

Unscheduled bleeding in combined oral contraceptive users: focus on extended-cycle and continuous-use regimens

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Abstract

Combined oral contraceptives (COCs) are highly effective when correctly used but unscheduled bleeding, which occurs fairly commonly during the early months, is disruptive for many women. The mechanisms underlying this bleeding are not fully understood. Several studies have shown that extended-cycle or continuous-use COCs are typically associated with higher initial rates of unscheduled bleeding than are conventional 21-day cyclical COCs. Some medicines, herbal supplements and smoking may increase unscheduled bleeding by interfering with estrogen metabolism. The most common

cause of unscheduled bleeding is non-adherence to a prescribed COC regimen. Compliance can be improved by appropriate counselling of women about the possibility of unscheduled bleeding and the importance of adherence to the pill regimen. If abnormal bleeding persists beyond 3–4 months and causes such as incorrect usage can be ruled out, other causes should be considered.

Keywords combined oral contraceptives, continuous-use COCs, extended-cycle COCs, unscheduled bleeding

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Introduction

Combined oral contraceptives (COCs) provide excellent contraceptive efficacy and also give many women improved cycle control, reduced cycle-related pain, and reduced volume of menstrual loss.^{1,2} Unscheduled bleeding requiring sanitary protection is a common side effect of COCs. Such bleeding occurs most commonly during the first 3 months of COC use³ but it may persist and continue to be disruptive and troublesome for many women.

There is increasing interest in the potential health and lifestyle benefits of extended-cycle or continuous-use COCs.⁴ Although these COC regimens are associated with higher initial rates of unscheduled bleeding compared with conventional 21-day cyclical COCs,⁵ for many women the benefits of reducing or even eliminating monthly bleeding may outweigh the inconvenience of such unscheduled bleeding. This review describes the occurrence, causes and management of unscheduled bleeding associated with COCs, particularly with regard to extended-cycle or continuous-use preparations.

Methods

Relevant articles were obtained through a PubMed search of the literature. Key search terms included “unscheduled bleeding” and “breakthrough bleeding” in combination with “combined oral contraceptive” or “combined oral contraception”.

Assessment of bleeding patterns

There is lack of uniformity in the analysis and reporting of bleeding patterns. Recognising this, the World Health

Key message points

- Unscheduled bleeding is a common side effect of combined oral contraceptives (COCs).
- Women should be counselled appropriately about the possibility of unscheduled bleeding and the importance of adherence to a pill regimen.
- Those considering extended-cycle or continuous-use regimens should be advised that unscheduled bleeding may be more common in the first 3–4 months of use.
- A short, hormone-free interval may be an effective clinical management strategy for disruptive unscheduled bleeding in women on continuous COC regimens.
- Persistent or new-onset unscheduled bleeding may be due to incorrect usage or to cervical or other pathology.

Organization (WHO) issued recommendations in 1986 for the standardised collection, analysis and reporting of bleeding associated with contraceptive use in clinical studies. The WHO recommended the use of ‘reference periods’ rather than cycles because of the variability in the length of menstrual cycles both within and between individual women. It was therefore proposed that bleeding outcomes be measured using reference periods of at least 90 days.^{6,7} Recently, Mishell and colleagues⁸ published new recommendations for the standardisation of data collection and analysis of bleeding in studies of hormonal contraception.

How prevalent is unscheduled bleeding and what causes it?

In studies of inadvertent pregnancies in COC users, the proportion of women who experienced unscheduled bleeding ranged from 16% to 21%.^{9,10} A recent literature review suggested that irregular bleeding is most common during the first cycle of COC use and that this decreases with longer-term use and strict compliance. The number of bleeding/spotting days for all COCs ranged between 10 and 24 days for the first 90-day reference period but decreased to between 7.5 and 15 days by reference period 4.¹¹

For women from many different cultures, regular patterns of vaginal bleeding are central to beliefs concerning fertility, absence of pregnancy and reproductive health. For some women, the presence of irregular or unpredictable bleeding is a barrier to social, sexual and cultural activities

