

Sexual side effects of oral contraceptives: clinical considerations

Cynthia A. Graham, PhD

ABSTRACT Oral contraceptives have offered many women worldwide the freedom to engage in heterosexual intercourse with minimal fear of pregnancy, as well as other health benefits. Ironically, these agents are also responsible for adverse sexual effects, such as decreased desire, which may limit or inhibit sexual activity. Recent research suggests that emotional and sexual side effects may be strong determinants of whether a woman continues to use “the pill.” However, because of limited research, it is impossible to determine which women are likely to experience adverse sexual effects or which formulations are responsible for such effects. Nevertheless, potential negative impact on sexuality must be discussed with patients when prescribing these agents. If side effects arise, proper and timely management is necessary, with diligent follow-up of sexual and nonsexual concerns.

The majority of women in the United States spend a good many years engaging in vaginal intercourse during their procreative period; hence, finding an effective contraceptive method directly relates to their sexual function and satisfaction. Each year, approximately 3 million unwanted pregnancies occur in this country, and 1.5 million end in abortion.¹ Oral contraceptives (OCs) remain the most popular reversible method of contraception in this country, enabling women to engage and enjoy vaginal intercourse with little fear of pregnancy. However, US surveys report annual discontinuation rates of 29% among OC users,² with a much higher percentage among adolescents.³

Research has shown that the presence of side effects is a major factor associated with early discontinuation of OCs,⁴ but few studies have attempted systematic assessment of these effects, thus limiting our understanding of these agents' impact on sexual function. Moreover, existing studies have focused on cycle control and physical side effects (eg, skin changes, bloating) on women, with only superficial attention paid to emotional effects, and even less to sexuality-associated changes.

Benefits of oral contraceptives

In addition to offering a safe contraceptive method, OCs may confer other clinical benefits for users. Some women report positive effects on their sexuality, mostly associated with the freedom from worries about pregnancy

Practice Tips

- When prescribing oral contraceptives discuss the possibility of adverse sexual effects, such as decreased sexual desire, suggesting that if such occur, switching to another OC or stopping the pill altogether should be considered.
- Discuss possible alternative methods of birth control when appropriate.
- Inquire directly about potential changes in sexual function in women using oral contraceptives. Patients may not volunteer this information unless asked directly by their physicians.
- Ask about any history of sexually transmitted infection in the patient and/or the partner. If positive, suggest use of a barrier contraceptive method as a complimentary or an alternative

Cynthia A. Graham, PhD

Clinical Assistant Professor
Gender Studies and Department of Psychiatry
Indiana University
Director of Graduate Education
The Kinsey Institute for Research in Sex,
Gender, and Reproduction
Bloomington, Indiana

and the ability to engage in spontaneous and uninterrupted sexual activity at will. It is also possible that women who are more positive about their sexuality are more likely to be using OCs.

Menstrual symptoms. Current low-dose OC formulations can offer the added benefits of reducing premenstrual or menstrual symptoms, such as breast tenderness, menstrual cramps, and bloating,⁵ which are often associated with the menstrual cycle, as well as regulating the cycle itself.

Additional benefits. Other possible benefits, with indirect impact on sexuality, may be associated with the specific hormonal combination of estrogen and progestin contained in many of the currently used low-dose formulations (Table 1).

The combination of ethinyl estradiol and norgestimate in some OC formulations is thought to increase sex hormone-binding globulin, which decreases free testosterone, thereby diminishing severity of acne in otherwise healthy women. However, few studies have examined sexual side effects on women using OCs to treat acne. European studies of the treatment of acne with OCs, including the antiandrogen cyproterone acetate, have shown adverse sexual effects in a proportion of women, indicating that further research is needed. In the United States, the only OC formulation approved by the FDA for the treatment of acne is Ortho Tri-Cyclen[®]. When prescribing this agent for this purpose, keep in mind that while improving acne, it may inadvertently affect the woman's sexual function. Inquiring about sexual function in this connection may therefore be appropriate.

