

A frameless LNG-IUD may be preferred over framed LNG-IUD for the treatment of primary dysmenorrhea

Sir,

I read with interest the article published by Iacovides *et al.* about primary dysmenorrhea (Iacovides *et al.*, 2015).

The article describes in detail the etiology of primary dysmenorrhea and its well-known repercussions on quality of life and makes a comment on this often poorly treated and even disregarded condition by health care providers. As treatment for primary dysmenorrhea, the article refers to non-steroidal anti-inflammatory drugs (NSAIDs) as the main first line treatment method and mentions briefly the use of hormonal intrauterine devices (IUDs) which have been shown to reduce menstrual bleeding and pain. (Lindh and Milson, 2013). We would like to add some considerations and practical experience in effectively blocking dysmenorrheic pain sensation in young women with this condition using intrauterine technology.

I refer to a clinical reports on 21 patients with primary and secondary dysmenorrhea treated with an experimental 'frameless' levonorgestrel-releasing intrauterine system (Wildemeersch *et al.*, 2014). The majority of these women also complained of heavy menstrual bleeding and poor quality of life with mood changes particularly during their menstrual period.

All women were treated successfully, i.e. no pain, scanty bleeding or no bleeding (amenorrhea) and much improved quality of life. This suggests that the strongly reduced bleeding was the main mechanism responsible for the alleviation of menstrual pain complaints in these patients. Continuous intrauterine levonorgestrel (LNG) delivery causes uniform suppression of the endometrium throughout the whole thickness of the mucosa, which is maintained by the high tissue concentrations, and reduces the prostaglandin synthesis in the endometrium. The contraceptive effect of the IUD is also welcomed by these women as they were sexually active. The positive results obtained in this study also suggest that the frameless design may be preferred over a framed LNG-IUD, as the absence of a frame is particularly advantageous in these women (Fig. 1). Clinical experience has shown that disproportion between the IUD and the uterine cavity can lead to partial or total expulsion, perforation of the uterine wall, pain, unintended pregnancy, and abnormal or heavy uterine bleeding leading to early removal of the device. Frameless IUDs are well tolerated as they are flexible and do not occupy much space in the uterine cavity as they are devoid of a plastic frame.

The LNG-IUD is a typically multipurpose device solving several problems simultaneously. Larger scale studies should however be conducted, preferably including a comparator, to confirm the excellent results of this potentially highly useful IUD.

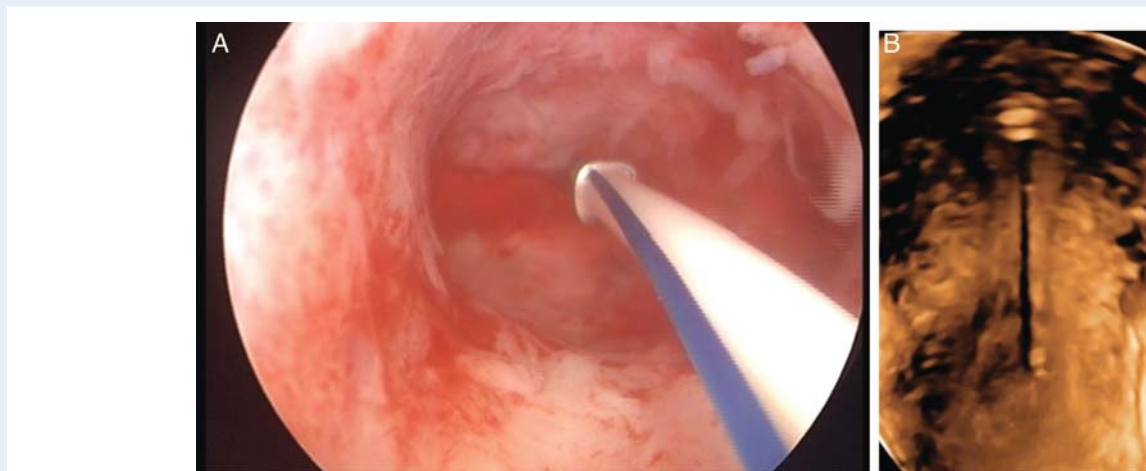


Figure 1 (A) Hysteroscopic view of the Frameless LNG-IUD, releasing 20 mcg of LNG/d, inserted in the uterine cavity. (B) 3-D sonography of the frameless, anchored IUD in the narrow uterine cavity.

