibroids in OC users [11]. Combined hormonal contraceptive use showed a 70% reduction in myoma size. The risk reduction is associated with duration of oral contraceptive use. There has been a 50 to 60% reduction in size of myoma after combined hormonal contraceptive use, reducing need for further medical or surgical management [12]. Increasing duration of hormonal contraceptive usage was associated with increased protection; there was a 30% risk reduction after10

years of use. These findings were confirmed by a large, case-control study demonstrating a 50% reduction in risk in women with more than 7 years of OC use compared with nonusers. However, not all studies have demonstrated a protective effect. A large study from the US, reported weak association between and use of combined OCs before the age of 17 years and fibroids, in which fibroids were diagnosed either at hysterectomy or by ultrasound. However, it suggested no clear pattern of association.[13].

Pelvic inflammatory disease (PID):

The possible mechanism by which combined hormonal contraceptive pills protect against PID is still speculated. Plausible explanation is that it makes the cervical mucus thicker preventing the ascending organism. Another probable mechanism is decreased menstrual blood flow preventing nidation of organism. This results in reduction of in-hospital stay, medication and surgical procedures. Hence, risk of ectopic pregnancy and infertility problems are also reduced. Besides the risk reduction between 50-70%, PID which occurs during pill intake was shown to have less severe inflammation as observed duringlaparoscopy [14].

Endometrial hyperplasia:

Endometrial hyperplasia can be either be prevented (as in patients with PCOS) or treated by combined hormonal contraceptives, showing a tissue level progestogen dominant effect.

Benign Breast disease:

Statistically significant decrease in risk of benign breast disease has been noted with longer duration of hormonal contraceptive intake. Reduced incidencefor fibrocystic breast disease (30%), fibroadenoma (60%), breast lumps (40%) have been noted with long term use of combined hormonal contraceptive use. Fibrocystic changes are significantly reduced after 1-2 years of pill usage and effectively lasts for up to1-yearpost discontinuation.

Ectopic Pregnancy:

OCs protect against ectopic pregnancies primarily by preventing pregnancy. Case-control studies show a 90% protection from ectopic pregnancies with current use. The risk of ectopic pregnancy among users of OCs is approximately 0.005 ectopic pregnancies per 1000 woman-years of use,similar to that found with vasectomy. In comparison, rates greater than or equal to 0.2 ectopic pregnancies per 1000 woman-years are associated with copper T380A, tubal sterilization and Norplant [15]. However, it should be noted that all methods of contraception reduce the risk of ectopic pregnancy compared with those using no contraception at all.

Iron-Deficiency Anemia:

Combination OCs helps in indirectly alleviating likelihood of iron-deficiency anaemia by decreasing menstrual blood loss and regulation of menstrual bleeding. This is beneficial for both current and past users of OCs [16].

Rheumatoid Arthritis:
Risk of rheumatoid arthritis is found to be reduced by about 30% on suage of oral contraceptives. Women who used oral hormonal contraceptives for more than five years the relative risk of developing mild disease was significantly more. However, long-term outcome of the disease is not significantly influenced by hormonal contraceptives [17].

Multiple Sclerosis:
Recent studiessuggest that age of occurrence of first symptoms of MS was significantly higher among women using oral hormonal contraceptives compared to nonusers (onset at 31 years versus 33 years). Increased duration of OC intake is proportional to the increase in age for onset of MS, from 24 years with less than 1 year of OC intake to 31 years with more than 10 years OC intake. Women who gave birth before the onset of MS had lessersignificantly age at primary symptomscompared to those who did not (31 years versus 33 years) [18].

Menstrual Migraine:
Basic principle in women with menstrual migraine without aura is either minimal changes in concentration of hormones or elimination of hormonal changes all together. If the standard 7- day free interval of oral hormonal contraceptive pills eliminating and a `long-cycle` or constant regimen is taken the alleviating effect of OCPs on menstrual migraine can be accomplished [19].

