

## Therapeutic Options for Unscheduled Bleeding Associated with Long-Acting Reversible Contraception

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### **KEYWORDS**

- Irregular bleeding Intrauterine device Contraceptive implant Levonorgestrel
- Etonogestrel

#### **KEY POINTS**

- Long-acting reversible contraception (LARCs), including intrauterine devices and implants, are highly effective forms of birth control.
- Irregular vaginal bleeding is one of the most common reasons for premature discontinuation of LARC devices.
- Nonsteroidal antiinflammatory drugs can decrease unscheduled bleeding associated with LARC use and are the most well studied for this indication.
- Other medications that can decrease unscheduled bleeding include antifibrinolytics (tranexamic acid), antiprogestins (mifepristone), and matrix metalloproteinase inhibitors (doxycycline).

#### INTRODUCTION

Long-acting reversible contraception (LARC), such as intrauterine devices (IUDs) and implants, are the most effective reversible contraceptives available.<sup>1</sup> A common side effect of both IUDs and implants is an alteration in menstrual bleeding patterns. Women can experience heavier bleeding with the copper IUD or unscheduled bleeding and spotting with the hormonal and copper IUD as well as the contraceptive implant. Dissatisfaction with bleeding, particularly heavy or unscheduled bleeding and spotting, is a common reason for early discontinuation of LARC methods.<sup>2</sup> Therapies that can prevent or treat unscheduled bleeding could improve patient satisfaction, increase uptake of LARC methods, and reduce early discontinuation, all of which would result in fewer unplanned pregnancies.

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The reason women experience unscheduled bleeding with IUDs and implants has not been clearly elucidated. Unscheduled bleeding falls into 2 categories: bleeding that occurs with initiation of a LARC method and bleeding that occurs with prolonged use of LARC. Bleeding that occurs with initiation of a levonorgestrel (LNG) IUD and etonogestrel (ENG) implant is common and is most likely the result of the endometrium transitioning to a thin state from consistent progestin exposure. The precise mechanism of unscheduled bleeding that occurs with prolonged exposure to progestin is unknown but is thought to be related to the progestin dilating superficial veins and capillaries, which are fragile and susceptible to focal bleeding. Other potential influences include changes in structural support in the endometrium, altered matrix metalloproteinase (MMP) activity, and changes in endometrial perfusion and hemostasis.

Structured direct counseling before LARC initiation to inform women about common bleeding patterns associated with each contraceptive method is critical to method initiation and acceptance. Emphasizing that unscheduled bleeding is not associated with decreased efficacy of the method is key. Advance knowledge of possible unscheduled bleeding may reassure users, that if bleeding irregularities occur, the method is still effective; users may be willing to wait longer for unscheduled bleeding or spotting to resolve.

Pregnancy should always be excluded first when new-onset amenorrhea is accompanied by signs or symptoms of pregnancy. If a woman with an IUD complains of both irregular bleeding and pelvic pain, it is important to verify proper placement by examination or ultrasound to ensure that the device is not in the cervix, embedded in the myometrium, or perforated through the uterus. Consideration should also be given to infections or pathologic causes like cervical or endometrial cancer. Cultures or endometrial biopsies can be done with an IUD in place.

Heavy, prolonged, and unscheduled bleeding are strongly associated with dissatisfaction and early discontinuation of LARC methods.<sup>3–6</sup> Clinicians must, therefore, be armed with evidence-based interventions to alleviate this common side effect. The authors review the current literature related to the treatment of unscheduled bleeding and spotting that accompanies IUD and contraceptive implant use, discuss major themes in the treatment of unscheduled bleeding, and identify areas where further research is needed. In the authors' review of the literature, they limited their search to human subjects and articles published in English. The authors excluded treatment modalities that are not available in the United States.

#### **COPPER INTRAUTERINE DEVICE**

With the copper IUD (copper T380A/Paragard [Teva Women's Health, Inc, Sellersville, PA, USA]), irregular spotting and prolonged or heavier menses are frequent in the first few months of use. Menstrual bleeding can be increased up to 55% to 74%, which is thought to be because of excessive prostaglandin release in the endometrial cavity.<sup>7,8</sup> The discontinuation rate for pain or bleeding in one trial of the copper T380A was 5% at 1 year, 8% at 2 years, and 9% at 3 years.<sup>9</sup>

#### Interventions for Heavy Bleeding

Treatments for heavy bleeding associated with copper IUD use include nonsteroidal antiinflammatory drugs (NSAIDs), antifibrinolytic agents, and antidiuretics. Some trials have also studied prophylactic interventions to prevent the initial increase in bleeding known to occur for most users. **Table 1** contains a summary of medical interventions shown to have a benefit in clinical trials for heavy bleeding in copper IUD users.

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