The risk of endometrial and ovarian cancer decreases in a duration-dependent manner with OC use. Such protective effects have been documented up to 30 years after cessation of OC use.^{6,7} A recent British study shows that ovarian cancer risk in particular is sig-

TABLE 1 Some commonly used low-dose oral contraceptives

Drug	Contents
Estrogen-progestin combination	
Levlen [®]	0.03 mg ethinyl estradiol; 0.15mg levonorgestrel
Levora [®]	0.03 mg ethinyl estradiol; 0.15 mg levonorgestrel
Lo/Ovral [®]	0.03 mg ethinyl estradiol; 0.3 mg norgestrel
Nordette [®]	0.03 mg ethinyl estradiol; 0.15 mg levonorgestrel
Alesse [®]	0.02 mg ethinyl estradiol; 0.1 mg levonorgestrel
LevLite [®]	0.02 mg ethinyl estradiol; 0.1 mg levonorgestrel
Demulen [®] 1/35	0.035 mg ethinyl estradiol; 1.0 mg ethynodiol diacetate
Loestrin [®] 1.5/30	0.030 mg ethinyl estradiol; 1.5 norethindrone acetate
Ortho-Cyclen [®]	0.035 mg ethinyl estradiol; 0.25 mg norgestimate
Ortho-Cept [®]	0.030 mg ethinyl estradiol/0.15 mg desogestrel
Ortho-Novum [®] 1/35	0.035 mg ethinyl estradiol/1.0 mg norethindrone
Zovia 1/35 [®]	0.035 mg ethinyl estradiol; 1.0 mg ethynodiol diacetate
Triphasic formulation	
Ortho Tri-Cyclen [®] 1	0.035 mg ethinyl estradiol; 0.18 mg/0.215 mg/0.25 mg norgestimate
Triphasil [®]	0.030 mg/0.040 mg/0.030 mg ethinyl estradiol; 0.050 mg/0.075 mg/0.125 mg levonorgestrel
Ortho Novum [®] 7/7/7	0.035 mg ethinyl estradiol; 0.5 mg/0.75 mg/1 mg norethindrone
Progestin-only formulations	
Micronor [®]	0.35 mg norethindrone
Nor-Q.D. [®]	0.35 mg norethindrone
Ovrette [®]	0.075 mg norgestrel

1. Ortho Tri-Cyclen[®] has received FDA-approval for the treatment of moderate acne in women age 15 years who have achieved menarche, desire contraception, and are unresponsive to topical anti-acne treatments (and have no contraindications to OC therapy).

nificantly reduced in women who use OCs at some point in their lives compared to nonusers.⁸

Another indirect effect of OC is its protection against osteoporosis, which in its advanced stages may significantly affect sexual function. A large meta-analysis showed positive effects of low-dose OCs on bone mineral density in 9 out of 13 studies.⁹

Negative aspects of oral contraceptives

Even with these benefits, and even with the use of current low-dose OC formulations, a substantial proportion (29%) of women who begin taking these agents discontinue their use within the first few months.

Reduced desire. Clearly, many women starting an OC regimen do not experience adverse sexual effects (Table 2), but research has shown that a minority of women experience significant reduction in sexual desire after starting an OC regimen.¹⁰ Although these agents have been used for over 40 years now, we still do not know what makes some women likely to have adverse sexual effects as a result of using an OC, nor do we know which formulations are likely to produce such effects. We also do not understand the mechanisms that may underlie the effects of OCs on sexuality.

Lack of compliance. Inappropriate use of OCs is common. One survey found that 50 out of 1000 “typical users” of OCs become pregnant over 1 year.² Most of these pregnancies are caused by the woman “skipping” days, or not following the regimen as instructed. Unless it is clearly explained, some women may not realize the risk involved in not taking the OC tablet on days that they are not sexually active. A woman who misses tablets or is late starting a new packet of OCs should be encouraged to use a back-up method of contraception until she has correctly taken seven consecutive tablets.

Sexually transmitted infections. It is important to explain to all women that, unlike condoms, use of OC provides no protection against sexually transmitted infections (STIs). Because barrier methods of contraceptions are the only means to prevent transmission of STIs, including HIV infection, it is good practice to inquire about any history of STIs, especially among young persons, before prescribing this type of contraception. Questions should also reflect the possibility of infection in the partner. If you suspect the presence or history of an STI, discuss the risk of infection exposure and/or transmission as well as the need for “safe sex,” before prescribing an OC. Consider mentioning the use of condoms as an added protection in such cases.

Lack of research—a gender bias?