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and hence represents a major disruption to their lives. In some societies due to social traditions there may be restriction of social, religious or domestic activities during the days of bleeding. Unscheduled bleeding with COCs may be sufficiently troublesome to lead some women to discontinue their use. In a study of 1657 women starting or restarting COCs in the USA, 12% of subsequent discontinuations were attributed to bleeding irregularities.¹²

COCs comprise an estrogen component [typically ethinylestradiol (EE)] and a progestogen component. The trend in COC formulations has been towards lower doses of both sex steroids, but lower doses of estrogen may be insufficient to sustain endometrial support, leading to unscheduled bleeding.¹³ In a study comparing COCs containing the same amount of progestogen with two different doses of EE, the formulation containing less EE was associated with a higher incidence of unscheduled bleeding.¹⁴ However, progestogen-induced decidualisation and endometrial atrophy may also contribute to the problem.³

Do variations in COC formulation or regimen affect the occurrence of unscheduled bleeding?

In addition to the dose of sex steroid hormones, the formulation and regimen of COCs may affect the incidence of unscheduled bleeding. In a study that compared two COCs containing 20 µg EE and either 100 µg levonorgestrel (LNG) or 500 µg norethisterone, the frequency of unscheduled bleeding was significantly less with LNG.¹⁵ There is also evidence that the ratio of estrogen to progestogen may affect the incidence of unscheduled bleeding.¹⁶

Prescribing schedules may also be important. Extended-cycle or continuous-use COCs are typically associated with higher initial rates of unscheduled bleeding than are conventional 21-day cyclical COCs.⁵ One study randomised women ($n = 682$) to receive a COC containing 150 µg LNG and 30 µg EE according to an extended-cycle regimen (84 days of active pills followed by a 7-day hormone-free interval) or a conventional cyclical regimen (21 days of active pills followed by a 7-day hormone-free interval) over 1 year.⁵ Women on the extended-cycle regimen reported a mean 37.6 (11% of 336 possible days) unscheduled bleeding/spotting days vs 18.3 (7% of 273 possible days) for women on the conventional cyclical regimen. In a separate study, 708 women were treated with a 91-day extended-cycle COC (150 µg LNG/30 µg EE).¹⁷ Each cycle consisted of 84 days of active pills followed by 10 mg EE daily for 7 days. The mean number of unscheduled bleeding/spotting days was highest during cycle 1 (14.3) and generally subsided over time (9.5, 7.2, and 7.6 days for cycles 2, 3, and 4, respectively).

Most recently, a large Phase III trial ($n = 2134$) evaluated the safety and efficacy of cycle-free LNG/EE (90 µg/20 µg), a continuous-use COC in clinical development for daily use without a hormone-free interval.¹⁸ It has recently been approved by the US Food and Drug Administration and is currently being evaluated by the European Medicines Agency. Over the 1-year trial (13 pill packs), the number of bleeding and spotting days per pill pack declined progressively; by pill packs 6 and 13, the incidence of bleeding was 33.8% and 21%, respectively. In a separate trial ($n = 641$) conducted over 12 months, women were randomised to receive 13 packs of cycle-free LNG/EE or a 21-day cyclical COC (LNG 100 µg /EE 20 µg).¹⁹ Among the women who received cycle-free LNG/EE, the percentage who experienced unscheduled bleeding decreased with each pill pack (50% at pill pack 3

vs 21% at pill pack 13). After pill pack 4, the median number of days of unscheduled bleeding and/or spotting was lower with cycle-free LNG/EE than with the cyclical preparation.

How do concomitant medications and smoking affect the occurrence of unscheduled bleeding?

Medicines and herbal supplements that induce the cytochrome P450 enzyme system may affect the metabolism of COCs, reducing their efficacy and increasing the risk of unscheduled bleeding. These concomitant medications may include the antituberculosis agent rifampicin,²⁰ antiretrovirals and St John's Wort.²¹ A comprehensive review of the literature on drug interactions between COCs and antibiotics identified case reports suggesting a relationship between use of griseofulvin and the occurrence of oligomenorrhoea, irregular menses, and unplanned pregnancy.²⁰

Smoking may increase the incidence of unscheduled bleeding by altering estrogen metabolism and consequently diminishing endometrial support.²² In a study that evaluated data from three trials ($n = 2956$) for six consecutive menstrual cycles, a significantly higher proportion of smokers reported unscheduled bleeding during each cycle ($p \leq 0.039$).²³ Smokers were 47% more likely to have unscheduled bleeding than non-smokers, with higher levels of smoking associated with a greater frequency of unscheduled bleeding.