Bone Mineral Density:
In a hypoestrogenic state, preservation of bone mineral density occurs with oral hormonal contraceptives usage, particularly in younger aged women, or in older premenopausal women with reduced ovarian function. With long-term use of oral hormonal contraceptives (5 years) protection increases in proportion to the increased duration of the use [20].Since the early 1990s, studies of both premenopausal and postmenopausal women seem to favour bone sparing effects of OCs. A cross-sectional, retrospective study investigated risk factors associated with low bone mineral density in about 2000 women, the majority (76%) of which were postmenopausal [21]. A past history of OC use provided protection against low bone mineral. Postmenopausal women who had previously used OCs for at least 10 years had the greatest protection against low bone mineral density compared with never users in the distal radius, ulna, and lumbar spine. No protection against fracture at these sites was noted in premenopausal OC users. A protective effect against hip fractures, however, was found in a population-based, case-control study of postmenopausal women who had formerly taken OCs during their premenopausal years [22]. Prior use of any OC produced a significantly lower risk of hip fracture in postmenopausal women compared with nonusers, especially with high dose formulations.

Voice:

Vocal cords are hormone-dependent structures and therefore pathological changes of circulating hormone parameters influence them, such as androgens in the climacterium. In androgen excess environment, oral hormonal contraceptives with a combination of ethinylestradiol and a progestogen having anti-androgenic properties can lead to voice improvement or resumption. Similar positive clinical effects can be experienced in climacteric women when lack of estradiol and dominance of androgen effects may become relevant. Also, in this situation a combination of estradiol/estradiol valerate and an anti-androgenic progestogen may improve or restore the voice in professional and non-professional singers [23].

Asthma:

Recent studies have indicated that oral hormonal contraceptives help to reduce asthmatic symptoms [24].

Toxic Shock Syndrome:

The effect of OC use on toxic shock syndrome (TSS) is unclear. Certain studies demonstrate a 50% reduction in risk with OC usage [25] while some studies fail to demonstrate this effect. Reduction in risk of TSS may be partially related to an overall decrease in menstrual blood flow in OC users or may be confounded by changes in absorbency and composition of sanitary napkins/ tampons used by women.

Conclusion:

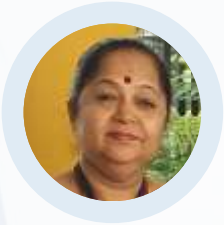
Over the last several decades, OCs have remained a safe and effective method of birth control. Various studies have observed and confirmed the substantial non-contraceptive health benefits and therapeutic roles of the OC pill. Most patients, however, are unaware of these benefits and tend to overestimate health risks associated with OCs.

To conclude, it needs to be recognised that hormonal contraceptives (estrogen/progestogen combination) are not only highly effective form of contraception but are useful medications for varied medical disorders in women. Thus, they are important for female health and should be judiciously used in clinical practice. Counselling and education about the many health and therapeutic benefits of OCs are necessary to help women make well-informed health-care decisions and improve compliance.

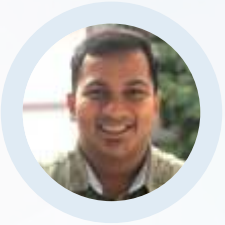
References:

