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Review article

The management of unacceptable bleeding patterns in etonogestrel-releasing contraceptive implant users☆

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Abstract

The aim of this guidance is to review the management of unacceptable vaginal bleeding patterns in etonogestrel (ENG)-releasing contraceptive implant users concentrating, where possible, on the evidence for pharmacological treatments and identifying a pragmatic approach where this is not possible.

This article was developed in accordance with methodology used for producing Royal College of Obstetricians and Gynaecologists' Green Top Guidelines.

The Cochrane Library (including the Cochrane Database of Systematic Reviews, DARE and EMBASE) and Medline (1966–2010) were searched using the relevant MeSH terms, including all subheadings, and this was combined with a keyword search. Search words included "progestogen only contraceptives," "contraceptive implants," "progestogen implants," "etonogestrel implants," "irregular bleeding," "unpredictable bleeding," "bleeding irregularity" and "bleeding pattern," and the search was limited to humans and English language. Enquiries for relevant information were also made to the pharmaceutical industry and researchers for missing studies.

Although this is not a systematic review, two of the authors (D.M., I.S.F.), qualitatively assessed those papers reporting quantitative results involving treatments given either to stop or prevent bleeding in ENG or levonorgestrel contraceptive implants users.

Keywords: Progestogen only contraceptives; Contraceptive implants; Progestogen implants; Etonogestrel implants; Irregular bleeding; Unpredictable bleeding; Bleeding irregularity; Bleeding pattern

1. Introduction

ENG contraceptive implants are becoming an increasingly popular birth control choice with approximately six million women using this method worldwide (data on file, Merck, Sharp, Dohme). This safe, highly effective, long-acting and reversible contraceptive is suitable for most women of reproductive age, with recent guidelines supporting its use in women with a history of venous thromboembolism or congenital and acquired cardiovascular disease [1,2].

2. How effective is the ENG contraceptive implant?

Recent data have shown that the ENG implant is one of the most effective reversible contraceptives with a method failure rate of 0.01 per 100 implants fitted [3].

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Recent reanalysis of initial trial data and postmarketing reporting figures show ENG implants to be one of the most effective female contraceptives with overall typical failure rates of 0.049 per 100 implants fitted (method failure rate −0.01 per 100 implants fitted) [3]. This has led to some health insurance schemes fully reimbursing the cost of implant provision in a number of high resource countries and other governments subsidising or providing it free at health care facilities.

Most women find ENG contraceptive implants highly acceptable with first year continuation rates of approximately 80% in published studies [4].

Continuation rates for ENG implants are generally good, however there are marked differences depending on geographical area, with 90.4% continuation rate at two years in developing countries compared to 55.4% in developed populations [4].This may reflect a disparity in health care provision, cultural differences in perception of "nuisance" side effects and their acceptance or an ethnic variation in menstrual bleeding pattern experienced by users [4,5].

Reasons given for implant removal vary but almost one third of European women who discontinue state that "bleeding problems" have led to the early discontinuation [4]. There is also some evidence that nuisance side effects are less well tolerated by younger women using implants [6] and those attending urban health clinics [7]. Interestingly, women from Southeast Asia have less vaginal bleeding — about 5 to 7 days fewer bleeding-spotting days per 90-day reference period — compared to women from Europe and the United States [5]. Body weight may help explain these findings with Southeast Asian women in this study weighing, on average, 7.7 kg less than other women. A positive correlation was found between numbers of bleeding/spotting days and body weight with less bleeding/spotting occurring in lighter women [5].

There is, therefore, a need to review the management of "unacceptable" bleeding in ENG implant users taking into account these factors and providing a standardized approach in its management based on currently available evidence at all levels.

2.1. Bleeding pattern definitions

For the purpose of this paper, the characterization of bleeding descriptions and patterns were based on World Health Organization-recommended definitions and are shown in Table 1 [8].

Table 1
Characterisations of bleeding descriptions and patterns [adapted from 8]

- Bleeding day — any day with vaginal discharge containing blood that required more than one sanitary towel or tampon per day
- Spotting-day — any day with vaginal discharge containing blood that required at most one sanitary towel or tampon per day
- Bleeding-free day — a day during which neither bleeding nor spotting was reported
- Bleeding-spotting episode — one or more consecutive days during which bleeding or spotting was entered in the diary, bounded by bleeding-free days
- Amenorrhea — no bleeding or spotting days throughout the 90-day reference period
- Infrequent bleeding — less than three bleeding-spotting episodes in a 90-day reference period, excluding amenorrhea
- Normal frequency — three to five bleeding-spotting episodes in a 90-day reference period
- Frequent bleeding — more than five bleeding-spotting episodes in a 90-day reference period
- Prolonged bleeding — any bleeding-spotting episode (uninterrupted) lasting more than 14 days in the 90-day reference period [as defined in 5]

2.2. What types of bleeding patterns occur in users of ENG implants?

Like other progestogen-only contraceptives, use of ENG implants is associated with unpredictable vaginal bleeding patterns [5].

Data from 923 women, in 11 clinical trials conducted around the world, were analyzed recently and this confirmed that ENG contraceptive implants were associated with unpredictable bleeding patterns [5]. Amenorrhea was reported in 22.2% of women, 33.6% had infrequent bleeding and 6.7% frequent and/or 17.7% prolonged bleeding [5]. A second integrated analysis of 942 women from the US, Chile, Asia and Europe (including some of the trial data in Mansour et al. [5]) reported that widespread changes in bleeding patterns were found in ENG implant users but that no one pattern predominated [9].

2.3. Do users of ENG implants experience less menstrual bleeding than women who have natural cycles?

Most ENG implant users report a reduction in frequency and volume of menstrual bleeding [10].

There are no published papers reporting quantitative blood loss measurements in ENG implant users but most women will experience a reduction in frequency and volume of menstrual bleeding [10]. A recent analysis of bleeding patterns in ENG implant users stated that the number of bleeding/spotting days was less in 75% of the 90-day reference periods compared to those observed during natural cycles. The analysis also reported that the median number of bleeding-spotting days was slightly lower in ENG users than in women experiencing natural cycles and comparable to those taking a combined oral contraceptive (COC) [5]. This analysis reported no change in hemoglobin concentration following ENG use [5].

2.4. Will these bleeding patterns improve over time and who is likely to discontinue early?

Initial studies suggested that the bleeding pattern experienced by ENG implant users would improve with time but two recent analyses concluded that individual patterns vary considerably [5,9].