Why has the issue of possible OC-associated adverse sexual effects in women not received the research attention it deserves? Most prospective studies conducted decades ago involved high-dose formulations that are no longer in use. With the introduction of lower-dose agents, interest in potential adverse sexual effects of OCs has waned considerably. A widely held view suggests that any OC-associated sexual and emotional adverse effects are both “transient” and “trivial.” Even if some such effects are transient (which is yet to be

TABLE 2 Possible impact of oral contraceptives on human sexuality

Negative consequences	Benefits
■ May diminish sexual desire	Fewer worries about pregnancy
■ Discontinuation of contraceptive method	Increased intercourse frequency, if desire intact
■ No protection from sexually transmitted infections	No interruption to sexual spontaneity, as in barrier methods
■ Forgetting to take the tablet	Reduced premenstrual symptoms

established regarding sexuality or mood), it has been shown that early adverse sexual effects are common reasons for discontinuing this contraceptive method.⁴ Compared with other clinical conditions, sexual side effects may indeed be deemed “trivial,” but we must not underestimate their impact on a woman’s quality of life as well as on her and her partner’s relationship satisfaction. Remember also that many women take OCs for a number of years, thus, ongoing effects on their sexual relationship may be of considerable concern.

Another obstacle to research has been the view that subjective variables, such as sexual desire and enjoyment, are extremely difficult to assess. These difficulties are compounded with regards to OCs, even when placebo controls are used.¹¹ Nevertheless, several studies investigating such variables have been conducted, including placebo-controlled ones, and these have demonstrated adverse effects on sexuality with OC use.^{5,12}

It is intriguing to note that studies on the male oral contraceptive pill—although still in the development phase—have already included assessment of possible adverse sexual effects.^{13,14}

Most studies conducted on low-dose OC formulations in women have been cross-sectional comparisons of OC-users and nonusers, a design that does not lend itself to investigating possible direct side effects on sexual function. Consequently, these studies report few or no differences in sexual function between OC-users and control groups, with little acknowledgment of any study-design limitations. In studies of established OC-users, women who experience adverse sexual effects are likely to have selected themselves out by discontinuing use of that contraceptive method.

Recent studies: hormonal effects and high discontinuation rate

In contrast to the large number of cross-sectional comparisons of OC-users and nonusers, only a handful of studies have involved either (1) placebo-controlled, double-blind assessment of the possible direct pharmacologic effects on women starting OCs, or (2) pre-OC assessment of characteristics of women about to start on such agents for contraceptive purposes, and follow-up to assess possible interactions between psychological factors and the direct hormonal effects of these drugs.

Adverse sexual effects. One example of the first type involved 150 women from Manila (Philippines) and Edinburgh (Scotland) who had been sterilized, or whose partners had been vasectomized.¹² This placebo-controlled, double-blind study design involved only physiologic (and not psychological) issues of contraception. (To ensure “blindness,” the women in this study did not know which OC they were on—36% of the Edinburgh placebo-receiving subjects and 20% of the Manila placebo-receiving subjects believed they had received an active OC, only 28% to 36% of Manila subjects and 76% to 80% of Edinburgh subjects taking an active OC believed they received an OC—and researchers had no knowledge of the participants' bleeding patterns.)

After 1 month of pretreatment assessment, the women were randomly assigned to one of three groups—low-dose combination OC (ethinyl estradiol 0.03 mg + levonorgestrel 0.15 mg), progestin-only OC (levonorgestrel 0.03 mg), or placebo. Treatment and assessment continued for 4 months, including daily ratings of mood, sexuality, and bleeding; detailed interviews on sexual functioning; and standardized measures of mood and relationship satisfaction, with only 4 women out of 150 discontinuing treatment.

Main results showed reduced sexual desire with use of the combined OC, and, to a lesser extent, reduced frequency of sexual activity in the Scottish women; half of the combined OC-users reported this as a negative effect. In Manila, sexual desire was not significantly reduced, possibly the result of a significantly lower sexual interest and more negative sexual relationships before starting OCs. In both centers the progestin-only OC was associated with no adverse sexual effects. Although this result was surprising, it could possibly occurred because the dose of progestin in the progestin-only formulation was quite low compared with

the higher level of progestin in the combined OC. These adverse effects of the combined OC may have proved transient if treatment had extended beyond 4 months; however, given that the highest OC discontinuation rates occur in the first few months, these findings warrant further consideration.