1. Johannes C huber, Eva-katrinbentz, JahannesOtt, Clemens B Tempfer. Non-contraceptive benefits of oral contraceptive. Expert Opin. Pharmacother. (2008) 9(13) .
2. Asbell B. The pill: a biography of the drug that changed the world. Random House New York; 1995.
3. Schindler AE. Non-Contraceptive Benefits of Oral Hormonal Contraceptives. Int J EndocrinolMetab. 2013;11(1):41-7.
4. Schindler AE. Antiandrogenicprogestins for treatment of signs of androgenisation and hormonal contraception. Eur J ObstetGynecolReprod Biol. 2004; 112:136-41.
5. Falsetti L, Gambera A, Tisi G. E cacy of the combination ethinyloestradiol and cyproterone acetate on endocrine, clinical and ultrasonographic pro le in polycystic ovarian syndrome. Hum Reprod. 2001;16(1):36-42.
6. Warren MP, Stiehl AL. Exercise and female adolescents: effects on the reproductive and skeletal systems. J Am Med WomensAssoc 1999;54:115–120,138
7. Huber JC, Bentz EK, Ott J, Tempfer CB. Non-contraceptive benefits of oral contraceptives. Expert spin Pharmacother. 2008;9(13):2317-25.
8. Attar E, Bulun SE. Aromatase and other steroidogenic genes in endometriosis: translational aspects. Hum Reprod Update 2006 ; 12 (1): 49 -56
9. Maia H Jr, Casoy J, Correia T, et al. The effect of oral contraceptives on aromatase expression in the eutopic endometrium of patients with endometriosis. GynecolEndocrinol2008 ; 24 (3): 123 -8
10. Davis L, Kennedy SS, Moore J, Prentice A. Modern combined oral contraceptives for pain associated with endometriosis. Cochrane Database Syst Rev 2007 ;(3):CD001019
11. Hannaford PC, Selvaraj S, Elliott AM, et al. Cancer risk among users of oral contraceptives: cohort data from the Royal College of General Practitioner's oral contraception study. BMJ 2007 ; 335 (7621): 651
12. Burkman RT. Oral contraceptives: current status. Clin Obstet Gynecol. 2001;44(1):62-72.
13. Wise LA, Palmer JR, Harlow BL, et al. Reproductive factors, hormonal contraception, and risk of uterine leiomyomata in African-American women: a prospective study. Am J Epidemiol 2004 ; 159 (2): 113 -23
14. Huber JC, Bentz EK, Ott J, Tempfer CB. Non-contraceptive benefits of oral contraceptives. Expert Opin Pharmacother. 2008;9(13):2317–25. doi: 10.1517/14656566.9.13.2317. [PubMed] [CrossRef] [Google Scholar]
15. Sivin I. Dose- and age-dependent ectopic pregnancy risks with intrauterine contraception. Obstet Gynecol 1991;78: 291–298
16. Dayal M, et al. Noncontraceptive Benefits and Therapeutic Uses of the Oral Contraceptive Pill. Seminars In Reproductive Medicine/Volume 19, Number 4 2001
17. Drossaers-Bakker KW, Zwinderman AH, van Zeben D, Breedveld FC, Hazes JM. Pregnancy and oral contraceptive use do not significantly influence outcome in long term rheumatoid arthritis. Ann Rheum Dis. 2002;61(5):405-8.

18. Holmqvist ST, Hammar M, Lindblom AM, Brynhirdsen J. Age at onset of Multiple sclerosis is correlated to use of combined oral hormonal contraceptives and child birth before diagnosis. Fert Steril. 2010;94:2835-7.
19. Kuhl H, Birkhauser M, Mueck A, Neulen J, Thaler C, Kiesel L, et al. [Long-cycle treatment in oral contraception]. Ther Umsch. 2009;66(2):101-8.
20. Williams JK. Noncontraceptive benefits of oral contraceptive use: an evidence-based approach. Int J Fertil Womens Med. 2000;45(3):241-7.
21. Kleerekoper M, Brienza RS, Schultz LR, et al. Oral contraceptive use may protect against low bone mass. Arch Intern Med 1991;151:1971–1976
22. Michaëlsson K,Baron JA,Farahmand BY,et al.Oral contraceptive use and risk of hip fracture: a case-control study. Lancet 1999;353:1481–1484
23. La FM, Ledger WL, Davidson JW, Howard DM, Jones GL. The effects of a third generation combined oral contraceptive pill on the classical singing voice. J Voice. 2007;21(6):754-61.
24. Mandhane PJ, Hanna SE, Inman MD, Duncan JM, Greene JM, Wang HY, et al. Changes in exhaled nitric oxide related to estrogen and progesterone during the menstrual cycle. Chest. 2009;136(5):1301-7.
25. Gray RH.Toxic shock syndrome and oral contraception [letter].Am J Obstet Gynecol 1987;156:1038



Preventive Role of Hormonal Contraception in Malignant Disease



Dr. Vidya Thobbi
MD, FICOG
Prof and HOD , Dept. of OBG, Al Ameen Medical college , Vijaypura
Chairperson F. D. M. E. Committee, FOGSI (2018-20).,
Treasurer, KSOGA.

