

Hormonal contraception: Is it time to abandon estrogen?

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Abstract

The efficacy of the contraceptive methods is high, and contraceptive effect is mainly due to progestogen, since it promotes inhibition of ovulation, thickening of the cervical mucus, and reduction in tubal motility. Therefore, one must reflect on the role of estrogen – is it time to abandon it? In this paper, we discuss the role of estrogen and progestogen in contraception, bleeding profile and non-contraceptive benefits.

Keywords: Hormonal contraception; Estrogens; Progestins

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Introduction

The use of contraceptives is an important strategy for reducing maternal and perinatal morbidity and mortality.^{1,2} Hormonal methods, containing a combination of hormones or progestogen alone, stand out among the contraceptives. According to data from the United Nations (UN), 100 million women use combined hormonal contraceptives worldwide.³ The available data from Latin America are inconsistent; nevertheless, the numbers are evidence of increased usage of hormonal contraception among the reproductive-age women in the region.⁴ In a data analysis of groups of women from 23 Latin American and Caribbean countries, the rate of use of contraceptive methods was 55.4% for Argentina (2011), 82% for Brazil (2013), 81.3% for Colombia (2015), and 65.5% for Mexico (2015).⁵ When contraception options are narrowed down to oral methods, the dissimilarities in rate of use between countries persist,^{4,5} for pills are little used in Mexico, while the proportion of users is larger in Chile (25%) and in Brazil (34.2%).⁵

The importance of hormonal contraceptives is undeniable when treating and preventing several gynecological disorders, such as dysmenorrhea, iron deficiency anemia, premenstrual syndrome, abnormal uterine bleeding, ectopic pregnancy, ovarian cysts, polycystic ovarian syndrome, and endometriosis,^{6,7} as well as when reducing oncological risks, namely those of endometrial, ovarian, and colorectal cancer.^{3,6,8,9} However, despite such potential benefits, there are a few adverse effects associated with their use.


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A study conducted by the World Health Organization (WHO) in 36 countries revealed that two-thirds of the sexually active women who had the desire to avoid or postpone pregnancy stopped using contraceptives for fear of the side effects (particularly of combined contraceptives), for concerns about their health, and for underestimating the probability of conception. As a result, one out of four pregnancies was unplanned.¹⁰ Thus, an assessment of the adverse effects of hormonal contraception is crucial, for such effects are the main cause of discontinuation and poor adherence.^{3,11,12} Data from the CHOICE study show that the three most important attributes of contraceptive methods are high effectiveness, safety, and few side effects.¹³ The combined contraceptives produce a range of effects, from general and common, such as nausea, headache, and breast pain, to very rare and serious, such as venous thromboembolism (VTE), cerebrovascular accident (CVA), and acute myocardial infarction (AMI).¹⁴ As for progestogens alone, the most common complaints are menstrual irregularities and water retention.^{9,12,15}

Currently, the search for methods with fewer adverse effects and less potential risks has taken on great proportions. The progestogen-only methods have few contraindications. This is the reason they are highly recommended in clinical situations where estrogen should not be used.¹⁶ The safety of progestogen-only use has been confirmed in numerous studies, and some of the most recent among them have been carried out with drospirenone.^{17,18} The WHO states that the contraceptives containing only progestogen do not increase the risk of VTE, AMI, or CVA.^{19,20} Therefore, progestogens alone represent a class of contraceptives that combine efficacy and safety and display a fairly wide array of uses.

→ Mechanism of action of progestogens alone

The action mechanism of progestogens is multimodal, for it is based on inhibition of ovulation, thickening of the cervical mucus, reduction in tubal motility, and desynchronization of the endometrial changes necessary for implantation. Theoretically, estrogen would increase contraceptive efficacy by suppressing the follicle-stimulating hormone and thus keeping the dominant follicle from developing. Nonetheless, the most important contribution estrogen makes to hormonal contraceptives is the reduction in unpredictable bleeding.^{12,15}

→ Efficacy of the contraceptive methods

The efficacy of the contraceptive methods is high, and there is no difference between combined methods (pills, patches and rings) and short-acting progestogens alone.^{12,21} In typical use, the failure rate of combined oral contraceptives (COCs) and oral progestogen-only pills (POPs) is 3 to 9 pregnancies for every 100 couples per year.¹⁰ Furthermore, the effectiveness of hormonal contraceptives is based on the progestogen component through the aforementioned multiple action mechanisms.^{14,22} It is a fact that progestogens can also be found in a few long-acting reversible contraceptive (LARC) methods, and these are significantly superior in efficacy to the short-acting ones, and this is an advantage of the LARCs.^{23,24}

