

Management of pain associated with the insertion of intrauterine contraceptives

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Submitted on December 18, 2012; resubmitted on April 9, 2013; accepted on April 16, 2013

TABLE OF CONTENTS

- Introduction
- Methods
- Pain Management Strategies: Critical Review of the Evidence and Expert Consensus
- Data Gaps and Areas for Further Research
- Summary and Conclusions

BACKGROUND: Most intrauterine contraception (IUC) placements do not require pain relief. However, small proportions of nulliparous (~17%) and parous (~11%) women experience substantial pain that needs to be proactively managed. This review critically evaluates the evidence for pain management strategies, formulates evidence-based recommendations and identifies data gaps and areas for further research.

METHODS: A PubMed literature search was undertaken. Relevant articles on management of pain associated with IUC insertion, published in English between 1980 and November 2012, were identified using the following search terms: 'intrauterine contraception', 'insertion' and 'pain'. RCTs were included; further relevant articles were also identified and included as appropriate.

RESULTS: Seventeen studies were identified and included: 12 RCTs and one non-randomized study of pre-insertion oral analgesia, cervical priming and local anaesthesia; one systematic review and one RCT on post-insertion analgesia and two non-randomized studies on non-pharmacological interventions. There was no conclusive evidence that any prophylactic pharmacological intervention reduces pain associated with IUC insertion. However, most of the regimens studied were adopted from hysteroscopy or abortion and effectiveness in specific subsets of women has not been studied adequately. A systematic review found non-steroidal anti-inflammatory agents (NSAID) to be effective in reactively treating post-insertion pain, but no benefit was found with prophylactic use.

CONCLUSIONS: No prophylactic pharmacological intervention has been adequately evaluated to support routine use for pain reduction during or after IUC insertion. Women's anxiety about the procedure may contribute to higher levels of perceived pain, which highlights the importance of counselling, and creating a trustworthy, unhurried and professional atmosphere in which the experience of the provider also has a major role; a situation frequently referred to as 'verbal anaesthesia'.

Key words: intrauterine contraception / pain / analgesia / local anaesthesia / cervical priming

Introduction

Long-acting reversible contraception (LARC) methods, including intrauterine contraception (IUC), are intrinsically highly effective and their effectiveness does not depend on user compliance (Trussell, 2011;

Winner *et al.*, 2012). Thus, with more widespread use of LARC methods, the rate of unintended pregnancy could be reduced. Women who have the best knowledge of IUC are more likely to use it personally. In a survey of female Fellows of the American College of Obstetricians and Gynecologists, the prevalence of personal IUC use

was >20-fold higher than among women in the general population (Association of Reproductive Health Professionals, 2004). Similarly, a high prevalence of IUC use has been reported among midwives (Gemzell-Danielsson et al., 2012). Our anecdotal observations also suggest a similar high prevalence of IUC use among various women's healthcare professionals (HCP), including physicians, nurse practitioners and nurse-midwives.

The Contraceptive CHOICE Project showed that when women requesting contraception were given unbiased information on LARC methods and then given a free choice of any contraceptive method provided free of charge, the majority (56%) chose IUC (Secura et al., 2010; Peipert et al., 2011).

Fear of pain during insertion, however, might prevent some women from choosing IUC (Hubacher et al., 2006; Allen et al., 2009) and HCPs' fears of painful and/or difficult placements may lead them to recommend or counsel women on other, less effective contraceptive methods (Heikinheimo et al., 2010).

Women's perception of pain is multifactorial and likely to be influenced by cultural differences and personal experiences; insertion-related pain is therefore difficult to predict. Nevertheless, factors associated with greater pain include nulliparity, not currently breastfeeding and longer time since last pregnancy; of these factors, nulliparity is the strongest predictor of pain (Chi et al., 1986, 1989; Lassner et al., 1995; Hubacher et al., 2006). The proportion of sexually active women of reproductive age who are nulliparous is increasing, with women delaying childbirth and having fewer children or choosing to remain childless (Anon, 2011). The proportion of Caesarean section births has also increased (Bailit et al., 2004; Villar et al., 2006; Barber et al., 2011; Stavrou et al., 2011), and women who have only ever had a Caesarean section are often viewed as nulliparous with respect to IUC placement.

Anticipated pain is often greater than the actual pain experienced (Murty, 2003), and the majority of nulliparous women experience no more than moderate pain during IUC insertion (Suhonen et al., 2004; Brockmeyer et al., 2008; Marions et al., 2011). In a prospective study in 117 nulliparous women, the majority (62%) reported that the pain associated with the procedure was similar in intensity to that of menstruation (Brockmeyer et al., 2008), although for some women, menstrual pain can be severe enough to require pain relief. In a non-interventional study in 224 nulliparous women, 9% reported no pain and 72% reported moderate pain during insertion of a levonorgestrel intrauterine system (LNG-IUS) (Marions et al., 2011).

However, among nulliparous women there is a subset (about 17%) for whom the insertion of IUC is associated with severe pain (Marions et al., 2011) and among parous women (mean of two prior births; $n = 46$) ~11% report severe pain (Heikinheimo et al., 2010). These women need effective pain relief.

The aim of this review is to critically evaluate the evidence for various pain management strategies and formulate evidence-based recommendations. In the absence of conclusive evidence, a group consensus is presented. Data gaps and areas for further research are also discussed. It is not within the scope of this article to review the evidence for the management of other side effects, such as vasovagal reactions.

Methods

A literature search was undertaken using PubMed. Relevant articles on management of pain associated with IUC insertion, published in English between

1980 and November 2012, were identified using the following search terms: 'intrauterine contraception', 'insertion' and 'pain'. We reviewed and included primary RCTs; further relevant supporting articles were identified and included as appropriate. Relevant references from the bibliographies of included articles were also reviewed and included when appropriate.

