The management of irregular bleeding in women using contraception

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Background

The pattern of menstrual bleeding seen in women during their reproductive years is the result of a finely tuned balance between endogenous oestrogens, which stimulate the endometrial lining, and progesterone, which temporarily maintains that lining in anticipation of a pregnancy. Many women have expectations of a 'normal monthly' cycle, and may be wary of anything that has the potential to disrupt its regularity. From a clinical perspective, any alteration in vaginal bleeding may indicate underlying pathology, and lead to further investigation and management.

Objective

The aim of this article is to provide a practical approach to the investigation and management of altered vaginal bleeding patterns in women using various methods of contraception.

Discussion

Around 70% of Australian women of reproductive age use some form of contraception. Any discussion of 'normal bleeding' becomes even more complex given that modern contraceptive methods almost inevitably modify the pattern of bleeding experienced by the user.

Although contraceptive use is commonly associated with alterations in patterns of bleeding, the potential for unrelated pathology should always be considered. This is particularly the case if the change in bleeding pattern is a new development and/or accompanied by other symptoms. The possibility of pregnancy (intrauterine, ectopic, miscarriage, trophoblastic disease) should always be excluded since no contraceptive method is 100% effective. Irregular bleeding may also be due to underlying pathology, such as cervicitis, pelvic inflammatory disease, endometriosis, polyps, uterine fibroids or neoplasm. A careful history, gynaecological examination and appropriate investigations are important in determining which cases can be safely managed in a primary care setting and which need prompt specialist referral.

If abnormal/irregular bleeding is determined to be secondary to contraceptive use, management will depend on the:

- potential to modify the method to achieve a more suitable bleeding pattern
- patient's readiness to cope with an altered bleeding pattern
- suitability of alternatives.

Some of the issues that must be considered are outlined in Box 1.

Combined hormonal contraceptive methods

The oral contraceptive pill remains the most popular contraceptive method among Australian women.[1] Progestogen in combined contraceptives provides the major contraceptive effect, and oestrogen is added primarily to stabilise the bleeding pattern as an atrophic endometrium may result in asynchronous 'breakthrough' bleeding (BTB). Irregular bleeding is common in the first three to four months of combined oral contraceptive pill (COCP) use, occurring in up to 30% of women in the first cycle.[2]

The rate of BTB usually declines over time; however, at 12 months of use, around 10% of women taking lower dose

Box 1. Irregular bleeding secondary to contraceptive use

- Adherence to recommended regimen – oral contraceptives require strict daily commitment.
- Poor gut absorption (ie significant vomiting, severe diarrhoea, chronic malabsorption) may compromise the efficacy and cycle control of oral contraceptives.
- Hormonal effects on the thickness/stability of the endometrium – this is intrinsic to progestogen-only contraception, but for combined methods depends on dose, formulation and delivery system.
- Interference with hormone metabolism – exogenous hormone metabolism is individually variable but can also be affected by smoking[21] and the use of liver enzyme-inducing medications such as:
  - antiepileptic medications (not all)
  - anti-tuberculosis drugs
  - several drugs used to treat human immunodeficiency virus (HIV)
  - St John's Wort (hypericum)
  - other drugs (eg bosentan, aprepitant, modafinil, sugammadex).

Note: Most broad-spectrum antibiotics have no effect on steroid metabolism, although they may reduce absorption should diarrhoea occur. Additional contraceptives are no longer recommended when antibiotics are prescribed for minor illnesses. Refer to www.fsrh.org/documents/ceu-clinical-guidance-drug-interactions-with-hormonal for more information.

Box 2. Managing persistent irregular bleeding in women using COCP

Change to an alternative progestogen – the variability of trial design makes it impossible to definitively rank progestogens as regards general cycle control, although preparations containing gestodene, or norethisterone at a dose of 1000 µg, may offer some advantages in terms of BTB control.[22,23]

Change the oestrogen dose or type – even with perfect adherence, COCPs containing 20 µg of ethinyloestradiol are associated with higher initial rates of BTB.[24] Consider changing to a preparation containing 30–40 µg of ethinyloestradiol or, alternatively, one of the newer oestradiol pills. Ethinyloestradiol 50 µg is sometimes recommended for women on known enzyme-inducing medications but, in general, has a minimal role in managing BTB because of an increased risk of significant side effects.