Dr. Rohan Palshetkar
MS - Obstetrics & Gynaecology,
Obstetrician, Infertility Specialist and
Gynecologist in Vashi, Navi Mumbai
Joint secretary FOGSI 2019

Every woman has the right to plan her pregnancy and contraceptives are one way of doing so. There is a wide variety of contraceptives that are available to women these days to avoid pregnancy. However, they do have their own health risks, but the also have substantial non-contraceptive health benefits. For example, IUDs are highly effective contraceptives, but they pose a threat for an increased risk of pelvic inflammatory disorder in high risk groups. Barrier methods are less effective contraceptives, but they have the added benefit of protection against sexually transmitted infections (STI). Oral contraceptives have the added advantage of being highly effective contraceptives but they increase the risk of cardiovascular disease. However they also have non-contraceptive benefits such as protection against ovarian and endometrial carcinoma very minimal effect on breast cancer. In this chapter, we wish to see what the evidence points towards the protective effect of hormonal contraceptives in Malignant Disease.

Several recent epidemiological studies have confirmed that combined oral contraceptives (COCs) provide substantial protection against endometrial and ovarian cancer, and this protection is long-lasting and may persist for 15 or more years after termination of OC use . In many studies COCs have been associated with an increased riskof cervical abnormalities and cervical cancer, but there might be alternative explanations for these epidemiological associations (COC users can start having sexual intercourse at an earlier age, they have more sexual partners, and they rarely use barrier methods of contraception), so OCs act as a promoter for HPV-induced carcinogenesis.

In this chapter, we wish to see what the evidence points towards the protective effect of hormonal contraceptives in Malignant Disease.

Ovarian Cancer

The 5 year survival rate for invasive epithelial ovarian cancer (most common) is less than 50%. This is most likely due to the reason that

women with epithelial ovarian carcinoma are diagnosed at an advanced stage. However, there is an effective strategy to reduce the risk of ovarian carcinoma in women. Meta-analysis of epidemiological studies have shown that there is almost a 40% reduction in the risk of development of ovarian cancer with 5 years of oral contraceptive pills. The protective effect increases significantly with the duration of OC use and continues for at least 25 years even after the pill is stopped. The mechanism underlying this protective effect is not well understood. Both according to the 'incessant' and 'gondatrophin' hypotheses OC use is anticipated to decrease the risk of epithelial ovarian cancer. The mechanism underlying this protective effect is not well understood. One of the theories is that OC pills protect against ovarian cancer by preventing ovulation.

One of the theories is that OC pills protect against ovarian cancer by preventing ovulation. However, there is now evidence that suggests the protective effect of OC pills is due to the favourableprogestogenic environment. OC pill use would protect if the hormonal exposure while on OCs was less stimulatory to the possibly different types of cells of origin of ovarian cancer than the hormonal exposure in normal ovulatory cycles. OC derive a 30% protection against epithelial ovarian cancer. High dose OC pills are more are being slightly more protective than low dose OC pills.The exposure to progesterone is higher when the woman is on OC pills rather than a regular cycle thus explaining the protective effect. It is proposed that a major source of protection from OC pills is due to their significantly reducing cell proliferation in the Fallopian tube fimbriae rise and in the ovarian cortical inclusion cysts. These two are considered the most likely cells for the origin of ovarian carcinoma.

Proliferating cell populations are more susceptible to carcinogenic effects with the rise in cancer risk with cell proliferation being secondary to increased chances of mutation and progression. Fallopian tube Fimbriae proliferation has been reported to be almost confined to the follicular phase of the menstrual cycle with virtually no proliferation within a few days after ovulation. Therefore, OC pills could protect against ovarian cancers arising in the fimbriae by mimicking the luteal phase of the cycle when progesterone exposure is high. Whether such changes occur in cortical inclusion cysts is not known. Cell proliferation within different types of cortical inclusion cysts during the menstrual cycle has not been

studied. Ovarian cancer risk is determined by the increased proliferative activity of the ovarian surface epithelium required to accomplish repair of the ovarian surface epithelium after each ovulation . A potent mitogen to ovarian cystadenomacells is an intra-ovarian estradiol concentration . OC use blocks ovulation and markedly decreases intra-ovarian estrogen levels.