Kinsey Institute's new findings. A recent study of the second type, conducted at the Kinsey Institute, involved comprehensive assessment of pre-OC use and follow-up over the first 12 months of use.¹⁵ Assessment included pre-OC attitudes and expectations about OCs, self-reported side effects, premenstrual and menstrual symptoms, sexual interest and enjoyment, and sexual activity frequency. Women were randomized into one of two low-dose OC types—monophasic (Ortho-Cyclen®) or triphasic (Ortho Tri-Cyclen®). After 12 months, 38% of the women were still taking OCs, 47% had discontinued, and 14% had switched to another OC. Reasons for discontinuation or switching are listed in Table 3.

This study included careful assessment of pre-OC characteristics, such as social and situational variables and expectations about the OC effects that may be associated with discontinuation, but only one baseline measure (number of previous contraceptive methods used) was predictive of discontinuation. In contrast, the variables that had been intended to assess change in sexual or emotional well-being with use of OC—decreased frequency of sexual thoughts, decreased psychosexual “arousability,” emotional side effects, and worsening of premenstrual symptoms—instead turned out to be strong predictors for discontinuation of the “pill.”

TABLE 3 Common reasons for discontinuing/switching oral contraceptives

Reason	Percentage (%)
Physical side effects	37
Emotional side effects	33
Problems with bleeding or spotting	18
Relationship ended	18
Forgetting to take oral contraceptive	16
Sexual side effects	8
Medical reasons	4

Data from Sanders SA, Graham CA, Bass JL, et al.¹⁵

Possible mechanisms underlying adverse sexual effects

We remain ignorant of the mechanisms underlying adverse effects of OCs on sexuality. Although general well-being and mood are related to sexual desire, it is unlikely that negative effects on sexuality are secondary to negative mood change.¹⁶ One study showed that current low-dose OCs significantly decrease free testosterone levels in women,¹⁷ and speculation has focused on this as the explanation for OC-induced reduced desire. The same study found decreased androgen levels when women were taking any of four low-dose formulations of OCs.¹⁷ However, to date, no studies have measured the change in testosterone level from baseline to post-onset of OC use and the impact on sexuality. It has long been believed that progestins have a negative effect on sexual desire, and some have seen the progestin component of the OC formulations as the culprit in adverse sexual effects. However, at this point this is speculative, as we have no data to support this assumption.

Moreover, we have very limited evidence on whether certain types of OC formulations are more likely to be associated with adverse effects on sexuality. Graham and colleagues' study¹² on progestin-only OCs and sexuality found that no decrease in sexual interest occurred with use of progestin-only OCs, but no conclusions should be reached from one study. The progestin level used in progestin-only formulations is significantly lower than that used in combination OCs. More evidence is needed to explain this discrepancy. Even though progestins contained in OCs vary in their androgenic properties, they all substantially reduce testosterone levels.¹⁷

As of now, progestin effects, and reduced free testosterone are two possible explanations, among others, for loss of sexual desire associated with OC use.

Clinical implications

Prescribing OCs (Table 4) provides an obvious opportunity to ask women about sexual issues. When discussing the benefits and risks of OCs, also include the possibility of adverse sexual effects, adding that if such occur, it may be useful to discuss them before discontinuing use of this contraceptive method. The likelihood is that some clinicians rarely inquire about possible sexual or emotional side effects, and some may not take women's reports about such changes seriously. Some may even feel that drawing attention to such

TABLE 4 Prescribing oral contraceptives: practical tips

- Ask about sexual function and any history of STIs in the patient and/or the partner
- Emphasize need to follow regimen correctly; noncompliance is a common reason for unwanted pregnancy
- Inform patients about the possible effects (positive and negative) of OCs on sexuality
- Inquire about any changes, positive or negative, in a woman's sexual functioning since starting the OC
- If the onset of loss of sexual desire coincides with use of OC, discuss the possibility of switching to another formulation or switching to another contraceptive method
- If the latter option is chosen, discuss possible alternative forms of birth control
- If patient reports loss of sexual desire or other sexual issues, take a thorough sexual history and investigate appropriate treatment. If necessary, consider referral to a sexual therapist

OC = Oral contraceptives; STI = Sexually transmitted infections.

effects increases their likelihood and should therefore be avoided.