What role does compliance play in unscheduled bleeding?

The most common cause of unscheduled bleeding is missed pills (non-adherence to a prescribed COC regimen). In a prospective study evaluating the effect of deliberate omission of two consecutive COC tablets (days 6/7 or days 11/12), missed pills resulted in an episode of unscheduled bleeding in 10 out of 12 cycles.²⁴ Even delaying taking COCs for a few hours may increase the risk of unscheduled bleeding.²²

Women generally admit to missing pills in far fewer self-reported cycles than if the pill-taking is objectively recorded. Potter *et al.*²⁵ compared self-reported data on pill-taking with data from an electronic device measuring compliance. In 3 months of pill use, the electronic and self-reported data agreed on the number of days when pills were missed in only 45% of cases; the level of agreement dropped from 55% in the first month to 38% in the third month. In each month, the proportion of women reporting no missed pills was much higher than the proportion recorded electronically (53–59% compared with 19–33%), and the proportion missing at least three pills according to the electronic data was triple that derived from the women's reports (30–51% vs 10–14%). In addition, the electronic data recorded substantially more episodes in which women missed pills on two or more consecutive days (88 vs 30). This study very clearly showed that 'compliance' was much worse than the individual women were prepared to admit.²⁵

In a study of 943 women in the USA, those who reported unscheduled bleeding or spotting were 1.6 to 1.7 times more likely to have missed two or more pills per cycle than those who did not.²⁶ In a study of 6676 women in Denmark, France, Italy, Portugal and the UK that examined adherence behaviour among OC users, 19% of the subjects stated that they generally miss one or more pills per cycle and 10% miss two or more.²⁷ Moreover, women who did not have an established pill-taking routine were over three times more likely to miss pills compared

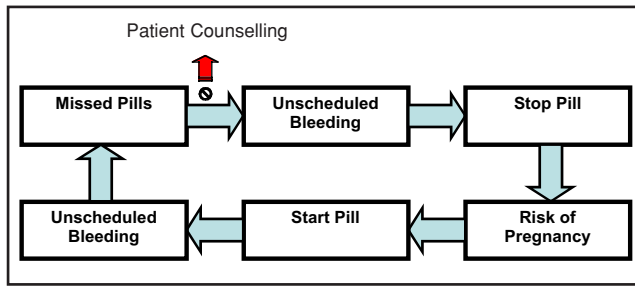


Figure 1 Proper patient counselling on adherence to a prescribed regimen may help avoid the cycle of unscheduled bleeding associated with oral contraceptives

with those with a routine. These women were also 4.6 times more likely to be among the group of women who missed two or more pills.

How important is proper patient counselling in managing unscheduled bleeding?

Correct COC use is influenced by the occurrence of side effects, the pill-taking routine, and whether a woman has read and/or understood relevant package information.²⁸ Those women who are aware of the possibility of unscheduled bleeding before beginning a new COC prescription are more likely to tolerate short-term changes to their bleeding profile.²⁹ However, side effects with COC are mild and are less important reasons for discontinuation than is widely believed.³⁰

The best way to ensure that women receive appropriate information about bleeding irregularities with COCs is proper patient counselling, particularly with regard to the importance of adherence to a prescribed pill regimen (Figure 1). This may minimise the risk of missed pills and the occurrence of unscheduled bleeding. Unfortunately, many women do not receive adequate counselling. Rosenberg *et al.*²⁷ reported that nearly 50% of women said that they did not receive appropriate information from their health care provider when their COC was first prescribed. These women were approximately 1.5 times more likely to be inconsistent COC users than those who were satisfied with the counselling they received. A survey of knowledge about COCs in 649 women waiting at pharmacies to receive new prescriptions for COCs indicated that a significant proportion of the women had not been counselled about common side effects of COCs.³¹ For instance, 65.5% and 46.1% of women had not been counselled about unscheduled bleeding and missed pills, respectively. Those who had been counselled had higher levels of understanding about COCs. There may also be disparities between the information that physicians believe they are providing about COCs and what patients report that they have been told.³² Written information may be useful in this regard.

