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Effect of Contraceptives on Fertility

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Abstract:

Pregnancy and childbirth carry risks of morbidity and mortality. Although the contraceptives that couples use to avoid pregnancy have their own health risks, they also have substantial noncontraceptive health benefits. Information about these risks and benefits is necessary for informed decision making. Oral contraceptives, for example, not only prevent pregnancy, but they also reduce the risk of endometrial and ovarian cancer and protect against acute pelvic inflammatory disease and ectopic pregnancies. However, oral contraceptives increase the risk of cardiovascular disease. IUDs provide effective contraception but increase the potential for infection in certain high-risk groups. Barrier methods of contraception provide less effective contraception, but they protect against sexually transmitted infections including human immunodeficiency virus (HIV). The importance of the noncontraceptive benefits and risks of contraceptives varies among societies because of variations in the prevalence of the diseases involved.

In this review we will discuss evidence on the effectiveness and health consequences of specific contraceptive methods on fertility.

Keywords: contraceptives; fertility; pregnancy

Introduction

Depending on their circumstances, women have different reproductive goals and contraception habits. Many women are now free to decide to become pregnant voluntarily rather than by accident thanks to the availability of extremely efficient reversible contraception. Any reversible method of contraception must not negatively impact future fertility, which is frequently a major worry for women [1]. Particularly in young women [2], whose general mistrust of effective contraceptive methods is exacerbated by misconceptions and a lack of information [2], [3], any fertility delay or impairment after stopping a particular method of contraception may be linked to decreased use and low user satisfaction.

Initial reports from the 1960s indicated that some women who had previously experienced regular menstruation might experience anovulation and infertility after stopping oral contraceptives [4], [5], [6], and [7]. Clinicians were concerned that using oral contraceptives to suppress ovulation for an extended period of time could result in a protracted ovulatory suppression state, delaying the return to regular menstruation and leaving some women amenorrheic for over a year. Since then, this so-called postpill amenorrhea syndrome has been disproved [8]. However, some doctors remain concerned about the impact of long-term oral contraceptive usage on fertility and reproductive function, especially as it may impact teenage maturation and reproductive development [3].

Fertility is a complicated topic that is influenced by a variety of elements (both male and female), such as environmental influences, behavioral/lifestyle factors, and underlying reproductive capacity. It is widely acknowledged that fecundity and age are negatively correlated [9], [10], and that this correlation is linked to decreased coital frequency [11], [12], decreased fertility [10], [13], and a higher prevalence of underlying gynecological disease [14]. Smoking has also been linked to decreased fertility in women [15], [16], [17], obesity [18], and exposure to various environmental pollutants (such as pesticides, solvents, and chlorinated hydrocarbons) [19], [20], and [21]. Therefore, a variety of underlying characteristics unique to the community being studied may have an impact on studies evaluating pregnancy rates or time to pregnancy after stopping the use of contraceptives.

This article's objective was to do a thorough analysis of the literature that compares the rates of pregnancy among women who wish to conceive after stopping different forms of contraception. The majority of reversible methods of contraception have not been well reviewed, despite recent evaluations concentrating on this feature for specific methods such oral contraceptives [22] and copper intrauterine devices (IUDs) [23]. When advising individuals or couples regarding the effect of using contraceptives

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on their future fertility, this information will be helpful, particularly for those who have not yet had children.

Contraceptive Methods

Generally, reversible contraceptive techniques can be classified as either hormonal (like progestin-only pills or estrogen-progestin patches) or nonhormonal (like diaphragms and condoms), as well as long-acting (like IUDs) or short-acting (like pills). The efficiency of reversible contraceptive methods in preventing pregnancy can also be categorized. In the United States, contraceptive techniques are only available with a prescription, with the exception of condoms, spermicide, and behavioral methods.

Hormonal Contraceptives

Pharmacology of Steroidal Hormone Components

Estrogen and progesterone are lipid or steroid hormones. Progestin, either alone or in combination with estrogen, is a component of hormonal contraception. The majority of progestins used in contraceptives, including levonorgestrel and norethindrone, are produced from testosterone; progesterone is the only progestin that occurs naturally. In order to inhibit ovulation, progestins suppress the hypothalamus's gonadotropin-releasing hormone, which in turn reduces the pituitary's luteinizing hormone. [24,,25] Furthermore, progestins directly impair the permeability of cervical mucus. Progestins decrease sperm survival and transit to the fallopian tube as well as endometrial receptivity. [26,27] By inhibiting gonadotropins and folliclestimulating hormone, estrogens increase the effectiveness of contraceptives by halting the growth of a dominant follicle. However, reducing irregular bleeding is the main way that estrogens contribute to progestin-based contraceptives. Ethinylestradiol is the estrogen component found in the majority of combined hormonal contraceptives.

