More Harm Than Good: The Lack of Evidence for Administering Misoprostol Prior to IUD Insertion

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Abstract

The administration of misoprostol prior to insertion of an intrauterine device has become a widespread practice. Because of its utility for cervical ripening before procedures such as dilatation and curettage, misoprostol has been assumed to be a safe and useful adjunct both to facilitate the ease of insertion of an IUD and to reduce the pain experienced by women during this procedure. As this practice has become more widely used, a body of literature has evolved to assess whether or not it truly improves the IUD insertion experience for providers and patients. A literature search showed that six controlled trials have been carried out to assess this practice (one is reported in abstract form only). The dosing and route of administration vary between the trials; however, there are quite consistent findings that not only does misoprostol administration not improve the ease of insertion of IUDs but it also leads to increased unpleasant side effects. The routine use of misoprostol for IUD insertion should be abandoned.

Résumé

L'administration de misoprostol avant l'insertion d'un dispositif intra-utérin est devenue une pratique répandue. En raison de son utilité à des fins de maturation cervicale avant la tenue d'interventions telles que la dilatation-curetage, il a été présumé que le misoprostol constituait une mesure d'appoint sûre et utile tant pour faciliter l'insertion d'un DIU que pour atténuer la douleur que connaissent les femmes au cours de cette intervention. En raison de la popularité grandissante de cette pratique, nous avons assisté à la publication d'un corpus d'articles traitant de la question de savoir si celle-ci améliore réellement l'expérience de l'insertion d'un DIU pour les fournisseurs de soins et les patientes. Une recherche documentaire a indiqué que six essais comparatifs avaient été menés en vue d'évaluer cette pratique (un de ceux-ci n'a été publié que sous forme de résumé). La posologie et la voie d'administration varient d'un essai à l'autre; toutefois, les résultats s'entendent assez uniformément pour indiquer qu'en plus de ne pas faciliter l'insertion des DIU, l'administration de misoprostol mène à une hausse des effets indésirables. L'utilisation systématique du misoprostol aux fins de l'insertion d'un DIU devrait être abandonnée.

Key Words: Misoprostol, IUD, IUS, intrauterine system, intrauterine device

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INTRODUCTION

Misoprostol is an inexpensive, widely available prostaglandin E_1 analogue approved by Health Canada for use as a protective agent for the gastric mucosa. It is used for a variety of purposes in the field of obstetrics and gynaecology, most notably as a cervical ripening agent prior to dilatation and curettage, and in the management of postpartum hemorrhage.

Copper-containing intrauterine devices and the levonorgestrel intrauterine system are becoming increasingly popular among Canadian women as effective, long-acting, and reversible contraceptives.[1] With increasing experience using these contraceptive devices, care providers have become more confident in recommending them for a wider variety of women, including adolescents and nulliparous women. Because insertion of an intrauterine device or system is painful for many women, and can be challenging in some circumstances, some care providers are hesitant to recommend this form of contraceptive, particularly to nulliparous women.[2] Widespread interest in finding ways to decrease patient discomfort and increase ease of insertion has led to a variety of techniques being employed, frequently including the use of misoprostol to prepare the cervix prior to IUD insertion. This practice became widespread, mainly through word of mouth,[2] before there was sufficient research evidence to support it. We conducted a review of the available evidence to determine if the use of misoprostol in this context is justified.

METHODS

A search of PubMed using the terms "misoprostol" or "prostaglandin" combined with "IUD," "IUS," "intrauterine device," or "intrauterine system" reveals that to date there have been six randomized controlled studies of the use of misoprostol prior to IUD insertion.[3–8] While one of these studies has been presented only in abstract form, the other five have been published in peer-reviewed journals. There is variation between studies in the dosing and route of administration of misoprostol; however, the overall findings in these studies are fairly consistent and suggest that the routine use of misoprostol prior to IUD insertion does not substantially increase ease of insertion as reported by the care provider, or reduce the number of failed insertions.

Some of the studies[4,6,9] investigated the use of misoprostol for cervical ripening in both multiparous and nulliparous women. Others[3,5,7,8] included only nulliparous women. There have been no studies assessing misoprostol use only in multiparous women.

RESULTS

Only one[3] of six studies reports an improvement in the ease of IUD insertion (reported by the care provider) with the pre-insertion use of misoprostol. In 2007, Saav et al. carried out a randomized study that was single-blind and not placebo-controlled.[3] Patients were randomized to receive either 400 μg of misoprostol sublingually with 100 mg of diclofenac, or 100 mg of diclofenac alone. The study included only nulliparous women. The authors reported that care providers described IUD insertion as "easy" in 74.4% of patients pre-treated with misoprostol compared with 55.0% of those who did not receive pre-treatment. This difference reached statistical significance ($P = 0.039$). The care providers in this study found the insertions overall to be far less difficult than they had expected. When asked, care providers guessed that 20 of the 40 women in the control group had been pre-treated with misoprostol, because the IUD insertion was so easy. In contrast to the study of Saav et al.[3], five other studies[4–8] did not demonstrate any improvement in ease of insertion reported by the care provider. These five studies may provide more reliable data, as they were all double-blind and placebo-controlled, while the study of Saav et al. was neither.