Seventeen studies were identified and included: 12 RCTs and one non-randomized study of pre-insertion oral analgesia, cervical priming and local anaesthesia; one systematic review and one RCT on post-insertion analgesia and two non-randomized studies on non-pharmacological interventions.

Pain management strategies: critical review of the evidence and expert consensus

No comprehensive strategy has been developed for managing pain associated with the insertion of IUC and no standard has been established. Current pharmacological strategies include: pre-insertion therapy (oral analgesia, cervical ripening/priming and local anaesthesia); therapy given during the procedure (local anaesthesia administered reactively) and post-procedure therapy (non-steroidal anti-inflammatory drugs [NSAIDs] and opioid analgesia). Non-pharmacological pain management strategies include psychological preparation and counselling before insertion and 'verbal anaesthesia' and distraction during the procedure. The evidence for each of these strategies is reviewed below.

Pre-insertion pharmacological therapy

Oral analgesia

Prophylactic administration of ibuprofen or another NSAID is widespread despite a lack of supporting evidence, possibly because providers and/or women believe that, as an effective analgesic, it might reduce pain caused by IUC insertion.

Three RCTs have evaluated the prophylactic use of oral analgesia versus placebo for reducing pain associated with IUC insertion (Hubacher et al., 2006; Chor et al., 2012; Karabayirli et al., 2012) (Table I).

In the first RCT, 2019 nulliparous or parous 'first-time' users of the copper intrauterine device (IUD) received either 400 mg ibuprofen or placebo at least 45 min before the procedure (Hubacher et al., 2006). Ibuprofen had no significant effect on patient-reported pain compared with placebo. Certain subgroups (e.g. nulliparous women) experienced more pain than others, but ibuprofen had no clinically relevant impact on the level of pain compared with placebo.

In the second RCT, 81 women received either 800 mg ibuprofen or placebo 45 min before the insertion of an LNG-IUS (Chor et al., 2012). Prophylactic use of ibuprofen had no significant impact on mean scores for anticipated pain, pain associated with tenaculum application or pain associated with the actual insertion.

In the third RCT, 103 women received 50 mg tramadol ($n = 35$), 550 mg naproxen sodium ($n = 34$) or placebo ($n = 34$) 1 h before IUC insertion (Karabayirli et al., 2012). Women reported the pain they experienced on insertion using a 0–10 visual analogue scale (VAS). Tramadol was associated with a significant reduction in pain compared with naproxen sodium ($P = 0.003$), and naproxen sodium was associated with a significant reduction in pain compared with placebo ($P = 0.001$).

A further UK-based, non-randomized, single-centre study of 109 nulliparous and parous women concluded that the pain scores reported by women who took pre-insertion analgesia (mainly ibuprofen) were not

Table 1 Studies of pre- and post-placement pharmacological interventions for the reduction of pain associated with IUC insertion.

Reference	n	Population	Interventions	Method of evaluation of pain ^a	Significance of pain reduction effect	Level of evidence ^b
Pre-insertion oral analgesia						
Hubacher <i>et al.</i> (2006)	2019	Nulliparous and parous	400 mg ibuprofen versus placebo	Overall pain measured on 0–10 VAS	Not significant (median score 1.0 in both treatment groups)	2
Chor <i>et al.</i> (2012)	81	Mainly parous (96%)	800 mg ibuprofen versus placebo	Measured at different time points on 0–10 VAS	Not significant (mean score during actual insertion 3.69 versus 3.34, $P = 0.91$)	2
Karabayirli <i>et al.</i> (2012)	103		50 mg tramadol versus 550 mg naproxen sodium versus placebo	Overall pain measured on 0–10 VAS	Significant reduction in mean pain score with tramadol versus naproxen sodium (2.31 versus 2.94, $P = 0.003$) and with naproxen sodium versus placebo (2.94 versus 4.88, $P = 0.001$)	2
Pre-insertion cervical priming						
Sääv <i>et al.</i> (2007)	80	Nulliparous	400 µg misoprostol (sublingual) versus placebo	Overall pain measured on 0–10 VAS	Not significant (median score 7.0 versus 6.5, $P = 0.20$)	2
Heikinheimo <i>et al.</i> (2010)	89	Mainly parous (94%)	400 µg misoprostol (sublingual) versus placebo	Overall pain measured as 'none', 'mild', 'moderate' or 'severe'	Not significant (no more than mild pain reported in 37 and 35% of subjects in the misoprostol and placebo groups, respectively)	2
Edelman <i>et al.</i> (2011)	40	Nulliparous	400 µg misoprostol (buccally) versus placebo	Measured at different time points on 0–100 VAS	Not significant (mean score during actual insertion 65 versus 55, $P = 0.83$)	2
Dijkhuizen <i>et al.</i> (2011)	199	Nulliparous and parous	400 µg misoprostol (vaginally) versus placebo	Overall pain measured on 0–100 VAS	Not significant (mean score 46 versus 40, $P = 0.14$)	2
Swenson <i>et al.</i> (2012)	108	Nulliparous	400 µg misoprostol (vaginally or buccally) versus placebo	Measured at different time points on 0–100 VAS	Not significant (mean score during actual insertion 58.4 versus 56.9, $P = 0.74$)	2
Pre-insertion local anaesthesia						
Olotto <i>et al.</i> (1996)	102	Nulliparous and parous	2% lignocaine gel (intracervically) versus placebo gel versus no treatment	Overall pain measured on 1–7 VAS	Significant reduction in pain (distribution of subjects with pain scores of 1–2, 3–4 and 5–7 differed significantly between treatment groups, $P < 0.025$)	2 (flawed study design) ^c
Maguire <i>et al.</i> (2012)	197	Nulliparous and parous	2% lignocaine gel versus placebo gel	Measured at different time points on 0–100 VAS	Not significant (mean score during actual insertion 51.0 versus 50.9, $P = 0.98$)	2
McNicholas <i>et al.</i> (2012)	199	Nulliparous and parous	2% lignocaine gel versus placebo gel	Measured at different time points on 0–10 VAS	Not significant (median score during actual insertion 5 versus 6, $P = 0.16$)	2
Mody <i>et al.</i> (2012)	50	Nulliparous and parous	1% lignocaine paracervical block versus no anaesthesia	Measured at different time points on 0–100 VAS	Not significant (median score during actual insertion 24.0 versus 62.0, $P = 0.09$)	2
Post-insertion pharmacological therapy						
Grimes <i>et al.</i> (2006)		Systematic review	NSAID versus placebo		Significant reduction in pain when used to reactively treat post-insertion pain. No significant effect when given prophylactically	1
Goldstuck and Ward (1983)	59	Mainly nulliparous	Meptazinol versus placebo	Pain relief rated as 'excellent', 'good', 'fair', 'poor' or 'inadequate' at 7 days after insertion	Not significant (pain relief rated as 'good' or 'excellent' in 67 and 69% of subjects, in the meptazinol and placebo groups, respectively)	2

