International Journal of Reproduction, Contraception, Obstetrics and Gynecology
Devalla A. Int J Reprod Contracept Obstet Gynecol. 2024 Dec;13(12):3777-3784
www.ijrcog.org
pISSN 2320-1770 | eISSN 2320-1789

DOI: https://dx.doi.org/10.18203/2320-1770.ijrcog20243626

Review Article

Contraception in perimenopause: a review of fecundity, fertility, and feasibility of contraceptives

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Received: 12 October 2024
Accepted: 08 November 2024

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ABSTRACT

Menopausal transition warrants effective contraception despite reduced fecundity and fertility. The associated maternal and perinatal morbidities and mortality in women after 40 years has prompted women to choose safe and reliable contraceptives. Although the majority of women globally opt for sterilization; however, the observed trends in the last decade have seen an increase in the use of Long-acting reversible contraceptives. Combined hormonal contraceptives have been disrepute traditionally but the current literature remarks the use of CHC in selected populations. A literature search was conducted till December 2023 using the PubMed, Embase, SCOPUS databases and recommendations by various organizations using related search terms. This review highlights the various contraceptive options currently dispensed in the armamentarium for women above 40 years. The aim is to focus on the associated co-morbidities that can affect the contraceptive choices in this group and the contraceptive effects on the menopausal symptoms. This would guide the clinicians in prescribing the methods considering the complex requirements.

Keywords: Contraception above 40, Contraception in older women, Hormone replacement therapy, Menopausal transition, Perimenopausal contraception

INTRODUCTION

A natural decline in fertility is anticipated after the age of 35 years, effective contraception is still necessary to prevent unplanned pregnancies.[1,2] The choice of a contraceptive method by a woman is heavily influenced by a diverse range of demographic, cultural, economic, lifestyle and social factors. There can be narrowing down to a few options from the available basket owing to previous failed experiences of a particular contraceptive. From a recent study, 4–36% of contraceptive pill users were likely to change their method within 12 months. For previous contraceptive pill users (n=377), most common reason for change was concern about side effects (from 26% Italy to 10% UK), however, awareness of many non-hormonal contraceptive methods was low.[3] Approaching contraceptive counselling from a place that considers the journey with contraception over a reproductive life span will help identify how beliefs, perceptions, and attitudes of women affect their contraceptive practices and choices.[4] The anticipated increased risks of congenital anomalies and chromosomal disorders, spontaneous abortions coupled with pre-existing metabolic derangements and medical co-morbidities have placed a need to address the contraceptive needs in this age group.[5] In 2021, the estimated number of women with an unmet need for family planning in India was 24, 194, 428.[6] With the recent upsurge in the fertility awareness and family planning initiatives, there is a likely shift from a permanent sterilization towards long-acting reversible contraceptive options with their growing awareness and tolerability. In this review, the author has attempted to provide a comprehensive overview on the unmet needs of contraception in the perimenopausal group, awareness of the modern contraceptive options including non-contraceptive benefits, co-morbidities in perimenopausal age and contraceptive choices, perspectives among Indian perimenopausal women beyond sterilization and

considering the Long-Acting Reversible Contraceptives (LARC).

LITERATURE SEARCH

A literature review was conducted for published articles in English language till 2023 December from PubMed, Embase, SCOPUS, ProQuest databases and recommendations by various organizations including WHO, Guttmacher and UNFPA. The following search terms were used for the literature search: "contraception above 40", "attitudes of perimenopausal women and LARC", "contraception for women of older age".

WHY IS THERE A NEED FOR THIS REVIEW?

Women in this age group have differing needs than their younger counterparts. The need for contraception cannot be underestimated as despite reduced fertility and fecundity, it still poses a risk of pregnancy. The perinatal outcomes in perimenopausal women are often poor. Figure 1 and 2 depict the poor pregnancy outcomes in the women of this age group.

There is not only a decline in natural fertility but the inclination towards further childbearing is considerably reduced in many women. The less frequent sexual intercourse and higher compliance with contraceptive regimens is also more relevant in this population. The fecundity rate is 0.06 for women aged over 40 years.[8] Moreover, combined estrogen and progestin hormone replacement therapy used for the treatment of perimenopausal symptoms cannot substitute for the contraceptive doses unless using an Mirena® IUS/estradiol regime.[9]

DETERMINANTS OF CONTRACEPTIVE UPTAKE

Complex co-morbidities and the emergence of perimenopausal symptoms may be affect the contraceptive choices. It is imperative for the clinicians to be aware of these changes to promote a mutually agreeable safe decision-making. General practise of a "one-size-fits-all" approach neglects the complex needs of these women; especially when hormone replacement therapy is not a contraceptive.[10] Suitability of Contraceptive Methods for Women over 40 years.