Change the delivery system – vaginal rings bypass issues of variable gastrointestinal absorption and daily commitment to use. BTB in ring users was shown to be significantly less common than in those taking a 30 µg levonorgestrel COCP.[10,25]

There is no good evidence that triphasic preparations offer any advantage over monophasic in terms of cycle control.[5]

COCPs still report some non-scheduled bleeding.[3] It is important not only to guide expectations as to the likelihood of some initial BTB, but to be proactive in encouraging women to seek advice if it persists, especially given that this is one of the most common reasons for COCP discontinuation.[4] One question that often concerns women and clinicians is whether BTB is a sign of reduced contraceptive efficacy. The Faculty of Sexual and Reproductive Healthcare in the UK states that this is not a concern in the absence of missed or late pills, vomiting or drug interactions.[5]

Over time, there has been an inexorable shift towards COCP preparations containing lower doses of oestrogen and progestogen, making regular pill-taking even more important if BTB is to be avoided. The dose and type of progestogen is also important. Progestogens vary greatly in their purity, half-life and receptor affinity. Combining the same dose of oestrogen with different types or doses of progestogen may result in markedly different rates of BTB.[6,7] In the absence of high-quality evidence, the most commonly accepted management advice, should a woman continue to experience persistent BTB after a three-month trial of initial COCP, is provided in Box 2.

Since the 1960s, most COCP regimens have scheduled a monthly withdrawal bleed at the end of active pill-taking. Such bleeding is usually lighter and of shorter duration, compared with a normal menstrual cycle, or may even be completely absent. Some women require reassurance that there are no long-term problems associated with such changes; alternatively, switching to a different preparation could be considered. In fact, there is no clinical imperative for scheduled, monthly withdrawal bleeding, and there are now two extended-use preparations licensed for use in Australia. However, women in Australia have for many years, albeit off-licence, taken active pills from conventional COCP preparations continuously to prolong the time between bleeds. Such ongoing use of active pills is, however, associated with higher rates of BTB and in the past it has been difficult to advise women as to how to manage this. Studies[8,9] now indicate that if a woman experiences three or more days of BTB during an extended-cycle regimen, she should be advised to take a four-day break from active hormones to allow the endometrium to shed completely. This results in fewer bleeding days overall than continuing with active pills.[8,10]

Progestogen-only contraceptives

In Australia, progestogen-only contraceptives include the progestogen-only pill (POP), levonorgestel intrauterine device (IUD), etonogestrel implant and depomedroxyprogesterone injection. Women considering these methods should be advised that they are unlikely to experience a regular bleeding pattern during long-term use, and pre-emptive explanation and reassurance can be invaluable here. In addition, women should be warned that bleeding might be extremely unpredictable, particularly during the first few months of use.

Conversely, the woman's attitude to amenorrhoea should also be explored because this is just as unacceptable for some. There are higher rates of eventual amenorrhoea on the contraceptive injection and hormonal IUD (50% at 12 months)[11,12] than with implants (20%).[13] All the medications listed in Box 1 also affect the bleeding pattern and efficacy of the POP and contraceptive implant, although they have no impact on the contraceptive injection or hormonal IUD.

All POPs presently available in Australia contain either norethisterone or levonorgestrel. Around 40% of women using these POPs continue to ovulate and may therefore experience a regular bleeding pattern.[14] The remainder can report anything from amenorrhoea to almost constant light bleeding. In those troubled by persistent irregular bleeding, a trial of the alternative progestogen may be worthwhile. Although POPs have an equivalent theoretical failure rate to COCPs, these must be taken within three hours of the usual time, or the incidence of BTB and contraceptive failure increases.[15] Pregnancy should therefore always be considered should a woman using POP report a significant change in her usual bleeding pattern.