CI, confidence interval; NSAID, non-steroidal anti-inflammatory drug; VAS, visual analogue scale.

^aFor studies in which pain was evaluated at different time points, the time points included one or more of the following: at speculum insertion, at tenaculum placement, during the actual insertion of the device, shortly after insertion of the device.

^bOxford Centre for Evidence-Based Medicine (2011) levels of evidence: Level 1, systematic review of randomized trials; Level 2, randomized trial or an observational study with dramatic effect; Level 3, non-randomized controlled cohort/follow-up study; Level 4, case-series, case-control studies or historically controlled studies; Level 5, mechanism-based reasoning.

^cStudy was associated with a number of limitations, e.g. assignment of treatment was not blinded to providers and the treatment groups were not well balanced with regard to parity.

significantly different to the pain scores reported by those who did not take any pre-insertion analgesia (Murty, 2003).

Study limitations. The analgesia regimens evaluated in these studies were not optimized for IUC insertion, e.g. type of analgesia, dose and timing before the procedure. Instead, the regimens used were extrapolated from other gynaecological settings (abortion and hysteroscopy).

Group consensus. There is currently no evidence to recommend routine prophylactic use of ibuprofen; there is no evidence that it reduces insertion-related pain.

Data from one small study suggest that the prophylactic use of the atypical opioid analgesic tramadol, or the NSAID naproxen sodium, may reduce pain on IUC insertion. However, larger follow-up studies are required to confirm these preliminary findings.

Cervical priming

In an online US-based survey of 1905 providers who regularly insert IUC in nulliparous women, 50% reported using misoprostol and 40% of misoprostol users reported that they routinely used it in all nulliparous women (Vard et al., 2011). However, wide variation was reported in the dose used, as well as in the route and timing of administration. This reflects the current lack of studies defining the optimal misoprostol regimen and the lack of data on the 'real-world' usefulness of cervical priming in this setting.

The impact of cervical priming with misoprostol on pain associated with IUC insertion has been evaluated in five placebo-controlled RCTs (Sääv et al., 2007; Heikinheimo et al., 2010; Dijkhuizen et al., 2011; Edelman et al., 2011; Swenson et al., 2012) (Table I).

In the first RCT, 80 nulliparous women received either 400 µg sublingual misoprostol or placebo 1 h before the procedure. In addition, an NSAID (to alleviate misoprostol-induced uterine cramping) was administered in both treatment groups. The primary end-point was ease of insertion rather than pain (Sääv et al., 2007).

The second RCT was conducted in 89 women who had already had on average two births and were having a repeat LNG-IUS inserted: 400 µg sublingual misoprostol or placebo was given 3 h before the procedure without coadministration of an NSAID. Again, the primary end-point was ease of insertion rather than pain (Heikinheimo et al., 2010).

In the third trial, 40 nulliparous women were randomized to receive 400 µg misoprostol or placebo administered buccally 90 min before the procedure. Administration of oral analgesia or local anaesthesia was at the discretion of the provider and was reported by treatment group (Edelman et al., 2011). The primary end-point was pain measured on a VAS (0–100 mm) (Howard, 2003) at various time points before, during and after insertion (Edelman et al., 2011).

The fourth trial was conducted in 199 women, of whom 95 were nulliparous and 104 were parous. Women received 400 µg misoprostol or placebo vaginally 3 h before the procedure. Co-administration of NSAIDs was not permitted. The primary end-point was placement failure not pain (Dijkhuizen et al., 2011).

In the fifth trial, 108 nulliparous women who requested IUC were randomized to self-administer either 400 µg misoprostol or placebo vaginally or buccally 3–4 h before the insertion procedure. Use of prophylactic analgesia and local anaesthesia was permitted at the discretion of the investigator. Again, the primary end-point was ease of insertion rather than pain. However, subjects reported pain on a 0–100 VAS

at the following time points: before insertion, immediately post-insertion and before clinic discharge (Swenson et al., 2012).

In one of the five trials, the use of misoprostol compared with placebo was shown to significantly increase ease of insertion from the blinded investigator's perspective (Sääv et al., 2007). However, none of the five RCTs demonstrated a significant reduction in patient-reported pain with misoprostol compared with placebo. In the most recent study (Swenson et al., 2012), which evaluated pain at different time points, no significant difference between the misoprostol and placebo groups was observed for pain during the actual insertion ($P = 0.74$). However, subjects randomized to misoprostol reported significantly more pain before insertion ($P = 0.003$) and a trend towards more pain immediately post-insertion ($P = 0.07$). This is likely to be related to misoprostol-induced uterine cramping.

Furthermore, in the above studies premedication with misoprostol was associated with an increase in pre-insertion side effects compared with placebo. These side effects included nausea, cramps and, particularly with sublingual administration, shivering. These are known side effects of misoprostol; their severity is dependent on the dose and route of administration. Sublingual and buccal administrations are generally associated with increased side effects compared with vaginal administration (Caliskan et al., 2007; Jabir and Smeet, 2009).