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Reply: LNG-IUDs in treating dysmenorrhea

Sir,

We appreciate Dr Wildemeersch's interest in our review and comments about the potential effectiveness of hormonal intrauterine technology in treating primary and secondary dysmenorrhea. Non-steroidal anti-inflammatory drugs (NSAIDs) are the most common treatment for dysmenorrhea and are given more extensive coverage in our review (Iacovides *et al.*, 2015).

We would like to take this opportunity to extend Dr Wildemeersch's discussion about the use of intrauterine devices (IUDs) as a treatment strategy for dysmenorrhea. The levonorgestrel-releasing IUD (LNG-IUD) is an effective contraceptive option in women and usage rates are increasing, although usage is still relatively low in women under the age of 20 years (Ott *et al.*, 2014); the age-group in which primary dysmenorrhea is common. More recently, smaller framed (28 × 30 mm) LNG-IUDs (LNG 13.5 mg) have become available (<http://www.medicines.org.uk/emc/medicine/28672/SPC/Jaydess+13.5+mg+intrauterine+delivery+system>. Accessed on 5/10/2015), thereby creating the opportunity for increased use of intrauterine technology in nulliparous women and adolescents. Insertion of a smaller IUD may be easier for these groups of women, who have smaller uterine dimensions compared with parous women. The frameless LNG-IUDs are promising for similar reasons, as highlighted by Dr Wildemeersch. However, it should be noted that recent published data showed that most insertions of a standard-size framed IUD (LNG 52 mg, size 32 × 32 mm) were uneventful in nulliparous adult women with small uterine measures (Kaislasuo *et al.*, 2014) and a smaller uterine cavity size predicted less bleeding and pain during use compared with adult women with larger uterine cavity measurements (Kaislasuo *et al.*, 2015).

The LNG-IUD has well-established non-contraceptive benefits, including reduction of severe dysmenorrhea and/or heavy menstrual bleeding associated with endometriosis, adenomyosis, and chronic pelvic pain (Bahamondes *et al.*, 2007). The reduction in menstrual pain is thought to be due to the effects of LNG on the endometrium leading to oligomenorrhea and amenorrhea, as well as inhibition of inflammatory mediators present in the peritoneum (Bahamondes *et al.*, 2007). However, the pain-reducing benefit of the LNG-IUD may not be immediately evident, and is influenced by dysmenorrheic pain severity at baseline: women with dysmenorrhea are more likely to experience greater pain when inserting (Kaislasuo *et al.*, 2014) and when using a LNG-IUD during the first 3 months of use (Kaislasuo

et al., 2015). Given the evidence that women with dysmenorrhea are hypersensitive to experimental pain (Iacovides *et al.*, 2015), they may also be hypersensitive to the pain of IUD insertion and the initial uterine irritation. Lack of immediate relief of menstrual pain in some women may also explain why pre-existing dysmenorrhea predicts removal of an IUD 1 year later (Maguire *et al.*, 2015). Self-reported bleeding and cramping are associated with lower user satisfaction with the LNG-IUD, however, the majority of women (>90%) are satisfied with their device at 6 months (Diedrich *et al.*, 2015). Further study is needed to follow up on associations between dysmenorrhea and IUD use so that women can be adequately counseled on what to expect. As with any treatment, side effects need to be considered; LNG-IUD use in women is associated with increased risk of acne, headache, migraine and mental side effects (<http://www.medicines.org.uk/emc/medicine/28672/SPC/Jaydess+13.5+mg+intrauterine+delivery+system>. Accessed on 5/10/2015).

For women who are seeking contraception in addition to menstrual pain relief, intrauterine devices as well as oral contraceptives, are good options. Short-term use (i.e. only during painful menstruation) of NSAIDs should not be excluded as an effective means of pain relief, particularly for nulliparous women not seeking contraception, and particularly since gastrointestinal side effects associated with NSAID use are of less concern with acute, rather than chronic, use (Iacovides *et al.*, 2015).

As commented by Dr Wildemeersch, current research on the effectiveness of intrauterine technology in alleviating dysmenorrhea is promising although we await collection of further data to confirm the efficacy of the new smaller framed and frameless LNG-IUDs in the long-term alleviation of dysmenorrhea in different populations, including adolescents, considering primary versus secondary dysmenorrhea. Finally, looking ahead to potential alternative treatments that are currently under development, we note the recent publication showing, for the first time, efficacy of PDC31 (prostaglandin F2α receptor inhibitor) in decreasing uterine activity and alleviating pain in primary dysmenorrhea (Böttcher *et al.*, 2014). Having more options available to women for treating dysmenorrhea is optimal and will improve management of this very common gynecological disorder.

References

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