Managing irregular bleeding on long-acting reversible hormonal contraceptives (LARCs)

Long-acting reversible hormonal contraceptives (LARCs) includes hormonal IUDs, implants and contraceptive injection. These methods have low practical failure rates, but pregnancy, infection and unrelated pathology still require exclusion. In the case of hormonal IUDs, irregular bleeding, which is usually accompanied by pain, can signal malposition of the device. IUD strings measuring longer than 4 cm from the cervical os strongly suggest the possibility of partial expulsion, and pelvic ultrasonography should be arranged to determine its position.

In most cases, however, irregular bleeding in women using progestogen-only contraceptive methods is due to a relatively atrophic, unstable endometrium. High-quality evidence for managing irregular bleeding on progestogen-only contraceptive methods is generally lacking. Box 3 lists a number of strategies that have at least some evidence suggesting they may prove useful in the short term. Unfortunately, none of these strategies has been shown to alter longer term bleeding patterns.

The addition of a combined-contraceptive method can only be considered where there are no contraindications to oestrogen. The reason high-dose norethisterone appears to be effective is that it is partially metabolised to ethinyloestradiol in the liver,[16] so that it behaves more like a very low-dose COCP. It should therefore be used with caution in women with an absolute contraindication to oestrogen[17] (eg those with a history of venous thromboembolism or migraine with aura). The non-hormonal options for managing troublesome bleeding (eg mefenamic, tranexamic acid) can be repeated monthly if required.

Given the higher rate of irregular bleeding in women who use implants, some elect to use a combined-contraception method (eg COCP, ring) concurrently. This practice is off-licence but is an acceptable way of taking advantage of the implant's reliability and the cycle-control offered by combined contraception. For the majority of women using the contraceptive injection or the levonorgestrel IUD, irregular bleeding settles over time and long-term use of additional hormonal contraception is rarely required. Women sometimes report more irregular bleeding as the implant or levonorgestrel IUD approaches the recommended time for removal. Anecdotally, early replacement may be associated with an improved bleeding pattern in some women and should be offered as an option. Similarly, reducing the interval between contraceptive injections to 10 weeks may prove useful.

Box 3. Managing irregular bleeding on LARC[26]

First-line options

- A combined hormonal contraceptive[13] taken continuously or cyclically for three months
- Five-day course of NSAID[27] (eg mefenamic acid 500 mg bd or tds)
- Five-day course of tranexamic[28,29] acid 500 mg bd

Second-line option

- Norethisterone 5 mg tds for 21 days

Unlikely to be effective[30]

- Doxycycline – although early studies showed promise, this was not borne out when larger trials were conducted

LARC, long-active reversible contraception; NSAID, nonsteroidal anti-inflammatory drug

Copper intrauterine device

Copper IUDs provide an effective, long-term, convenient and hormone-free method of contraception. Most women who use copper IUDs experience regular menstrual bleeding, although irregular spotting between bleeds is not uncommon, particularly in the first six months of use. Copper IUDs also tend to increase the amount and duration of menstrual loss. Studies indicate that the user should expect a 50–55% increase above her usual menstrual flow.[18,19] Nonsteroidal anti-inflammatory drugs and tranexamic acid appear to be effective in reducing heavy or prolonged menstrual bleeding in women who use copper IUDs, provided there are no contraindications to their use.[20] Similarly to hormonal IUDs, partial expulsion must also be considered as a possible cause for irregular bleeding, particularly if it is associated with pelvic pain or dyspareunia.

Key points

- Before commencing any contraceptive method, women should be informed as to the likely changes in both short-term and long-term bleeding patterns.
- It is important to consider the possibility of pregnancy, sexually transmissible infections and other pathology in all women presenting with irregular bleeding, regardless of their contraceptive method.
- Irregular bleeding is common in the first three to four months of oral contraceptive use, but should this persist for no obvious reason (eg issues of adherence or factors known to interfere with steroid metabolism), a change in COCP preparation (or a change of method) should be considered.
- There are a number of strategies that can be used to terminate a bleeding episode in women using long-acting,

progestogen-only contraception. However, none of these strategies has been shown to influence long-term bleeding patterns. Should the bleeding pattern remain unacceptable to the woman, an alternative contraceptive method should be considered.

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