The authors of four of these RCTs concluded that women should not be routinely premedicated with misoprostol before IUC insertion because the potential harms outweigh the possible benefits (Heikinheimo et al., 2010; Dijkhuizen et al., 2011; Edelman et al., 2011; Swenson et al., 2012).

Study limitations. To date, several aspects of cervical priming regimens for IUC insertion and removal remain unclear: the minimal dose of misoprostol and the optimal route, and the timing of administration to achieve the necessary degree of cervical softening before placement. No trial to date has sought to establish a standard on these variables. In addition, no trial has evaluated the benefits of misoprostol specifically among cases where insertion of IUC might be expected to be more difficult, such as when there is stenosis of the internal or external cervical os or when a previous insertion attempt has failed.

The regimens used in these five RCTs were based on experience from surgical abortion (Singh et al., 1998, 1999a, b, c). However, markedly less dilation is needed for IUC insertion. It is therefore likely that the doses of misoprostol administered in these studies were too high, causing unnecessarily high rates of side effects (mainly pain associated with uterine cramping). It is also possible that misoprostol induces more painful uterine contractions in non-pregnant women than pregnant women in whom the myometrium is protected from prostaglandin by an increased level of progesterone.

Although three of the five RCTs were conducted exclusively in nulliparous populations (Sääv et al., 2007; Edelman et al., 2011; Swenson et al., 2012), two studies involved mixed cohorts of multiparous and nulliparous women with conclusions drawn from the overall study populations. In the mixed cohort studies, failing to analyse subsets of nulliparous women and those who have only ever undergone Caesarean section deliveries may have led to erroneous conclusions being drawn and benefits for certain subgroups could have been missed.

The second study (Heikinheimo et al., 2010) included women who had already had on average two deliveries and nulliparous women represented only 6% of the study population. This study was conducted in a

highly selected cohort of women who had previously had IUC successfully inserted.

The main limitation in four of the studies was that ease of insertion or insertion failure was the primary outcome; pain was not the primary endpoint in these trials and therefore overall pain was evaluated rather than differentiating between pain associated with misoprostol-induced uterine contractions and cervical pain caused by dilation. In addition, the different time points when pain occurred were recorded in only two studies. Painful uterine cramping and other unpleasant side effects associated with misoprostol are dose-dependent. It is possible that when misoprostol was given *without* an NSAID, for example, in the study by Heikinheimo and colleagues (Heikinheimo *et al.*, 2010), the pain experienced in the placebo group was mostly related to IUC insertion and cervical in origin, whereas the pain experienced in the misoprostol group may have been associated with uterine cramping caused by the prostaglandin.

The time taken for misoprostol to exert its effect on the cervical tissue (and on uterine contractility) may vary according to the route of administration, e.g. sublingual administration has a more rapid effect than vaginal or buccal administration (Aronsson *et al.*, 2004; Meckstroth *et al.*, 2006; Tang *et al.*, 2007). In the study by Edelman *et al.* (2011), misoprostol was administered buccally 90 min before the procedure. This timeframe might be sufficient to cause uterine cramping but might not be long enough to soften the cervical tissue (Meckstroth *et al.*, 2006). Based on studies on cervical priming prior to surgical abortion, misoprostol should be administered at least 3 h in advance if administered buccally or vaginally. This is in contrast to sublingual administration, which results in a rapid onset of action, based on pharmacokinetics in pregnant women (Tang *et al.*, 2007).

In addition, the results of the study by Edelman *et al.* (2011) are difficult to interpret because additional oral analgesia and local anaesthesia (by various techniques) were given at the discretion of the investigator in both treatment arms but not reported in the publication, and only 40 women were evaluated.

Studies on the prophylactic use of mifepristone or spasmolytics for IUC placement have not been reported. The effect of cervical priming with mifepristone has been investigated in two RCTs conducted in other gynaecological settings; the first in 30 women undergoing surgical abortion, the second in non-pregnant premenopausal women about to undergo either cervical dilatation and diagnostic curettage or laparoscopic sterilization. In both the pregnant and non-pregnant controls, 600 mg of mifepristone given orally 48 h prior to surgery increased the mean pre-operative cervical dilation and reduced the force required to dilate the cervix (Gupta and Johnson, 1990).

Group consensus. A small group of women experience severe pain during IUC insertion and need special attention. Currently there is no accepted standard for prevention or treatment of these symptoms. Although there were limitations in the design and conduct of the above studies, and therefore in the conclusions that could be drawn, there is currently no clear evidence to support the routine use of misoprostol at the 400 µg dose in all women for pain control. There is no clear evidence that pain is reduced from the woman's perspective and potential harms may outweigh the possible benefits of the misoprostol regimens used in RCTs to date. In addition, in the absence of studies, there is no evidence to support routine use of mifepristone in the context of IUC placement.

For most nulliparous, nulligravid or parous women, IUC insertion can be performed successfully without cervical priming and with a minimum amount of discomfort (Bahamondes *et al.*, 2011). Whether selective use of misoprostol has a role in management of pain in certain subsets of women (e.g. nulliparous women and those in whom the insertion is non-routine/difficult) has yet to be adequately studied.

There is currently some evidence that misoprostol eases insertion from the provider's perspective. If misoprostol is to be used for cervical priming/ripening to improve technical ease in certain groups of women, we recommend that an NSAID (e.g. diclofenac or ibuprofen) is co-administered to manage the prostaglandin-mediated side effects (e.g. uterine cramping).

Pre-insertion local anaesthesia

The term 'local anaesthesia' has a different meaning to different providers and includes a number of formulations (e.g. gel, injections and spray) and techniques for administration (intracervical and paracervical).

Lignocaine gel: The application of local anaesthetic lignocaine gel before IUC insertion has been evaluated in three RCTs (Oloto *et al.*, 1996; Maguire *et al.*, 2012; McNicholas *et al.*, 2012) (Table I).