For each of the personal characteristics or medical conditions, the WHO-Medical Eligibility Criteria provides various categories as: category 1, category 2, category 3, category 4 (Table 1).[11]

Table 1: WHO-Medical eligibility criteria for selective of contraceptives.

Category	Definition	With clinical judgement	With limited clinical judgement
1	A condition for which there is no restriction for the use of the contraceptive method	Use method in any circumstance	Yes, use the method
2	A condition where the advantages of using the method generally outweigh the theoretical or proven risks	Generally, use method	
3	A condition where the theoretical or proven risks usually outweigh the advantages of using the method	Use of method not usually recommended unless other more appropriate methods are not available or not acceptable	No, do not use the method
4	A condition that represents an unacceptable health risk if the contraceptive method is used	Method not to be used	

Table 2: Non-contraceptive benefits offered by LARC/SARC methods.[2]

Type of contraceptive	Non-contraceptive benefit
Levonorgestrel IUS	Used in heavy menstrual bleeding, treatment of endometrial hyperplasia, prevents endometrial cancer
Copper IUD	Prevents endometrial cancer
Combined hormonal contraceptive	Reduces heavy menstrual bleeding, bone loss, vasomotor symptoms, prevention (better if started before 40 years) of ovarian, endometrial and possibly colorectal cancers.
Female sterilization	Help reduce ovarian cancer
Depot medroxyprogesterone acetate	Reduces heavy menstrual bleeding (esp in endometriosis), reduces risk of endometrial and ovarian cancers

LARC: Long-acting Reversible Contraceptives, SARC: Short acting Reversible contraceptives

Table 3: When to stop a contraceptive.

Method used	41-49 years old	>50 years old
Combined hormonal contraception/ Depo-provera	Continue if satisfied with method and there are no C/I	Stop and switch method
Condoms, diaphragms, Cu-IUD, Fertility awareness methods	Stop two years after last menses	Stop one year after last menses or at the age of 55 years
Progesterone only pill, Nexplanon, Levonorgestrel IUS	As a contraceptive: continue if suitable and no C/I or stop two years after two FSH levels >30 U/l at least 6 week apart	Stop one year after one FSH level >30 IU/l or at the age of 55 years.

Differences in the contraceptive uptake

Unlike the United Kingdom and Canada, the United States has a high prevalence of sterilization among older women of reproductive age.[12] In other countries, such as the UK, a substantial proportion of women over age 40 use intrauterine devices (IUDs).[13] Oral contraceptives and condoms are also popular among older women in the US, Canada and the UK.[14]

India runs a successful National Family planning programme since 1952 with multiple amendments over the years to cater to the growing demands of the population control. The dissipation of barrier contraceptives (Nirodh) and combined oral contraceptives (Mala-N), Long-acting reversible contraceptives (Copper containing Intrauterine devices and Depot Injection-Antara) by the ASHA workers and is considered quite successful. Moreover, the female and male sterilization procedures have been vigorously pursued through the National programmes. Despite all this, there is unequal distribution and availability of the options through different states.[15]

Sterilization versus LARC versus SARC

Is there a need to shift from Sterilization towards LARC/SARC?

Early menopause: In a study by Langton et al investigated over 1.6 million person-years in 2579 members experiencing early menopause, it was observed that tubal ligation was responsible for an increased risk of early menopause (HR=1.17, 95% CI, 1.06-1.28). Furthermore, women who never used contraception/ Oral contraceptives versus who used oral contraceptives had a higher risk of experiencing menopausal symptoms earlier (95% CI, 0.87-1.17, P for trend=0.71).[16]

Possible negative long-term impact on the ovarian reserve

Demand for sterilization reversal: Globally, for decades, female sterilization has been accepted as the only method of contraceptive for two or higher order births including India, accounting for 37% of the world's statistics as per NFHS 4 survey.[17] This has decreased over the years with reversal of sterilization showing a gradual rise. As much as 41% increase in reversal rates have been reported in a study from US over the last 30 years.[18] The results from predicted probabilities provide enough evidence that the regret due to bad quality of care in sterilization operation had increased with each subsequent round of NFHS.[19]

Minimum additional benefits: Except for reports on decreasing rates of epithelial ovarian cancer, this method has not been shown to provide much additional benefits. LARC/SARC methods offer numerous non-contraceptive benefits which are tabulated in Table 2.[20] Lesser failure rates with modern LARC methods.