Progestin-Only Contraception

There are numerous progestin-only contraceptive options available. The progestin's dosage, strength, and half-life, as well as user-dependent elements like following the prescribed regimen, all affect how effective they are. [28.29]

The efficacy of progestin-only pills to inhibit ovulation varies depending on whether they include drospirenone or norethindrone. Unlike a regular combination contraceptive pill, which contains 1000 µg of norethindrone, norethindrone pills only contain 300 µg. Because norethindrone pills contain less progestin, there is a greater chance of breakthrough bleeding and less regular ovulation suppression. Other progestin-mediated effects sustain the effectiveness of the contraceptive. Drospirenone-only pills help suppress ovulation because they contain a little more progestin than a hormonal contraceptive that combines progestin and estrogen. Ovulation suppression was maintained in one trial where participants postponed taking a drospirenone-containing pill by 24 hours, simulating a missing dose. Only one participant out of 127 showed signs of ovulation. [30] Progestin-only contraceptive pills have the following advantages: minimal impact on hemostatic parameters, safety profile, simplicity of beginning and withdrawal, and fertility return within one cycle. [31] Depot medroxyprogesterone acetate (DMPA) is an injectable progestin that is given at 12- to 14-week intervals. It comes in intramuscular (150 mg) and subcutaneous (104 mg) formulations. Even though DMPA is linked to irregular uterine bleeding, this pattern gets better the longer the drug is used. 46% of DMPA users experienced amenorrhea in the ninety days after their fourth dose, according to a systematic evaluation of DMPA-related bleeding patterns (13 studies involving 1610 participants). [32] The only type of contraception that can postpone a return to fertility is DMPA. Due to its ability to block the hypothalamic-pituitary-ovarian (HPO) axis and its persistence in adipose tissue, the contraceptive effect and irregular cycle may extend for up to 12 months following the last dose. DMPA may be most appropriate for people who benefit from amenorrhea (such as patients with bleeding disorders or developmental difficulties), but not for people who wish to become pregnant right away after stopping the medication. DMPA and progestin-only contraceptive tablets typically result in 4–7 births per 100 women annually. [29,33]

Similar to permanent techniques like tubal ligation or vasectomy, progestinonly long-acting options like the levonorgestrel (LNG) IUD and the subdermal implant often have efficacy rates of less than one pregnancy per 100 women year. [29,33] These techniques are also linked to a restoration to fertility within one cycle following cessation. With amenorrhea rates as high as 20% at 12 months and 40% at 24 months, the LNG IUD is effective for at least 7 years. [34] However, initiation necessitates a face-to-face meeting with an IUD placement-trained doctor. The etonogestrel subdermal implant is simple to insert and remove, and it can last up to five years [35]. In-person visits are also necessary for initiation and cessation. Because of the unpredictable nature of the implant's bleeding profile, up to 11% of patients remove it within the first year. [36] The bleeding pattern during the first three months (such as protracted, frequent, or irregular episodes) is associated with subsequent bleeding patterns, according to an analysis of 11 research (923 participants) from Europe, Asia, South America, and the US. [36] Those who experience prolonged or frequent bleeding during the first three months, however, have a 50% chance of improving within the next three months. [36]

Combined Hormonal Contraception

The weekly transdermal patch, monthly vaginal ring, and daily oral pill are examples of combined hormonal therapies that contain both progestin and estrogen. The success of these procedures, when fully adhered to, is two pregnancies per 100 users annually. However, the effectiveness varies depending on the user's adherence, with an average of 4 to 7 pregnancies per 100 women year. [29,33] A recent cohort study of almost 10,000 people in the US showed how important patient adherence to hormonal contraception is. Short-acting reversible techniques (pills, patches, and rings) had a pregnancy rate of 4.55 per 100 participant-years, while long-acting reversible methods (IUD, implant) had a pregnancy rate of 0.27. 13. The risk of pregnancy was higher for women under 21 who used short-acting techniques than for those who were 21 or older (adjusted hazard ratio, 1.9 [95% CI, 1.2-2.8]). [30] There were no age-related risk differences for the long-acting reversible IUD or implant techniques. Age-stratum absolute rates were not provided.

The processes by which progestin-only approaches and combined hormonal contraceptives prevent conception are identical. Their capacity to create a steady, predictable bleeding pattern is their biggest benefit over progestin-only techniques. About 90% of users of combined hormonal contraception pills (n = 1003) over a 90-day standard reference period reported regular scheduled withdrawal bleeds, while no one experienced amenorrhea, according to a study that compared the bleeding diaries of 5257 women using nine different methods of contraception (nonhormonal, combined hormonal contraception, and progestin-only). [37] Sometimes, throughout the week of the placebo, people do not experience a withdrawal bleed. If the patient or physician is worried that pregnancy might be the cause of the lack of bleeding, a pregnancy test may be conducted. Patients can be confident that the absence of withdrawal bleeding does not signify a medical condition or decreased fertility if pregnancy is ruled out. This is because the HPO axis is suppressed.