The first trial was a single-centre UK-based study, which evaluated the efficacy of 2% lignocaine gel, inactive placebo gel or 'no treatment' applied to the cervical canal for reduction in pain in 102 nulliparous or parous women (Oloto *et al.*, 1996). Intracervical application of 2% lignocaine gel resulted in a significant reduction in pain compared with no active treatment (placebo gel or no treatment; $P < 0.025$). Using a scale of 1–7, pain scores of 1–2, 3–4 and 5–7 were reported by 34 versus 10%, 48 versus 60% and 18 versus 29% of women in the lignocaine gel versus no active treatment groups, respectively. However, the trial was associated with several limitations; assignment of treatment was not blinded to providers, which may have influenced the results (e.g. knowing that active gel was being used may have allowed the provider to proceed with greater confidence). In addition, the treatment groups were not well balanced; a higher proportion of nulliparous women were allocated to the 'no treatment' group.

The second study was a randomized, double-blind trial of 197 women treated with intracervical 2% lignocaine gel or placebo gel prior to uterine sounding and insertion of IUC (Maguire *et al.*, 2012). There was no decrease in pain in the lignocaine group compared with the placebo group. Pain (measured by 100 mm VAS) was greatest during sounding and was similar between groups (51.6 mm in the placebo group versus 55.5 mm in the lignocaine group; $P = 0.33$). No treatment effect was seen in a stratified analysis accounting for parity.

The third study was a double-blind RCT in which women received 2% lignocaine or placebo gel applied at the planned tenaculum site and into the endocervical canal 3 min before IUC insertion (McNicholas *et al.*, 2012). Women rated their pain on a 10-point VAS immediately after tenaculum placement and immediately after IUC insertion. No significant difference was observed between the treatment groups at either of the time points studied for the overall cohort of 199 nulliparous and parous women, nor in the individual subgroups of nulliparous and parous women.

Injectable local anaesthesia: This involves a series of injections of a local anaesthetic into the vaginal fornices around the cervix (paracervical block) or into the cervical stroma (intracervical block). Pain reduction is achieved by blocking nerve fibres. Various techniques and provider experiences have been discussed in the literature (Hepburn, 1980;

Kurz and Meier-oehlke, 1983; Thiery, 1985; Bacon, 2011; Eady, 2011; Gray, 2011; Jones, 2011; Hutt, 2011a, b).

Only one RCT has evaluated the impact of injectable local anaesthesia on pain associated with insertion of IUC. This study evaluated a 1% lignocaine paracervical block compared with no local anaesthesia on patient-reported pain in 50 nulliparous and parous women undergoing IUD insertion (Mody et al., 2012). The women rated pain on a 100 mm VAS at the following time points during the procedure: speculum insertion, tenaculum placement, paracervical block administration, IUC insertion and 5 min after completion of the procedure. After adjustment for differences in BMI, no significant difference in pain was observed between the treatment groups at any of the time points studied.

In a systematic review and meta-analysis of data on the efficacy of local anaesthesia for pain control during outpatient hysteroscopy (Cooper et al., 2010), intracervical and paracervical injections of a local anaesthetic significantly reduced patient-reported pain, whereas transcervical and topical application of a local anaesthetic did not. A meta-analysis showed that paracervical injections provided superior pain reduction compared with the other techniques. However, the main problem with studying local anaesthesia in transcervical procedures is the huge variation in techniques, which are often inadequately explained, and the difficulty in evaluating diverse techniques. In addition, the terms 'paracervical' and 'intracervical' are frequently used but clinicians have different understandings of what these terms mean. For example, in one study of intracervical anaesthesia that was included in the systematic review and meta-analysis, 2 ml of 1% lignocaine was injected at the tenaculum site, which would have had no effect on the internal os. In another study of intracervical anaesthesia that was included, women received 100 mg tramadol, which might be expected to be a strong confounding factor. This systematic review is therefore a good example of the difficulties encountered when trying to conduct a meaningful analysis on the comparative effectiveness of different local anaesthesia techniques. However, from a rational standpoint, in a paracervical block local anaesthetic is injected without knowing the exact location of the target nerve, and therefore a larger volume is injected compared with an intracervical block in which the inner os is targeted directly either via the cervical canal or via cervical tissue. Importantly, however, hysteroscopy is not comparable with IUC insertion (e.g. IUC insertion requires less cervical dilation) and extrapolation of data between procedures should be viewed with caution.

Group consensus. There is currently no clear evidence from RCTs to recommend routine prophylactic use of local anaesthesia in any form for IUC insertions. Furthermore, there is no evidence that local anaesthesia prophylaxis is needed routinely in this setting. However, complications arising from the procedure, need for dilation and insertion pain are difficult to predict. Injectable local anaesthesia should therefore be at hand for reactive administration, intracervically or paracervically.

Post-insertion pharmacological therapy

NSAIDs

A systematic review of RCTs concluded that NSAIDs were effective in reactively treating pain after IUC insertion. However, prophylactic administration of NSAIDs after the procedure seemed to provide no significant pain reduction benefit, and caused side effects including stomach upsets and sleepiness (Grimes et al., 2006).

Group consensus. There is currently no evidence to recommend the routine prophylactic use of an NSAID immediately after IUC insertion because there is no clear evidence of benefit. However, if a woman does develop pain after the procedure, NSAIDs can be taken.

Despite a lack of conclusive supporting evidence, prophylactic use of NSAIDs after insertion of IUC is widespread, possibly because they are inexpensive, available over the counter and associated with relatively few side effects. They may also reduce anxiety through a possible placebo effect.

Opioid analgesia

In an RCT ($n = 59$) comparing meptazinol, a partial μ -opioid receptor agonist, with placebo for the relief of pain after copper IUD insertion, no significant difference was seen between treatment groups in the patients' global assessment of their therapy. Sixty-seven per cent and 69% of patients randomized to meptazinol and placebo, respectively, assessed their pain relief treatment as 'good or excellent', indicating either a strong placebo effect or that the procedure is pain-free or well tolerated by most women (Goldstuck and Ward, 1983).