Keep in mind that many women are reluctant to raise a sexual concern with their physician because they are not sure how the physician will respond. By inquiring about potential changes in sexual function with OCs, you will communicate to patients that you are open to talking about sexual matters. Women are much more likely to discuss sexual problems when physicians inquire directly, which can be done in the context of a general health assessment simply by asking, "How are things in your sexual life?" or "Do you have any concerns in the sexual area?"¹⁸

Especially in young women, take a thorough sexual history. Bear in mind the high incidence of STIs among young people and the asymptomatic or recurrent nature of some infections.

Conclusion

Oral contraceptives have the potential to cause sexual side effects in a subgroup of women, and these adverse effects may be highly relevant to discontinuation. More

research is needed to identify characteristics of women most likely to experience sexual side effects as well as which OC formulations are likely to be responsible for these effects. Encourage women to discuss sexual and emotional effects of OCs with you in much the same way as they report other side effects, such as bleeding, headaches, or breast tenderness. ♂

References

1. Abma J, Chandra A, Mosher W, et al. Fertility, family planning and women's health: new data from the 1995 National Survey of Family Growth. National Center for Health Statistics. *Vital Health Stat* 23(19):1-114, 1997.
2. Hatcher RA, Trussell J, Stewart F, et al. *Contraceptive Technology*, 17th ed. New York: Ardent Media, 1998.
3. Zibners A, Cromer BA, Hayes, J. Comparison of continuation rates for hormonal contraception among adolescents. *J Pediatr Adolesc Gynecol* 12(2):90-94, 1999.
4. Rosenberg MJ, Waugh MS. Oral contraceptive discontinuation: a prospective evaluation of frequency and reasons. *Am J Obstet Gynecol* 179: 577-82, 1998.
5. Graham CA, Sherwin BB. A prospective treatment study of premenstrual symptoms using a triphasic oral contraceptive. *J Psychosom Res* 36(3):257-66, 1992.
6. Schlesselman JJ. Risk of endometrial cancer in relation to use of combined oral contraceptives: a practitioner's guide to meta-analysis. *Hum Reprod* 12:1851-63, 1997.
7. Ness RB, Grisso JA, Klapper J, et al. Risk of ovarian cancer in relation to estrogen and progestin dose and use characteristics of oral contraceptives. *Am J Epidemiol* 152:233-41, 2000.
8. Beral V, Hermon C, Kay C, et al. Mortality associated with oral contraceptive use: 25 year follow-up of cohort of 46000 women from Royal College of General Practitioners' oral contraception study. *BMJ* 318(7176):96-100, 1999.
9. Kuohong W, Borgatta L, Stubblefield P. Low-dose oral contraceptives and bone mineral density: an evidence-based analysis. *Contraception* 61:77-82, 2000.
10. Bancroft J, Sartorius N. The effects of oral contraceptives on well being and sexuality. *Oxf Rev Reprod Biol* 12: 57-92, 1990.
11. Goldzeiger JW, Zama NM. Oral contraception side effects: where's the beef? *Contraception* 52(6):327-35, 1995.
12. Graham CA, Ramos R, Bancroft J, et al. The effects of steroidal contraceptives on the well-being and sexuality of women: a double-blind, placebo-controlled, two center study of combined and progestagen-only methods. *Contraception* 52(6):363-69, 1995.
13. Anderson RA, Bancroft J, Wu FCW. The effects of exogenous testosterone on sexuality and mood of normal men. *J Clin Endocrinol Metab* 75(6):1503-7, 1992.
14. Sjogren B, Gottlieb C. Testosterone for male contraception during one year: attitudes, well-being and quality of sex life. *Contraception* 64(1):5965, 2001.
15. Sanders SA, Graham CA, Bass JL, et al. A prospective study of the effects of oral contraceptives on sexuality and well-being and their relationship to discontinuation. *Contraception* 64(1):51-58, 2001.
16. Graham CA, Sherwin BB. The relationship between mood and sexuality in women using an oral contraceptive as a treatment for premenstrual symptoms. *Psychoneuroendocrinology* 18(4):273-81, 1993.
17. Coenen CMH, Thomas CMG, Hollanders JMG, et al. Changes in androgens during treatment with four low-dose contraceptives. *Contraception* 53(3):171-76, 1996.
18. Basson R. Clarifying the complaint of low sexual desire in men and women. *Med Asp Human Sex* 1(4):39-42, 2001.