Nonhormonal Contraceptives

Behavioral Methods

Fertility awareness-based techniques and penile retraction prior to ejaculation are examples of behavioral contraceptive treatments. Patients may refer to these techniques using euphemistic terminology like the rhythm method, natural family planning, or other imprecise terms. Patient education, cycle regularity, the patient's dedication to daily symptom assessment (first morning temperature, cervical mucus consistency), and the patient's capacity to refrain from sexual activity or ejaculation during the period of maximum fertility are all necessary for the effectiveness of withdrawal and fertility awareness. Pregnancy rate data are often of low quality and heavily influenced by the design of the study. [38] Fertility awareness strategies failed to prevent 22 pregnancies per 100 woman-years, according to a meta-analysis of higher-quality prospective studies of women at risk for unwanted pregnancy. [39]

Condoms and Diaphragms (Barrier Methods)

Other nonhormonal techniques include physical barriers (condoms and diaphragms) or substances that kill sperm or reduce their motility (pH modulators and spermicides) to stop sperm from entering the upper reproductive canal. These procedures typically have a first-year success rate of 13 pregnancies per 100 women annually. [29,33]

Copper-Bearing IUD

One extremely successful nonhormonal reversible technique is the copperbearing IUD. 12,18 The average annual use pregnancy rate is 1%. [29,33] The user's HPO axis remains unaffected, therefore menstrual cyclicity and ovulation continue. Through the direct actions of copper salts and endometrial inflammatory alterations, the main mode of action is spermicidal. [38] The main drawback of the copper IUD is that, primarily in the first three to six months of use, it might make menstruation more frequent, uncomfortable, and prolonged. 36 The risk of tubal infertility later on is not increased by IUD use. [40] Testing for sexually transmitted infections (STIs) can be done in conjunction with IUD installation if necessary. [41-43] The risk of pelvic inflammatory illness is not increased by the accelerated STI testing procedure during IUD implantation. Those who already have gonorrhea or a chlamydial infection (0%–5%) or do not (0%–2%) have a low absolute risk of developing pelvic inflammatory illness following IUD installation. [44]

Emergency Contraception

When taken after unprotected sexual activity, emergency contraception (EC) lowers the risk of pregnancy. When put within five days of unprotected sexual activity, a copper IUD, the most effective form of EC, lowers the probability of conception to 0.1%. [45] Another benefit of a copper IUD is that it gives users continuous contraception. EC had not previously thought about LNG IUDs as a viable alternative. But in a recent randomized noninferiority trial, women who requested EC and had at least one unprotected sexual encounter in the previous five days were randomly assigned to either a 52-mg LNG IUD (n = 355) or a copper IUD (n = 356). With a between-group absolute difference of 0.3% [95% CI, -0.9% to 1.8%], [46] LNG IUD was not inferior than copper IUD. However, it was not disclosed what percentage of study participants engaged in unprotected sexual activity throughout their menstrual cycle, putting them at risk for pregnancy. Given the scant and ambiguous evidence supporting the use of a 52-mg LNG IUD alone for EC, it makes sense to insert the IUD and administer an oral EC right away if the patient needs EC.

One dose of either an antiprogestin (ulipristal acetate, 30 mg) or a progestin (LNG, 1.5 mg) makes up oral EC. These two substances function by preventing or postponing ovulation. Abortifacient neither. While ulipristal acetate requires a prescription, LNG EC can be purchased over-the-counter. For optimal effectiveness, the drug should be taken as soon as possible after unprotected sexual activity; however, ulipristal acetate can be administered up to five days later. [47-49] After three days, the effectiveness of LNG is reduced. When taken within the first 72 hours of sexual activity, the two agents seem to be equally effective (ulipristal acetate EC: 15 pregnancies of 844, LNG EC: 22 pregnancies of 852); the estimate of the reduction in pregnancy without EC use is 90% lower. However, pharmacodynamic and clinical studies showed that the ulipristal acetate treatment effect lasts for up to 120 hours without any pregnancies (0/97). 46 Pregnancy prevention rates were lower than anticipated in actual EC use studies including 3893 participants; this appears to be connected to several acts of unprotected intercourse before and after EC use. [50,51] EC must be taken again if additional unprotected sexual activity takes place 24 hours after EC use and a regular method of contraception has not been initiated. [52] There are no significant side effects from repeated usage of LNG EC, and there is no particular research on repeated dosing for ulipristal acetate EC. [53] Before beginning a user-controlled technique, like condoms, clinicians should go over the EC alternatives with each patient. Oral EC may be prescribed to these patients to be used right away at home if necessary.