Group consensus. There is no evidence to support the routine use of narcotics for the treatment of pain after IUC insertion, and therefore, it is not recommended. There is no clear evidence of clinical benefit, and providers should question the cause of such pain that it warrants narcotic pain relief (e.g. have complications occurred?). Use of opioids may be appropriate only in very rare cases.

Non-pharmacological pain management strategies

Pre-insertion counselling

In a study evaluating the benefits of a psychological preparation interview, clear benefits in reducing patient-perceived pain at IUD insertion were reported (Newton and Reading, 1977). The authors suggested that psychological preparation may reduce the perception of pain by reducing uncertainty, providing information/reassurance on what to expect and increasing motivation leading to higher tolerance of discomfort.

Management of women's anxiety

A UK-based study of IUC insertions performed at a single centre (Murty, 2003) concluded that women who were more anxious and who anticipated that the procedure would be painful, even if it was not as bad as they expected at the time of the procedure, recalled 6 months later that it was a painful experience. In addition, women who choose to take oral analgesia before the procedure may be the most anxious, and higher anxiety levels may contribute to perceived pain.

Group consensus. Strategies aimed at reducing women's anxiety before and during the insertion procedure are important and may be effective in reducing pain associated with IUC insertion. The most anxious women may be those with mood disorders, a history of sexual trauma, a previous negative reaction to vaginal examination or a previous insertion that was painful and those who have heard from a peer about a painful procedure. These contributory factors have not been studied in any detail.

Data gaps and areas for further research

Oral analgesia

There is a general paucity of data on the use of pre-insertion oral analgesia. Furthermore, the regimens currently used in this context have been extrapolated from gynaecological procedures, such as hysteroscopy and surgical abortion.

Cervical priming

There are insufficient data on the use of cervical priming for reduction of pain associated with IUC insertion in non-routine cases and in nulliparous or nulligravid women. There are also insufficient data to determine the optimal dose, route and timing of misoprostol administration. The current regimens are derived from other gynaecological procedures, such as surgical abortion and hysteroscopy, in which wider cervical dilation is needed.

Future studies of misoprostol should focus on the evaluation of pain before, during and after IUC insertion rather than on overall pain, to differentiate the possible cause of pain at different time points. A lower misoprostol dose for IUC insertions could also be explored because less cervical dilation is required in this setting compared with other gynaecological procedures. Furthermore, dose reduction has the potential to induce less pain from prostaglandin-induced uterine cramping. Evaluation of other substances, such as mifepristone or spasmolytic drugs, is also recommended.

Local anaesthesia

There is a lack of studies evaluating the efficacy of different techniques for administering local anaesthesia to help reduce pain associated with IUC insertion. The available data on the use of local anaesthesia are mainly derived from studies of hysteroscopy. Studies are needed to directly compare different formulations (e.g. gel versus spray versus injectables), different administration techniques (e.g. intracervical versus paracervical) and different injectable anaesthetic drugs.

Non-pharmacological interventions

Studies evaluating the impact of non-pharmacological interventions (e.g. pre-insertion counselling and the effect of an assistant providing reassurance and distraction during the procedure) are lacking. Data from such studies are needed to share best practices internationally.

Summary and conclusions

Although IUC insertions can be performed in the majority of women without pharmacological interventions to reduce pain, a relevant percentage of women would benefit from such measures. After critical evaluation of the evidence, it can be concluded that no prophylactic pharmacological intervention has been adequately evaluated to support its routine use for reduction of pain during or after IUC insertion. Most regimens have been adapted from other gynaecological procedures and their effectiveness in providing pain relief in specific subsets of women has not been studied.

There is some evidence to suggest that non-pharmacological interventions might reduce pain levels. Women's anxiety about the procedure

may contribute to higher levels of perceived pain during IUC insertion, highlighting the importance of pre-insertion counselling, and 'verbal anaesthesia' and distraction during the procedure to help minimize anxiety. Further studies focusing on non-pharmacological interventions need to be conducted and reported in the literature to disseminate best practice advice internationally.

Acknowledgements

The authors acknowledge medical writing support provided by Sonya Haslam, which was funded by Bayer HealthCare.

Authors' roles

All authors participated in study design, data analysis, manuscript drafting and discussion. The authors have given their approval of the final version of the manuscript.

Funding

The assistance provided by Sonya Haslam in preparing the manuscript was funded by Bayer HealthCare. No other funding was provided for the study.

Conflicts of interest

The authors were invited and assisted by Bayer HealthCare to write the manuscript. However, no honorarium was received from the sponsor. K.G.-D. serves on advisory boards and has received financial support to undertake research studies and to speak at educational meetings and conferences from Bayer HealthCare, Merck/MSD, Exelgyn, HRA-Pharma and Gedeon Richter. D.M. has received financial support to attend pharmaceutical advisory board meetings, undertake research studies and to speak at educational meetings and conferences from Astellas, Merck, HRA Pharma, Consilient Healthcare, Vifor Pharma and Bayer HealthCare. C.F. has received financial support to attend advisory board meetings from Bayer HealthCare. A.M.K. serves on advisory boards for Bayer HealthCare and Merck. The University of Florida College of Medicine receives research funding from Bayer and Teva. L.B. serves on advisory boards for Bayer HealthCare and Merck. The University of Campinas receives research funding from Bayer and MSD.