How should providers counsel patients regarding unscheduled bleeding, particularly with regard to extended-cycle and continuous-use COCs?

Patient counselling should include information about the potential for unscheduled bleeding, a clear explanation of how to take the COC, information about the possible consequences of missed or delayed pills, and the benefits of a pill-taking routine. Providers should stress the likely transient nature of unscheduled bleeding and encourage questions, particularly for those women who are first-time COC users or who have not used COCs recently.¹²

Although unscheduled bleeding during the first 3–4

months of cyclical COC use is common, extended-cycle or continuous-use COCs may be associated with a longer duration of unscheduled bleeding as well as higher rates in the initial months of use.³³ Women considering extended-cycle or continuous-use COCs should be counselled about the need to weigh the convenience of no (or fewer) planned bleeds against the inconvenience of increased unscheduled bleeding. The benefit of a pill-taking routine should be emphasised.

Providing clear and appropriately targeted educational materials regarding the proper use of COCs, particularly written information, is useful and also used by patients. This has a significant impact on raising awareness and increasing contraceptive knowledge³⁴ and many of these resources are available online.

Are there any clinical strategies to manage unscheduled bleeding with extended-cycle and continuous-use COCs?

Currently, there is little evidence from well-designed, randomised studies on clinical strategies for the management of unscheduled bleeding associated with extended-cycle and continuous-use COCs. However, a recent prospective study assessed the occurrence and management of unscheduled bleeding during continuous use of a COC (drospirenone 3 mg/EE 30 µg) over 168 days.³⁵ Instituting a 3-day hormone-free interval was more effective in resolving unscheduled bleeding/spotting than was continuing active pills ($p < 0.0001$).

What should be done for prolonged unscheduled bleeding?

If unscheduled bleeding on COCs persists beyond 3–4 months and causes such as incorrect usage can be ruled out, pathological or physiological causes should be considered. In women with persistent unscheduled bleeding or spotting on a COC and in whom pathological causes have been excluded, we usually recommend changing to another formulation. One study of 65 COC users with unscheduled bleeding found that 29.2% tested positive for endocervical *Chlamydia trachomatis*, compared with 10.7% in matched controls.³⁶ Thus persistent unscheduled bleeding warrants physical examination to rule out any local lower genital tract causes such as cervical ectropion and invasive cervical cancer, and appropriate investigations should be instituted based on the history and examination findings. Possible upper genital tract causes of unscheduled bleeding include endocervical or endometrial infection, endocervical cancers, endometrial polyps, submucous myomas, cervical cancer and pelvic inflammatory disease.²²

Unscheduled bleeding is a common unwanted effect of combined oral contraceptives and may occur with all regimens. Clinicians should be aware that appropriate counselling and continuing support may improve compliance, and should remember to rule out pathology as a cause of the bleeding.

Statements on funding and competing interests

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Competing interests None identified.

References

- 1 The ESHRE Capri Workshop Group. Endometrial bleeding. *Hum Reprod Update* 2007; **14**: 1–11.