There are numerous studies which have shown that oral contraceptive pills reduce the risk of ovarian cancer. Iverson et al (1) published a study in 2017 seeing the lifetime cancer risk with oral contraceptive pills. 46,022 women were recruited in the study in 1968 and 1969 and were observed for 44 years. It was seen that OC pills had a protective effect not only on ovarian cancer but also endometrial and colorectal cancer. The longer duration women used oral contraception , there is greater decrease in risk of ovarian cancer. In 2008 study done by Collaborative group on Epidemiological Studies of Ovarian cancer in 23257 women with ovarian cancer and 87303 controls shown that even after cessation of oral contraceptives , this reduction in risk for ovarian cancer persisted for more than 30 years but it increases with time – if women had used oral contraception for 5 years , risk reductions if that had ceased less than 10 years is 29% , if that had ceased 10 -19 years previously is 19% , if that had ceased 20 -29 years previously is 15%(2). Before 75 years of age , risk reduction is greater if oral contraceptives used for more than 10 years , it significantly decrease cancer incidence from 1.2 to 0.8 per 100 users . It prevents about 2 ovarian cancers and one death from the disease before 75 years of age for every 5000 woman -year of use.

Pike & Spicer 1993 , conducted Meta-analysis of population-based epidemiological studies shows a reduction in ovarian cancer risk of approximately 7.5% per year of OC use(3)

In hereditary ovarian cancer ,main strategies to reduce ovarian cancer in woman carrying BRCA1 OR BRCA2 mutation is prophylactic oophorectomy and ultrasound screening , but it has been observed that risk off ovarian cancer is reduced in greater extent with use of oral contraceptives for more than 6 years . A study done by Narod and group on hereditary ovarian cancer and oral contraception with 207 women with hereditary ovarian cancerand 161 of their sisters as contols in case-control study in which 179 women was with BRCA1 and 28 women with BRCA2 mutation. The study shown that there is decrease in risk of hereditary ovarian cancer by 60% when used for more than six or more years (4).

There is limited Information is avialable on progestin-only contraceptive methods in ovarian cancer epidemiology . In a case–control study , with 441 epithelial ovarian cancer patients and 2065 hospital control subjects, only one case and 22 control women had used the progestin-only pill for more than 3 years risk estimation was not given but study shown progesterone only pills also have protective effect on ovarian cancer(5). The large cohort study from the Royal College which included only small patientsamples , only 3% were POP users(6). A hospital-based case–control study done by The WHO Collaborative Study of Neoplasia and Steroid Contraception , comparing 220 cases from 7 countries with 1537 age-matched controls, found no cases and only 2 controls who had exclusively used oral POPs(6).

Endometrial Carcinoma

The incidence of endometrial cancer continues to rise unabated. Over the past 20 years, the incidence has risen by more than 50%. In the UK alone, more than 9000 new cases are diagnosed each year and it is responsible for the deaths of more than 2000 women. The incidence in women under 50 increased by 2% every year between 1992 and 2012 [7]. An ageing population, changing patterns of hysterectomy use and tamoxifen therapy may all contribute to these trends, but the overwhelming culprit is undoubtedly the obesity epidemic. Across Europe, it has been estimated that 60% of endometrial cancer cases may be due to excess weight.

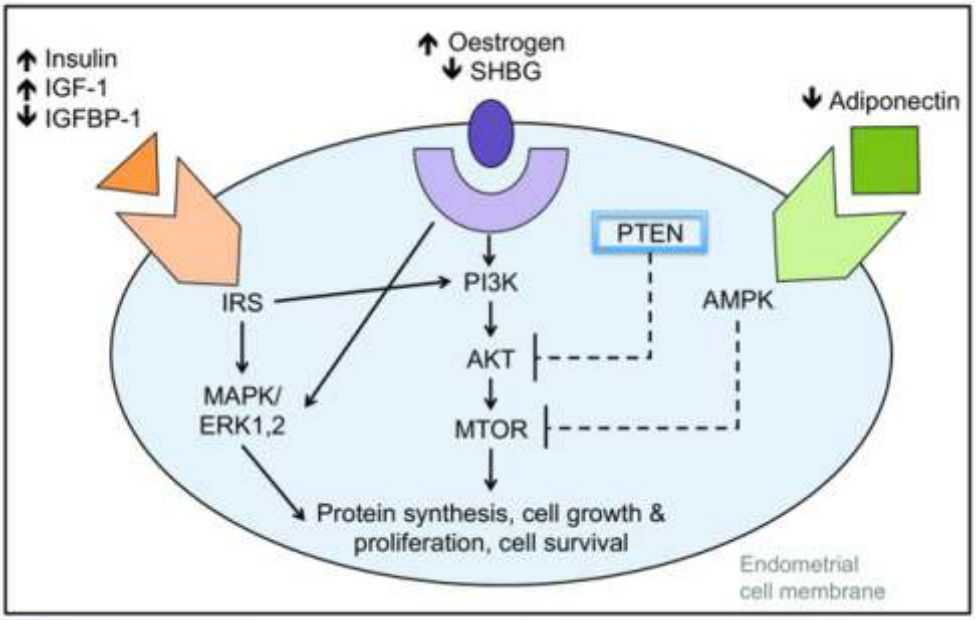
There are two different clinicopathological subtypes of endometrial cancer are recognized:

1 . Estrogen-related type 1 (endometroid) , comprising 70–80% of newly diagnosed cancer

2 . Non estrogen-related type 2 (nonendometroid such as papillary serous and clear cell).

Most endometrial cancers are what Bokhman termed type 1 endometrial cancers, where low-grade cancer develops in a hyperplastic endometrium, often on a background of obesity or diabetes [8]. The biological mechanisms driving type 1 endometrial carcinogenesis are incompletely understood, but adipose-derived oestrogen, unopposed by progesterone in obese postmenopausal women, is the best-supported hypothesis [9]. Obesity per se is not the whole story, however; insulin resistance, systemic inflammation and genetic predisposition all contribute to susceptibility, providing opportunities for targeted prevention strategies. Other risk

factors such as tamoxifen, nulliparity, unopposed oestrogen therapy and polycystic ovary syndrome (PCOS) are well described. Many of the recognised risk factors interact with key, pro-proliferative, signal transduction pathways (Fig. 1).



Open in a separate windowFig. 1
An overview of signal transduction pathways dysregulated in endometrial carcinogenesis

Worldwide, the prevalence of obesity (body mass index, BMI > 30 kg/m2) has doubled in the last three decades; each year, 2.8 million people around the world die as a result of being overweight or obese. Obesity accounts for 44% of the disease burden of diabetes and 23% of that of ischaemic heart disease [10].
Despite improving survival rates, deaths from endometrial cancer have increased by almost 20% in the last decade. Whilst across all stages 5-year survival reaches 79%, higher BMI is associated with increased all-cause mortality (per 10% increase in BMI OR 1.09; 95% CI 1.03–1.16), and disproportionate treatment-related morbidity [11].

Long-term follow-up data provides convincing evidence that use of combined oral contraceptives (COC) is associated with a significant and enduring reduction in the lifetime risk of endometrial cancer. Iversen et al. demonstrate that the protective effects of COC persist for at least 30 years, in this updated follow-up study of users who were recruited between 1968 and 1969 [12]. The faculty of Sexual and Reproductive Health advises that at a BMI > 35 kg/m2, the risks of COC are likely to outweigh the benefits (UKMEC 3 recommendation), which precludes its use as chemoprevention in the most obese women [13].
Unopposed action of estrogen causes endometrial hyperplasia. UNOPPOSED estrogen cause increase in the mitogenic action of estrogen in the absence of progestin in stimulating endometrial-cell division . Unopposed-serum estrogen is increased and sex-hormone-binding globulin is decreased in obese post-menopausal women , so that bioavailable estrogen concentration is increased in them . Estrogen replacement therapy increases serum unopposed estrogen. Obesity increases risk in premenopausal women by anovulation and their serum estradiol level is sufficiently high to cause maximal endometrial-cell proliferation. During pregnancy progesterone effectively opposes estrogen, so increasing parity is associated with decreasing risk. In early menopause serum unopposed-estrogen concentration reduces to a very low level , which reduces endometrial cancer risk.

Oral, injectable and intrauterine progestin use has been shown to reduce the risk of endometrial cancer.The progestin medroxyprogesterone acetate (MPA) at 5 mg/day reduces such cell proliferation to effectively zero within 6 days despite of continued estrogen use. But short duration progestin use does not completely reduces the risk of endometrial hyperplasia.

A case-control study of endometrial cancer done by M.C Spike found that there is only a small reduction of the estrogen replacement therapy-induced endometrial cancer risk from use of 7 days of progestin, but a complete abolition of the increased endometrial cancer risk with 10 or more days of progestin use in oral contraceptive pills [3].