References

- Allen RH, Bartz D, Grimes DA, Hubacher D, O'Brien P. Interventions for pain with intrauterine device insertion. *Cochrane Database Syst Rev* 2009;CD007373.
- Anon. The reproductive health report: the state of sexual and reproductive health within the European Union. *Eur J Contracept Reprod Health Care* 2011;**16**(Suppl 1):S1–S70.
- Aronsson A, Bygdeman M, Gemzell-Danielsson K. Effects of misoprostol on uterine contractility following different routes of administration. *Hum Reprod* 2004;**19**:81–84.
- Association of Reproductive Health Professionals. New developments in intrauterine contraception: use of intrauterine contraception in the United States. Available at: <http://www.arhp.org/Publications-and-Resources/Clinical-Proceedings/CP-Archives> (1 November 2011, date last accessed), 2004.
- Bacon L. Option of local anaesthetic for IUD fittings. *J Fam Plann Reprod Health Care* 2011;**37**:253–254.

- Bahamondes MV, Hidalgo MM, Bahamondes L, Monteiro I. Ease of insertion and clinical performance of the levonorgestrel-releasing intrauterine system in nulligravidas. *Contraception* 2011;**84**:e11–e16.
- Bailit JL, Love TE, Mercer B. Rising cesarean rates: are patients sicker? *Am J Obstet Gynecol* 2004;**191**:800–803.
- Barber EL, Lundsberg LS, Belanger K, Pettker CM, Funai EF, Illuzzi JL. Indications contributing to the increasing cesarean delivery rate. *Obstet Gynecol* 2011;**118**:29–38.
- Brockmeyer A, Kishen M, Webb A. Experience of IUD/IUS insertions and clinical performance in nulliparous women—a pilot study. *Eur J Contracept Reprod Health Care* 2008;**13**:248–254.
- Caliskan E, Filiz T, Yucesoy G, Coskun E, Vural B, Corakci A. Sublingual versus vaginal misoprostol for cervical ripening PRIOR TO manual vacuum aspiration under local anaesthesia: a randomized study. *Eur J Contracept Reprod Health Care* 2007;**12**:372–377.
- Chi IC, Galich LF, Tauber PF, Wilkens LR, Waszak CS, Siemens AJ, Lippes J. Severe pain at interval IUD insertion: a case-control analysis of patient risk factors. *Contraception* 1986;**34**:483–495.
- Chi IC, Wilkens LR, Champion CB, Macherer RE, Rivera R. Insertional pain and other IUD insertion-related rare events for breastfeeding and non-breastfeeding women—a decade's experience in developing countries. *Adv Contracept* 1989;**5**:101–119.
- Chor J, Bregand-White J, Golobof A, Harwood B, Cowett A. Ibuprofen prophylaxis for levonorgestrel-releasing intrauterine system insertion: a randomized controlled trial. *Contraception* 2012;**85**:558–562.
- Cooper NA, Khan KS, Clark TJ. Local anaesthesia for pain control during outpatient hysteroscopy: systematic review and meta-analysis. *BMJ* 2010;**340**:c1130.
- Dijkhuizen K, Dekkers OM, Holleboom CA, de Groot CJ, Hellebrekers BW, van Roosmalen GJ, Janssen CA, Helmerhorst FM. Vaginal misoprostol prior to insertion of an intrauterine device: an RCT. *Hum Reprod* 2011;**26**:323–329.
- Eady A. Local anaesthetic administration for IUD/IUS insertions. *J Fam Plann Reprod Health Care* 2011;**37**:254–255.
- Edelman AB, Schaefer E, Olson A, van Houten L, Bednarek P, Leclair C, Jensen JT. Effects of prophylactic misoprostol administration prior to intrauterine device insertion in nulliparous women. *Contraception* 2011;**84**:234–239.
- Gemzell-Danielsson K, Cho S, Inki P, Mansour D, Reid R, Bahamondes L. Use of contraceptive methods and contraceptive recommendations among health care providers actively involved in contraceptive counseling—results of an international survey in 10 countries. *Contraception* 2012;**86**:631–638.
- Goldstuck ND, Ward PJ. Treatment of pain following IUD insertion with meptazinol—a new centrally acting analgesic. *Contracept Deliv Syst* 1983;**4**:33–37.
- Gray S. Option of local anaesthetic for IUD fittings. *J Fam Plann Reprod Health Care* 2011;**37**:189–190.
- Grimes DA, Hubacher D, Lopez LM, Schulz KF. Non-steroidal anti-inflammatory drugs for heavy bleeding or pain associated with intrauterine-device use. *Cochrane Database Syst Rev* 2006;CD006034.
- Gupta JK, Johnson N. Effect of mifepristone on dilatation of the pregnant and non-pregnant cervix. *Lancet* 1990;**335**:1238–1240.
- Heikinheimo O, Inki P, Kunz M, Parmhed S, Anttila AM, Olsson SE, Hurskainen R, Gemzell-Danielsson K. Double-blind, randomized, placebo-controlled study on the effect of misoprostol on ease of consecutive insertion of the levonorgestrel-releasing intrauterine system. *Contraception* 2010;**81**:481–486.
- Hepburn S. Method of local anaesthesia for IUD insertion. *Contracept Deliv Syst* 1980;**1**:371–377.
- Howard FM. Chronic pelvic pain. *Obstet Gynecol* 2003;**101**:594–611.
- Hubacher D, Reyes V, Lillo S, Zepeda A, Chen PL, Croxatto H. Pain from copper intrauterine device insertion: randomized trial of prophylactic ibuprofen. *Am J Obstet Gynecol* 2006;**195**:1272–1277.
- Hutt S. Injectable local anaesthesia for IUD/IUS fittings. *J Fam Plann Reprod Health Care* 2011a;**37**:59.
- Hutt S. Women should be routinely offered ILA for IUD fittings. *J Fam Plann Reprod Health Care* 2011b;**37**:253–254.
- Jabir M, Smeeth RI. Comparison of oral and vaginal misoprostol for cervical ripening before evacuation of first trimester missed miscarriage. *Saudi Med J* 2009;**30**:82–87.