- 2 Breakthrough bleeding number one problem with OC use. *Contracept Technol Update* 1991; **12**: 185–190.
- 3 Schrager S. Abnormal uterine bleeding associated with hormonal contraception. *Am Fam Physician* 2002; **65**: 2073–2080.
- 4 Nelson AL. Extended-cycle oral contraception: a new option for routine use. *Treat Endocrinol* 2005; **4**: 139–145.
- 5 Anderson FD, Hait H. A multicenter, randomized study of an extended cycle oral contraceptive. *Contraception* 2003; **68**: 89–96.
- 6 Mishell DR Jr, Guillebaud J, Westhoff C, Nelson AL, Kaunitz AM, Trussell J, *et al*. Combined hormonal contraceptive trials: variable data collection and bleeding assessment methodologies influence study outcomes and physician perception. *Contraception* 2007; **75**: 4–10.
- 7 Belsey EM, Machin D, d'Arcangues C. The analysis of vaginal bleeding patterns induced by fertility regulating methods. World Health Organization Special Programme of Research, Development and Research Training in Human Reproduction. *Contraception* 1986; **34**: 253–260.
- 8 Mishell DR Jr, Guillebaud J, Westhoff C, Nelson AL, Kaunitz AM, Trussell J, *et al*. Recommendations for standardization of data collection and analysis of bleeding in combined hormone contraceptive trials. *Contraception* 2007; **75**: 11–15.
- 9 Sparrow MJ. Pill method failures. *N Z Med J* 1987; **100**: 102–105.
- 10 Kovacs GT, Riddoch G, Duncombe P, Welberry L, Chick P, Weisberg E, *et al*. Inadvertent pregnancies in oral contraceptive users. *Med J Aust* 1989; **150**: 549–551.
- 11 Bachmann G, Korner P. Bleeding patterns associated with oral contraceptive use: a review of the literature. *Contraception* 2007; **76**: 182–189.
- 12 Rosenberg MJ, Waugh MS. Oral contraceptive discontinuation: a prospective evaluation of frequency and reasons. *Am J Obstet Gynecol* 1998; **179**(3 Pt 1): 577–582.
- 13 Kaunitz AM. Oral contraceptive estrogen dose considerations. *Contraception* 1998; **58**(3 Suppl.): 15S–21S.
- 14 Akerlund M, Rode A, Westergaard J. Comparative profiles of reliability, cycle control and side effects of two oral contraceptive formulations containing 150 micrograms desogestrel and either 30 micrograms or 20 micrograms ethinyl estradiol. *Br J Obstet Gynaecol* 1993; **100**: 832–838.
- 15 Endrikat J, Hite R, Bannemerschult R, Gerlinger C, Schmidt W. Multicenter, comparative study of cycle control, efficacy and tolerability of two low-dose oral contraceptives containing 20 microg ethinylestradiol/100 microg levonorgestrel and 20 microg ethinylestradiol/500 microg norethisterone. *Contraception* 2001; **64**: 3–10.
- 16 Lawson JS, Yuliano SE, Pasquale SA, Osterman JJ. Optimum dosage of an oral contraceptive. A report from the study of seven combinations of norgestimate and ethinyl estradiol. *Am J Obstet Gynecol* 1979; **134**: 315–320.
- 17 Anderson FD, Gibbons W, Portman D. Safety and efficacy of an extended-regimen oral contraceptive utilizing continuous low-dose ethinyl estradiol. *Contraception* 2006; **73**: 229–234.
- 18 Archer DF, Jensen JT, Johnson JV, Borisute H, Grubb GS, Constantine GD. Evaluation of a continuous regimen of levonorgestrel/ethinyl estradiol: phase 3 study results. *Contraception* 2006; **74**: 439–445.
- 19 Teichmann AT, Kluff C, Grubb GS, Constantine G, Spielmann D. Comparative trial of continuous-use and 21-day cyclic levonorgestrel and ethinyl estradiol oral contraceptive. *Obstet Gynecol* 2006; **107**: 12S.
- 20 Dickinson BD, Altman RD, Nielsen NH, Sterling ML. Drug interactions between oral contraceptives and antibiotics. *Obstet Gynecol* 2001; **98**(5 Pt 1): 853–860.
- 21 Murphy PA, Kern SE, Stanczyk FZ, Westhoff CL. Interaction of St. John's Wort with oral contraceptives: effects on the pharmacokinetics of norethindrone and ethinyl estradiol, ovarian activity and breakthrough bleeding. *Contraception* 2005; **71**: 402–408.
- 22 Darney PD. OC practice guidelines: minimizing side effects. *Int J Fertil Womens Med* 1997; **Suppl. 1**: 158–169.
- 23 Rosenberg MJ, Waugh MS, Stevens CM. Smoking and cycle control among oral contraceptive users. *Am J Obstet Gynecol* 1996; **174**: 628–632.
- 24 Endrikat J, Wessel J, Rosenbaum P, Dusterberg B. Plasma concentrations of endogenous hormones during one regular treatment cycle with a low-dose oral contraceptive and during two cycles with deliberate omission of two tablets. *Gynecol Endocrinol* 2004; **18**: 318–326.
- 25 Potter L, Oakley D, de Leon-Wong E, Cañamar R. Measuring compliance among oral contraceptive users. *Fam Plann Perspect* 1996; **28**: 154–158.
- 26 Rosenberg MJ, Waugh MS, Burnhill MS. Compliance, counselling and satisfaction with oral contraceptives: a prospective evaluation. *Fam Plann Perspect* 1998; **30**: 89–92, 104.
- 27 Rosenberg MJ, Waugh MS, Meehan TE. Use and misuse of oral contraceptives: risk indicators for poor pill taking and discontinuation. *Contraception* 1995; **51**: 283–288.
- 28 Rosenberg MJ, Burnhill MS, Waugh MS, Grimes DA, Hillard PJ. Compliance and oral contraceptives: a review. *Contraception* 1995; **52**: 137–141.
- 29 Belsey EM. The association between vaginal bleeding patterns and reasons for discontinuation of contraceptive use. *Contraception* 1988; **38**: 207–225.
- 30 Westhoff CL, Heartwell S, Edwards S, Ziemann M, Stuart G, Cwiak C, *et al*. Oral contraceptive discontinuation: do side effects matter? *Am J Obstet Gynecol* 2007; **196**: 412e1–412e7.
- 31 Gaudet LM, Kives S, Hahn PM, Reid RL. What women believe about oral contraceptives and the effect of counselling. *Contraception* 2004; **69**: 31–36.
- 32 Rajasekar D, Bigrigg A, Docherty G. Nationwide audit of pill knowledge amongst family planning users in Scotland. *Eur J Contracept Reprod Health Care* 1999; **4**: 95–102.
- 33 Nelson AL. Communicating with patients about extended-cycle and continuous use of oral contraceptives. *J Womens Health (Larchmt)* 2007; **16**: 463–470.
- 34 Little P, Griffin S, Kelly J, Dickson N, Sadler C. Effect of educational leaflets and questions on knowledge of contraception in women taking the combined contraceptive pill: randomised controlled trial. *BMJ* 1998; **316**: 1948–1952.
- 35 Sulak PJ, Kuehl TJ, Coffee A, Willis S. Prospective analysis of occurrence and management of breakthrough bleeding during an extended oral contraceptive regimen. *Am J Obstet Gynecol* 2006; **195**: 935–941.
- 36 Krettek JE, Arkin SI, Chaisilwattana P, Monif GR. *Chlamydia trachomatis* in patients who used oral contraceptives and had intermenstrual spotting. *Obstet Gynecol* 1993; **81**(5 Pt 1): 728–731.