LARC methods (Long-acting reversible contraceptives)

LARC methods are the most effective modern contraceptive methods for preventing unintended pregnancy. LARC methods do not rely on user adherence and are also suitable for women with medical disorders and nulligravida women, safe and cost-effective.[21,22]

According to 2020/21 data indicate that 56% of women are using long-acting reversible contraceptives, a 10% increase from the year before.[23] This was observed to be lowest in women between 40–49 (6.6%).[24]

Intrauterine devices

The biggest advantage of using Cu-IUD is it can act as an emergency contraceptive and as a method of ongoing contraception in eligible women. However, it is unsuitable for women with heavy menstrual bleeding and dysmenorrhea, both may get aggravated.

Hence, this contraceptive has a limited role in women over 40 years with menstrual abnormalities. Nonetheless, it could be an alternative option for women with medial co-morbidities and oncological risks.[25]

LNG-IUS

It is approved in three doses 13.5 mg, 19.5 mg and 52 mg as a contraceptive but only the latter is approved for endometrial protection.[26] Whereas Cu-IUD has no benefits in climacteric symptoms, LNG-IUS can ameliorate to some extent. But LNG-IUS should be cautiously prescribed in women with mood disorders and migraine.

An off-label prescription of LNG-IUS beyond 52 years has not been recommended widely, though it may be retained up to 7 years or until menopause if amenorrheic.[25] The IUS has one of the lowest failure rates of all contraceptive options (0.1% typical and perfect use failure rate).

LNG-IUS has multiple benefits in perimenopausal women with heavy menstrual bleeding and symptomatic small non-cavitatory fibroids, due to its ability to decrease endometrial growth and prostaglandin ratio by promoting the formation of arachidonic acid in the endometrium.[27] A study conducted by Abu Hashim et al showed endometrial atrophy after 24 months of LNG-IUS insertion in 100% of women with a documented typical endometrial hyperplasia.[28] LNG-IUS combined with progesterone optimises the outcomes in patients with atypical hyperplasia and selected cases with early-stage endometrial cancer.[29,30]

Controversy surrounds LNG-IUS and the risk of breast cancer. Current medical eligibility criteria refutes its use (MEC-4) in current history of breast cancers, MEC-3 in past history of breast cancers but can be used (MEC-1) in women who are BRCA1/BRCA2 carriers/family history of breast cancer.[25,31]

Progesterone containing implant

Various types of subdermal implants are available worldwide with the 68 mg etonogestrel (Nexplanon® or Implanon NXT®) being the most common. It is the most effective contraceptive available worldwide with a failure rate of 0.05/100 women-years.[32] There are no associations with the loss of bone density or metabolic effect, and it is recommended in obese women as well.[26,33] There are currently no recommendations as to till what period this can be retained in the perimenopausal transition.[34] Like other progesterone contraceptives, it is absolutely contraindicated in breast cancer but unlike LNG-IUS it offers no protection in women with endometrial hyperplasia.[25]

Progesterone containing injectable

DMPA is an injectable contraceptive whose effects last for three months. There are not enough eligible data about its use during perimenopause due to its limited use in some countries. DMPA is related to a small loss in bone mineral density that is generally regained after cessation, however, it could reduce bone density that represents a critical factor that occurs physiologically during the climacteric period. Therefore, it is not a first-line contraceptive method after the age of 45 years, although there are no formal contraindications.[35] The dose of DMPA is relatively high compared with the progestin doses in other progestin-only and oestrogen-containing contraceptive methods, with several unique implications for its use. Of the benefits, amenorrhea rates are higher than other methods up to 50% at 1 year of use, with the prevalence of amenorrhea further increasing with ongoing use.

SARC methods (Short-acting reversible contraceptives)

Combined hormonal contraceptives

Aside from birth control, women can enjoy many other benefits from hormonal contraception. While the strongest beneficial effect of CHCs on BMD was seen in perimenopausal women with low oestrogen levels, it is still not clear whether this effect might mitigate fracture risk.[36]

The greatest risk occurs within the first 3 months of initiation (OR 12, 95% CI 7.1–22.4).[2] The incidence of VTE sharply increases after age 40, thus demonstrating that age plays an important role. A meaningful Danish cohort study found that the incidence of VTE in COC users rose from 8.7 per 10000 women-years for women aged 30–34 to 20.8 per 10000 women-years for women aged 45–49.[37] The risk of VTE in patients using COCs is influenced by both the type of progestin and the dose of oestrogen contained. A study performed by Sugiura et al shows that COCs with 20 µg of EE have a lower risk of pulmonary embolism and serious arterial thromboembolic events than COCs with 30–40 µg EE. In addition, using COC-containing levonorgestrel (LNG) is associated with a 50% lower risk of pulmonary embolism (PE) compared with using a COC with a third-generation progestin.[38] The increased maternal morbidity and mortality of pregnancy related to older age should be addressed, including the fact that any contraindication of hormonal contraceptives also increases the risk of significant adverse events during pregnancy.