- Jones K. Use of injectable local anaesthesia for IUD/IUS fitting. *J Fam Plann Reprod Health Care* 2011;**37**:253.
- Karabayirli S, Ayrim AA, Muslu B. Comparison of the analgesic effects of oral tramadol and naproxen sodium on pain relief during IUD insertion. *J Minim Invasive Gynecol* 2012;**19**:581–584.
- Kurz KH, Meier-oehlke P. Jet injection-local anesthesia for fitting and removal of IUDs. *Contracept Deliv Syst* 1983;**4**:27–32.
- Lassner KJ, Chen CH, Kropsch LA, Oberle MW, Lopes IM, Morris L. Comparative study of safety and efficacy of IUD insertions by physicians and nursing personnel in Brazil. *Bull Pan Am Health Organ* 1995;**29**:206–215.
- Maguire K, Davis A, Rosario TL, Westhoff C. Intracervical lidocaine gel for intrauterine device insertion: a randomized controlled trial. *Contraception* 2012;**86**:214–219.
- Marions L, Lökvist L, Taube A, Johansson M, Dalvik H, Øverlie I. Use of the levonorgestrel-releasing-intrauterine system in nulliparous women—a non-interventional study in Sweden. *Eur J Contracept Reprod Health Care* 2011;**16**:126–134.
- McNicholas CP, Madden T, Zhao Q, Secura G, Allsworth JE, Peipert JF. Cervical lidocaine for IUD insertional pain: a randomized controlled trial. *Am J Obstet Gynecol* 2012;**207**:384–386.
- Meckstroth KR, Whitaker AK, Bertisch S, Goldberg AB, Darney PD. Misoprostol administered by epithelial routes: drug absorption and uterine response. *Obstet Gynecol* 2006;**108**:582–590.
- Mody SK, Kiley J, Rademaker A, Gawron L, Stika C, Hammond C. Pain control for intrauterine device insertion: a randomized trial of 1% lidocaine paracervical block. *Contraception* 2012;**86**:704–709.
- Murty J. Use and effectiveness of oral analgesia when fitting an intrauterine device. *J Fam Plann Reprod Health Care* 2003;**29**:150–151.
- Newton JR, Reading AE. The effects of psychological preparation on pain at intrauterine device insertion. *Contraception* 1977;**16**:523–532.
- Oloto EJ, Bromham DR, Murty JA. Pain and discomfort perception at IUD insertion—effect of short-duration, low volume intracervical application of two percent lignocaine gel (Instillagel™)—a preliminary study. *Br J Fam Plann* 1996;**22**:177–180.
- Peipert JF, Zhao Q, Allsworth JE, Petrosky E, Madden T, Eisenberg D, Secura G. Continuation and satisfaction of reversible contraception. *Obstet Gynecol* 2011;**117**:1105–1113.
- Säävi I, Aronsson A, Marions L, Stephansson O, Gemzell-Danielsson K. Cervical priming with sublingual misoprostol prior to insertion of an intrauterine device in nulliparous women: a randomized controlled trial. *Hum Reprod* 2007;**22**:2647–2652.
- Secura GM, Allsworth JE, Madden T, Mullersman JL, Peipert JF. The Contraceptive CHOICE Project: reducing barriers to long-acting reversible contraception. *Am J Obstet Gynecol* 2010;**203**:115.e1–115.e7.
- Singh K, Fong YF, Prasad RN, Dong F. Randomized trial to determine optimal dose of vaginal misoprostol for preabortion cervical priming. *Obstet Gynecol* 1998;**92**:795–798.
- Singh K, Fong YF, Prasad RN, Dong F. Does an acidic medium enhance the efficacy of vaginal misoprostol for pre-abortion cervical priming? *Hum Reprod* 1999a;**14**:1635–1637.
- Singh K, Fong YF, Prasad RN, Dong F. Evacuation interval after vaginal misoprostol for preabortion cervical priming: a randomized trial. *Obstet Gynecol* 1999b;**94**:431–434.
- Singh K, Fong YF, Prasad RN, Dong F. Vaginal misoprostol for pre-abortion cervical priming: is there an optimal evacuation time interval? *Br J Obstet Gynaecol* 1999c;**106**:266–269.
- Stavrou EP, Ford JB, Shand AW, Morris JM, Roberts CL. Epidemiology and trends for Caesarean section births in New South Wales, Australia: a population-based study. *BMC Pregnancy Childbirth* 2011;**11**:8.
- Suhonen S, Haukkamaa M, Jakobsson T, Rauramo I. Clinical performance of a levonorgestrel-releasing intrauterine system and oral contraceptives in young nulliparous women: a comparative study. *Contraception* 2004;**69**:407–412.
- Swenson C, Turok DK, Ward K, Jacobson JC, Dermish A. Self-administered misoprostol or placebo before intrauterine device insertion in nulliparous women: a randomized controlled trial. *Obstet Gynecol* 2012;**120**:341–347.
- Tang OS, Gemzell-Danielsson K, Ho PC. Misoprostol: pharmacokinetic profiles, effects on the uterus and side-effects. *Int J Gynaecol Obstet* 2007;**99**(Suppl 2):S160–S167.
- Thiery M. Pain relief at insertion and removal of an IUD: a simplified technique for paracervical block. *Adv Contracept* 1985;**1**:167–170.
- Trussell J. Contraceptive failure in the United States. *Contraception* 2011;**83**:397–404.
- Villar J, Valladares E, Wojdyla D, Zavaleta N, Carroli G, Velazco A, Shah A, Campodónico L, Bataglia V, Faundes A et al. Caesarean delivery rates and pregnancy outcomes: the 2005 WHO global survey on maternal and perinatal health in Latin America. *Lancet* 2006;**367**:1819–1829.

-
- Ward K, Jacobson JC, Turok DK, Murphy PA. A survey of provider experience with :
misoprostol to facilitate intrauterine device insertion in nulliparous women. :
Contraception 2011;**84**:594–599. : Winner B, Peipert JF, Zhao Q, Buckel C, Madden T, Allsworth JE, Secura GM.
Effectiveness of long-acting reversible contraception. *N Engl J Med* 2012;
366:1998–2007.