This review found that within the first 12 months after stopping contraceptive, 83.1% (95% CI = 78.2-88%) of women were pregnant. There was no discernible difference in the first-year fertility return between IUD and hormonal treatments. Likewise, the type of progesterone used in contraception and the length of time using oral contraceptives had no discernible effects on the return of fertility after stopping contraception. However, there was conflicting evidence on the impact of parity on the restart of pregnancy after stopping contraception.

This review's fertility return rate was similar to earlier studies and publications that evaluated particular forms of contraception [54–57]. Pregnancy rates among LNG-IUS ex-users, copper IUDs, and oral contraceptives also overlapped and were similar to earlier findings. The results, however, were marginally less than the 85.2–94% reported by women who stopped using barrier methods or who did not use any form of contraception [58,59]. This discrepancy could be because hormonal contraceptives frequently take months to leave the body, which causes a brief postponement of the start of pregnancy for months [56,57].

The one-year pregnancy rate after stopping an implant ranges from 37.5% to 90%, which is similarly consistent across studies [54,55]. According to Affandi et al. [54], there are studies that show a remarkably low risk of conception within a year after stopping contraceptive, with reports of 37.5 and 48.8% for Norplant and Implanon ex-users, respectively. However, the rate of fertility return is comparable to other techniques when the study with the low rate of conception following the withdrawal of contraception is eliminated. Furthermore, no discernible variations between the various implant types were noted. The fact that implants are impregnated with the same hormone, which makes no difference, could help to explain this.

Resumption ranged from 71 to 96%, with an average of 84.75%, and fertility returned after IUD termination was not hampered in any way. Furthermore, pregnancy is unaffected by the kind of IUD, how long it is used, or whether hormones are added to the device [54–58]. According to Mansour et al. [54], the pregnancy rate after IUD termination ranges from 86.1 to 92.3%, which is similar for both natural method users and non-users. This research also shows that fertility quickly resumes following IUD termination. According to other research, the kind and length of IUD use had little bearing on the rate of pregnancy following cessation [55,56].

Despite the widespread belief that oral contraceptive may hinder conception, this review found that 87% of women were able to conceive. Other researchers found that fertility returned similarly after stopping oral contraception, which is consistent with this conclusion [54–57]. Nonetheless, this review and meta-analysis acknowledges that there may be a small lag in fertility recovery following the withdrawal of hormonal contraception until the hormone's blood bioavailability is fully eliminated. Additionally, it has been seen that using hormonal contraception for three months prevents pregnancy, but this impact is negligible for users who are 12 months along and nonexistent for those who are 24 months [54–59]. Currently, there is no longer a concern about decreased fertility that was linked to early use of high-dose oral contraceptive pills. This is because low-dose contraceptive regimens are available for usage [57–59].

Our analysis also demonstrates that the restoration of fertility was not substantially impacted by the length of time spent using contraception. It is consistent with the findings of several other studies [54–59] and the several papers that were part of the review [54–62]. However, there is evidence that suggests women who used oral contraceptives for a longer period of time may have had a slightly lower pregnancy rate than women who used them for a shorter period of time [54]. This could be due to the effect of aging, as fertility declines with age.

The potential association between prolonged use of hormonal contraception and the rate of restart of pregnancy, however, might not be revealed through acceptable and trustworthy conclusions because none of the research were randomized control trials and the majority of the studies had small sample sizes.

Restoring Fertility After Contraception

Likewise, our analysis revealed that the kind of progestin had no discernible impact on the short- or long-term pregnancy rate. This is due to the fact that dose is more important than duration. But at the moment, only formulations with minimal dosages are being used. As a result, reproductive delays after stopping the usage of contraception may not be prevalent. Furthermore, women who stop long-term or continuous OC regimens experience a similar return in fertility as those who stop cyclic OCs [54–58]. Previous investigations evaluating the restoration of fertility after stopping oral contraception also reported same outcome [54–60].

There was conflicting evidence on parity's impact on fertility rates. This review's conclusion indicates that parity may or may not increase fertility. The review's studies specifically contrasted nulliparous and multiparous women without taking into account the infertility rate [54]. Therefore, it is assumed that multiparous women who have been shown to be fertile will have a greater pregnancy rate. In all situations, the fertility rates of women who want to get pregnant after stopping a form of birth control may be impacted by the baseline incidence of infertility.

Conclusion

usage of contraception, type of contraception, duration of usage, and type of progesterone did not influence the resumption of fertility after stopping contraception. Nevertheless, there was conflicting evidence about the impact of parity on the restart of pregnancy after stopping contraception. In order to provide women the freedom to choose and use contraception for as long as they choose, it is crucial to inform them that using it in the past, regardless of its type or length, does not have a detrimental effect on their ability to conceive in the future.

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