An injectable depot progestin,Medroxyprogesterone acetate, as is given intramuscularly for contraception . It causes cervical mucus and endometrial changes , in addition to this it also prevents ovulation. A prospective study was done in 5000 women using injectable medroxyprogesterone acetate for contraception , a relative risk of ovarian cancer was found 0.8 after 4–13 years of follow-up [14].

Progesterone has effect on breast , to reduce this effect progestins need to be delivered to the endometrium . An intra-uterine device has the direct endometrial route of administration so it has even lower serum progestin levels. LNG-IUS has some advantages over other progestins due to the higher level of levonorgestrel in the uterus and especially in the endometrium than the level observed than in the plasma . The direct endometrial route of administration with an intra-uterine device has even lower serum progestin levels. The LNG-IUS can cause an endometrial glandular atrophy and a decidualization of the stroma.

Data from the Finnish Cancer Registry showed a standardised incidence ratio of 0.46 for endometrial cancer in users of the LNG-IUS. The NOWAC study was a Norwegian population-based prospective cohort study. Median follow-up was 12.5 years; 9% of the cohort reported LNG-IUS use during or prior to 1998–2007. After adjusting for BMI, activity, age at start of follow-up, combined oral contraceptive use, menopausal status and parity ever-users of LNG-IUS had RR of endometrial cancer of 0.34 (95% CI 0.18–0.65) compared with never-users [15].

If a woman is not accepting for this routes of administeration , then giving progestins for 13 days every 3–4 months may provide satisfactory protection of the endometrium with proportionally less effect on the breast than monthly administration. Two clinical trials done by Ettinger et al. 1994, Williams et al. 1994 of administering 10 mg MPA/day for 14 days every 3 months have been published in which the dose of conjugated estrogen was 0.625 mg/day , both these studies suggest that this approach may be satisfactory with such low-dose estrogen [3].

Blocking of ovarian function with a GnRHagonist , will significantly reduce breast cancer risk , even if low dose sex steroids are used along with it. Cohort study done by Rebbeck et al. (1999) in women with BRCA1 mutations who underwent bilateral prophylactic oophorectomy but had no history of breast or ovarian cancer and had not had a prophylactic mastectomy . Control subjects were as above but had not undergone oophorectomy. This study shown that women whose surgery was before 50 years of age, there is 47% overall reduction in breast cancer

risk and a 67% reduction in incidence 5 or more years after surgery [3]. This report suggested that the reduced breast cancer risk was a direct result of the reduced ovarian steroid levels. The reductions in risk observed in this study are even greater than predicted above and very close to that seen with tamoxifen. Use of GnRHA is

equivalent to oophorectomy is strongly supported by the results of the ZIPP randomized trial . In ZIPP randomized trial (Baum 1999) the GnRHA, depot Zoladex, was given to premenopausal breast cancer patients, and a 40% reduction in contralateral disease was observed (Baum 1999) [3]. Early menopause is associated with a much reduced risk of breast cancer. Spicer et al. 1994 , carried out a small randomized trial of such a GnRHA, depot Lupron, plus add-back estrogen plus progestin (GEP) regimen in women at high risk of breast cancer . It causes same effects as at menopause occurs. There was significant reduction in mammographic densities at 1 year suggest that the aim of the regimen to reduce breast cancer risk has been accomplished [3].

Almost 25 years ago, the harmful effects of unopposed oestrogen HRT in women with a uterus were apparent. Sequential HRT has also been shown to increase the risk of endometrial cancer, with risk being inversely proportional to the number of days progestin is given for. Continuous combination has not been shown to increase endometrial cancer risk and may even reduce it, presumably because of the protective effects of progesterone on the endometrium [16].

Recent years have seen the emergence of the first oestrogen-based, progestin-free oral menopausal HRT for non-hysterectomised women. Conjugated oestrogens with the SERM bazedoxifene (CE/BZA) minimise estrogenic effects on endometrium and breast whilst effectively addressing menopausal symptoms and protecting against osteoporosis. A similar randomised, double-blind study of 17 -estradiol/raloxifene did not provide adequate endometrial protection. CE/BZA has been studied in five RCTs involving more than 7500 women and no increase in endometrial hyperplasia was found. It may be an option for women who poorly tolerate the side effects of progestins [17].