The incidence of TS and myocardial infarction (MI) was 20- and 100-times higher in an older cohort (aged 45–49 years) versus a younger cohort (aged 15–19 years) of Danish women, respectively, also, considering COC use, the overall risk of stroke increases by 2.2-times and that of MI by 2.3-times.[38] A significantly increased risk of TS in women who use CHCs was also shown in a Cochrane review including 24 observational studies.[39]

In recent years, COCs containing E2 rather than EE have been developed.[34] The most important exponents are a quadriphasic preparation containing E2V+dienogest (DNG) and a monophasic preparation containing micronised E2+nomegestrol acetate (NOMAc). Both have a short HFI, which results in better menstrual cycle control. It seems These preparations share some similarities with postmenopausal HT preparations, rather than COCs, and so have theoretical safety benefits for women over 40. However, there is currently insufficient evidence to define a specific recommendation for the use of these preparations in women over 40.[40]

The INAS SCORE study by Dinger et al shows that E2V/DNG is associated with lower cardiovascular risk compared to COCs containing LNG or other progestins. A similar recent large post-marketing study that includes a total of 101,498 women, with 49,598 using E2-NOMAc

and 51,900 using EE-LNG for up to 2 years, has found a risk of VTE and PE in NOMAc-E2 which is similar to or even lower than that of LNG-based COCs users [HR adjusted of 0.59 (95% CI 0.25–1.35) (adjusted for age, BMI, family history of VTE and current duration of use).[41,42]

Progesterone only pill

Administration is daily and continuous, without breaks. Most of the commonly used preparations contain LNG (30 µg), norethisterone (350 µg) and desogestrel (75 µg). The type of progestin that has the greatest efficacy on ovulation inhibition is desogestrel, which is comparable to that of CHCs.[43,44] With the decline in fertility with age, the traditional POP becomes increasingly effective in older users.

A new option for a POP was recently released with a product containing 4 mg of drospirenone (DRSP), it suppresses ovulation and thickens cervical mucus because of its higher doses of progestin. This allows more leeway in the dosing schedule and maintains effectiveness, even with a missed or late pill. DRSP has strong anti-mineralocorticoid and antiandrogenic properties. The anti-mineralocorticoid properties may lower blood pressure and reduce fluid retention, helping to combat bloating and some of the weight changes observed in perimenopause. The antiandrogenic properties have been shown to have a better impact on arterial cardiovascular risk.[45]

The use of POPs may be beneficial in this age group because of the lack of association they have with VTE, stroke or MI.

The risk of breast cancer in users of POPs is controversial. Nevertheless, if there is also an increase in risk, it remains minimal and will continue to reduce after the cessation of POPs.[46] Information is limited about its effect on BMD.[47]

When to stop using contraception?

The consensus regarding the continuation of contraception is for 2 years, if the last menses were before 50 years of age and for 1 year if it were above 50 years. In women where the last menstrual period is unknown/uncertain, the contraception (with a few exceptions) may be continues till 55 years as most of the women become postmenopausal.

The women who likely bleed after this age are thought to have poor egg reserve and egg quality to cause a pregnancy.[25,48]

Contraceptives may mask the menopausal symptoms

Contraceptive methods do not influence the onset or duration of menopause; however, they may obscure the indicators that signify the commencement of the menopausal transition. This phenomenon occurs because a significant number of women experience amenorrhea while utilizing certain forms of contraception, particularly those involving Progesterone-containing injectable methods.[49]

Contraception–a substitute for Hormone replacement therapy?

It is imperative to acknowledge that the administration of contraception ought to be maintained in tandem with sequential hormone replacement therapy (HRT) in situations where the perimenopausal or menopausal condition remains ambiguous. Progestogen-only contraceptives are regarded as safe for application as a contraceptive method alongside sequential HRT. Combined hormonal contraceptives may be utilized, for individuals under the age of 50 who fulfil the requisite eligibility criteria, as a feasible substitute for HRT in the management of menopausal symptoms, potentially providing a measure of protection for skeletal health. This methodology signifies a secure and effective alternative to HRT for healthy, non-smoking, perimenopausal women, while also affording additional benefits such as the regulation of menstrual bleeding, contraceptive efficacy, and protective effects against ovarian and endometrial cancers. Historically, initial combined hormonal contraceptive (CHC) formulations contained concentrations surpassing 100 µg of ethinylestradiol (EE), whereas modern formulations generally encompass dosages ranging from 15 µg to 35 µg. The formulation associated with the minimal dosage is the vaginal ring (NuvaRing® [MSD]), which concurrently provides the highest degree of control over menstrual bleeding.[50]