Winning the Publications Game: How to Write a Scientific Paper Without Neglecting Your Patients (3rd edition). Tim Albert. Oxford, UK: Radcliffe Publishing, 2009. ISBN-13: 978-1-84619-247-0. Price: £21.99. Pages: 114 (paperback)

This is the slightly revised third edition of an excellent publication that I recommend to anyone thinking about writing an article and getting it published. The style is commendably clear and the author is encouraging, which is unusual for books about writing. As the author says, look at why you want to write and what you need to write, sit down and do it. It doesn't take long, but it is work.

The book is laid out, as in the previous editions, following the 10-stage process that goes from the first idea to after publication.

Throughout the author points out that writing is not a difficult process, but should be regarded as producing a good product and marketing it well. If only more authors followed Tim Albert's advice about setting their brief out clearly before starting writing! The brief he recommends contains five steps: the message, the market, the length, the deadline and the co-authors. All too often, reviewing articles reveals that the authors have not stated the message they wish to convey. If they don't know, how will their readers? Many articles arrive at a journal clearly originally intended for another or without having consulted the authors' instructions – another 'must' Tim Albert outlines. Clarity of thought and writing is helped by looking at the following suggested questions: Why did we start? What did we do? What did we find? What does it all mean?

It is difficult to pick out points to illustrate

the worth of the book – to do so would involve an unnecessary reproduction of the contents of each chapter. For example, another of the things that irritates reviewers is when authors quote the findings of papers incorrectly. Tim Albert recommends that authors should actually read the references that they quote! To nitpick, I found the summary of achievements that appear at the end of each chapter slightly incongruous in a book; they are more applicable to course material (to convince the funders that you know what you are doing!).

If you want to write articles, this is an excellent concise primer. If you already write successfully, read it to improve your technique.

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