References

1. Iverson Let al, Lifetime cancer risk and combined oral contraceptives: the Royal College of General Practitioners' Oral Contraception Study. Am J Obstet Gynecol. 2017 Jun;216(6):580.e1-580.e9. doi: 10.1016/j.ajog.2017.02.002. Epub 2017 Feb 8.
2. Collaborative Group on Epidemiological Studies of Ovarian Cancer. Ovarian cancer and oral contraceptives: collaborative reanalysis of data from 45 epidemiological studies including 23 257 women with ovarian cancer and 87 303 controls. The Lancet. 2008 Jan 26;371(9609):303-14.
3. Pike MC, Spicer DV. Hormonal contraception and chemoprevention of female cancers. Endocrine-related cancer. 2000 Jun 1;7(2):73-83.
4. Narod SA, Risch H, Moslehi R, Dørum A, Neuhausen S, Olsson H, Provencher D, Radice P, Evans G, Bishop S, Brunet JS. Oral contraceptives and the risk of hereditary ovarian cancer. New England Journal of Medicine. 1998 Aug 13;339(7):424-8.

5. Narod SA, Risch H, Moslehi R, Dørum A, Neuhausen S, Olsson H, Provencher D, Radice P, Evans G, Bishop S, Brunet JS. Oral contraceptives and the risk of hereditary ovarian cancer. New England Journal of Medicine. 1998 Aug 13;339(7):424-8.
6. Mueck AO, Seeger H, Rabe T. Hormonal contraception and risk of endometrial cancer: a systematic review. Endocrine-Related Cancer. 2010 Dec 1;17(4):R263-71.
7. Beavis AL, Smith AJB, Fader AN. Lifestyle changes and the risk of developing endometrial and ovarian cancers: opportunities for prevention and management. Int J Womens Health. 2016;8:151–167.
8. Burn J, Gerdes A-M, Macrae F, Mecklin J-P, Moeslein G, Olschwang S, et al. Long-term effect of aspirin on cancer risk in carriers of hereditary colorectal cancer: an analysis from the CAPP2 randomised controlled trial. Lancet Lond Engl. 2011;378(9809):2081–2087.
9. MacKintosh M, Crosbie E. Obesity-driven endometrial cancer: is weight loss the answer? BJOG Int J ObstetGynaecol. 2013;120(7):791–794.
10. Statistics on obesity, physical activity and diet: England, 2012. [cited 2012 Nov 7]. Available from: http://www.ic.nhs.uk/statistics-and-data-collections/health-and-lifestyles/obesity/statistics-on-obesity-physical-activity-and-diet-england-2012.
11. Uccella S, Bonzini M, Palomba S, Fanfani F, Ceccaroni M, Seracchioli R, et al. Impact of obesity on surgical treatment for endometrial cancer: a multicenter study comparing laparoscopy vs open surgery, with propensity-matched analysis. J Minim Invasive Gynecol. 2016;23(1):53–61.
12. Iversen L, Sivasubramaniam S, Lee AJ, Fielding S, Hannaford PC. Lifetime cancer risk and combined oral contraceptives: the Royal College of General Practitioners' Oral Contraception Study. Am J Obstet Gynecol. 2017;216(6):580.e1–580.e9.
13. Faculty of Sexual & Reproductive Healthcare. The UK Medical Eligibility Criteria for Contraceptive Use. Royal College of Obstetricians &Gynaecologists; 2009.
14. Riman T, Persson I, Nilsson S. Hormonal aspects of epithelial ovarian cancer: review of epidemiological evidence. Clinical endocrinology. 1998 Dec;49(6):695-707.
15. Jareid M, Thalabard J-C, Aarflot M, Bovelstad HM, Lund E, Braaten T. Levonorgestrel-releasing intrauterine system use is associated with a decreased risk of ovarian and endometrial cancer, without increased risk of breast cancer. Results from the NOWAC Study. GynecolOncol. 2018;149(1):127–132.
16. Sjogren LL, Morch LS, Lokkegaard E. Hormone replacement therapy and the risk of endometrial cancer: a systematic review. Maturitas. 2016;91:25–35.
17. Parish SJ, Gillespie JA. The evolving role of oral hormonal therapies and review of conjugated estrogens/bazedoxifene for the management of menopausal symptoms. Postgrad Med. 2017;129(3):340–351.