→ The role of estrogen in controlling bleeding

The bleeding pattern with progestogen use is variable. The WHO groups the variations into amenorrhea and infrequent, frequent, irregular and prolonged bleeding.²⁵ Changes to this classification, including the regular pattern, have been proposed.²⁶ Unfavorable bleeding patterns are those which are frequent (more than five bleeding episodes within a 90-day span) and those which are prolonged (bleeding episodes that last more than 14 days). The other patterns are deemed favorable.

The mechanisms involved in the progestogen-caused unfavorable bleeding have not been well established. Possible explanations include increased changes in tissue perfusion combined with local angiogenic factors, permeability of superficial blood vessels, and changes in the functions of the endometrial steroid hormone receptor.²⁷ In fact, the unfavorable bleeding pattern is the most common reason mentioned for discontinuation of POPs, and it occurs in up to 25% of the users.²⁸ There are measures that seek to control such unfavorable bleeding,^{26,27,29,30} however, not all users go into complete remission. In this sense, the presence of estrogen in the contraceptive formulations reduces the discontinuation of the method due to bleeding.³¹ A study with formulations containing 20 mcg of ethinylestradiol (EE) associated with 3 mg of drospirenone (DRSP) or with 150 mcg of desogestrel (DSG) showed incidences of unplanned bleeding ranging from 8.8% to 17.3% (EE20+DRSP) and from 9.4% to 16.3% (EE+DSG),³² while other authors found rates of 2.0% to 6.4% with the vaginal ring.³³

→ The benefits of estrogen beyond contraception

Both women and healthcare professionals underestimate the non-contraceptive benefits of the oral methods, concerned as they are about their harmful effects. However, besides reducing the menstrual flow and improving dysmenorrhea,

oral contraception decreases the incidence of endometrial and ovarian cancer by 40% to 50%. This effect correlates with usage time and lasts for up to 10 years or more after discontinuation of the pill. The combined methods have a specific effect on colorectal cancer, with a reduction in risk of approximately 40% through a decrease in bile acids in the colon.³⁴ Other benefits have been documented, such as prevention of osteopenia when undertaken in perimenopause and a reduction in the incidence of uterine myomas, in benign functional changes in the breast, and in acute pelvic inflammatory disease.³⁵ Yet, it is worth emphasizing that the classical treatments for premenstrual syndrome were designed with combined methods³⁶ and that evidence provided by progestogen-only methods is scarce.

Still, estrogen has a favorable effect on acne,³⁷ and in patients with hyperandrogenic syndromes, e.g., the polycystic ovarian syndrome, the use of combined methods contributes to the treatment of hirsutism as it promotes a rise in sex hormone-binding globulin (SHBG) and the attendant reduction in free testosterone. In parallel, the progestogen present in COCs inhibits the pituitary release of LH, aiding in the reduction of androgen production by the theca cells.³⁸

Notwithstanding our concerns with the risk of VTE associated with COC use, pregnancy and the puerperium are also associated with a rise in the risk of thromboembolic events. In fact, the thromboembolic risk in the pregnancy-puerperal cycle is many times greater compared to the use of any combined contraceptive.^{39,40} Furthermore, estradiol (E2)-containing pills have shown a better safety profile than those with ethinyl estradiol.^{41,42} Moreover, the new combination containing estetrol (E4) and drospirenone showed less impact on several hemostasis parameters, which suggests that it may have less residual risk of thromboembolic events than other contraceptives.^{43,44} Knowledge of the particularities of the hormonal contraceptive methods aids the gynecologist in comprehending what to do to avoid increasing the patient's potential risk of thromboembolism.

Conclusion

There is no single answer to the question "What is the best contraceptive method?" In fact, one should think about what is the role of estrogen and progestogen-only pills in current hormonal contraception? It is necessary to ponder the objectives of contraception, potential additional benefits, risks associated with the choice of a method as well as potential contraindications and medical eligibility criteria. Contraceptive counseling is a medical act, and it must be guided by a comprehensive medical evaluation and lead to shared decision-making with the patient about the seemingly most adequate method. Although the methods with no estrogen are certainly sufficient for an adequate protection against pregnancy, there is still ample space for the several applications of the combined methods; in short, the choice must always suit the individual patient.

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