The practice of 'tricycling,' defined as the consecutive consumption of three packs of pills, results in a mere five HFIs/bleeds per year, in contrast to traditional methods. The most recent formulations, such as Qlaira® (2-day Bayer) and Zoely® (4-day MSD), present shorter HFIs. These formulations similarly employ estradiol (E2) as a substitute for ethinyl estradiol (EE), akin to hormone replacement therapy (HRT).

The combination of Mirena with estrogen replacement therapy (ERT) represents the sole form of continuous combined (potentially bleed-free) HRT sanctioned for use in perimenopausal women. An aspect that may induce ambiguity among Mirena users pertains to the appropriate timing for the removal or replacement of the device. In scenarios where the device is inserted in women under the age of 45 who require contraception, Mirena should be replaced after a span of 5 years, the Faculty of Sexual and Reproductive Healthcare (FSRH) advocates for extended use if the device is fitted in women aged over 45 years. Conversely, if the device is utilized exclusively for the management of heavy menstrual bleeding (HMB), it necessitates replacement solely in the event of the recurrence of unacceptable bleeding. However, in contexts where the device is utilized as the progestogen element of HRT (for the purpose of safeguarding the endometrium), it is crucial that it is replaced after 5 years (notably, while

the license stipulates a duration of 4 years, the FSRH recommends 5 years) irrespective of the bleeding status or contraceptive necessity. Consequently, it is vital to ascertain during each follow-up consultation whether there have been any modifications in contraceptive requirements (for example, should the woman enter into a new partnership with a partner lacking a vasectomy); or whether estrogen replacement therapy has been instigated.[51]

Gaps in counselling for effective contraception

The age-related background risk for the development of cardiovascular disease commences an upward trajectory during the perimenopausal phase. This demographic exhibit elevated incidences of breast, endometrial, and ovarian cancers, which warrant careful consideration in the context of prescribing combined oral contraceptives. Endometrial carcinoma is predominantly characterized as a pathology of advanced age, however, specific risk factors, including prolonged polycystic ovarian syndrome, obesity or genetic mutations, render even younger women vulnerable. Women aged over 40 years face a heightened susceptibility to osteoporotic fractures in comparison to their younger peers, with the decline in bone mineral density markedly intensifying around the menopausal transition due to the absence of estrogen. The demand for tubal ligation reversal procedures has seen a notable increase in recent years, particularly during the early 2000s.[52]

Perspectives from Indian scenario

In India, the family planning initiative exclusively advocates for female sterilization as the singular method of contraception. It is imperative to transition from a permanent approach to a spacing strategy in order to furnish users with a diverse array of options that can mitigate feelings of regret.[53]

Trends in pregnancy rates and contraceptive choices

The chronological age at which a woman bears her final offspring exerts a significant influence on maternal and child health. Over a span of three decades (1992–2021), there has been a notable decrease of 15.8% in the median age at last childbirth for women aged 40–49 years.[54] Women aged 40 to 49 demonstrated a twelve-fold increase (OR: 1.12, 95% CI, 1.10–1.14) in the likelihood of utilizing modern contraceptive methods.[15] Because of the dominance of sterilization in Indian family planning policy, the results may have limited generalizability beyond India.

Role of social media

The influence of social media has been significantly noted in the formation of contemporary contraceptive preferences among women. A recent empirical investigation revealed that tweets predominantly addressed the decision-making process regarding contraceptive methods (26.7%) and their associated side effects (20.5%), with particular emphasis on long-acting reversible contraceptive methods and the depot medroxyprogesterone acetate injection. Additionally, tweets pertaining to the logistical aspects of usage or adherence were frequently observed in discussions surrounding short-acting reversible contraceptives. A minor fraction of tweets explicitly sought information (6.2%) or dispensed advice (4.2%).[55]

CONCLUSION

A choice for all. Freedom to plan, power to choose. This theme emphasizes the right of people to make informed decisions about their reproductive health. Millennial women in India are opting for smaller families, averaging just two children each. However, family planning is about more than just contraception, it is integral to the health and well-being of women, families, and communities. It empowers women, girls and youth by providing them with the rights and choices.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Devalla A. Contraception in perimenopause: a review of fecundity, fertility, and feasibility of contraceptives. Int J Reprod Contracept Obstet Gynecol 2024;13:3777-84.