Even if cervical preparation with misoprostol prior to IUD insertion has not been demonstrated to improve ease of insertion, its use would still warrant consideration if there were an advantage with regard to patient comfort. A Cochrane review[10] of interventions for pain with IUD insertion found no improvement in patient-reported pain scores with the use of misoprostol before IUD insertion; however, this review included only the study by Saav et al. because no other studies had been reported at the time the review was undertaken. The study by Saav et al. did not show a difference in pain scores between the misoprostol and control groups on a visual analogue scale.

The study by Saav et al. did describe a trend towards increased side effects in the treatment group. A statistically significant increase in shivering was experienced by women pre-treated with misoprostol compared with control subjects. There was also a trend towards increased rates of diarrhea (30.8% in the misoprostol group vs. 15.0% in the control group), and vomiting (5.1% vs. 2.5%), but neither of these reached statistical significance. Doubt may be cast on the validity of the side-effect comparison in this study because women were not blinded to treatment group and no placebo was used.

In a double-blind, multicentre, randomized controlled study reported by Dijkhuizen et al. in 2011,[6] women received either 400 μg of misoprostol or a placebo (inserted vaginally) three hours before IUD insertion. This study included both nulliparous and multiparous women. There was a statistically significant increase in side effects experienced by the misoprostol group (56.6%) compared with control subjects (42.4%) (RR 1.3, 95% CI 1.0 to 1.7; $P = 0.05$); the most commonly reported side effect was abdominal cramping. In this study there was also a non-significant trend towards increased pain estimation at the time of IUD insertion by women in the misoprostol group compared with controls. Nulliparous women assigned to receive misoprostol reported higher rates of side effects than nulliparous women who received placebo (60.4% vs. 45.5%), although this difference did not reach statistical significance. This was also true for multiparous women: those who received misoprostol reported more side effects than those who received placebo (52.9% vs. 39.6%). This difference also did not reach statistical significance for multiparous women.

Edelman et al. reported another double-blind, randomized controlled study of misoprostol that demonstrated significantly more nausea in the misoprostol group than in controls (29% vs. 5%, $P = 0.05$) as well as significantly more cramping (47% vs. 16%, $P = 0.04$).[5] The route of administration of the 400 μg misoprostol or placebo in this study was buccal. As in the study by Dijkhuizen et al.,[6] a non-significant trend was found towards increased pain with IUD insertion in the treatment group compared with controls. This study included nulliparous women only.

A double-blind, multicentre, randomized controlled study by Heikinheimo et al. compared misoprostol pre-treatment with placebo in a group of women who were having an IUD removed followed by insertion of a new IUD.[4] The dose of misoprostol was again 400 μg, but in this study it was administered sublingually. This study included both nulliparous and multiparous women. There was a significant increase in side effects seen in the misoprostol group compared with the placebo group (51.2% vs. 10.9%). Most side effects were gastrointestinal (oral pain, diarrhea, and nausea), with uterine contractions also reported. While there was no statistically significant overall difference between groups with regard to pain associated with insertion, more women in the misoprostol group reported severe pain than in the placebo group (23.3% vs. 10.9%). The study report did not include a comparison of outcome measures between nulliparous and multiparous women.

In a randomized, double blind, placebo-controlled study by Swenson et al.,[8] published in 2012, the misoprostol group reported significantly more pain before IUD insertion than the placebo group (17.1 mm on a visual analogue scale vs. 4.7 mm, $P = 0.003$) as well as a non-significant trend towards more pain post-insertion (35.1 mm vs. 27.5 mm, $P = 0.074$). In this study patients were provided with 400μg of misoprostol or placebo and could administer it vaginally or buccally. Most women (94%) used the misoprostol vaginally. All participants were nulliparous.

A randomized controlled trial by Scavuzzi et al.[7] randomized nulliparous women to receive 400 μg of misoprostol, or placebo, administered vaginally one hour before IUD insertion. This study did not detect any difference in cervical dilatation as measured by Hegar dilators, ease of insertion, or patient-reported pain. There was also no difference in side effects between the groups.

The studies described above covered a wide variety of patients, including nulliparous and multiparous users and women who were having an IUD removed and replaced. The dose of misoprostol used was the same in each study, although the route of administration varied. None of the studies demonstrated a clinical benefit to the use of misoprostol for cervical preparation before IUD insertion.

No study was designed to directly compare nulliparous and multiparous subjects. The single study[3] that showed an improvement in ease of insertion with the use of misoprostol involved only nulliparous subjects. Several other studies[5,7,8] that specifically assessed nulliparous women did not show any improvement in the ease of insertion or in reported pain with the use of misoprostol compared with placebo.

It should be noted that none of the above studies specifically addresses the issue of patients who have previously experienced a failed IUD insertion attempt. One case series[10] used misoprostol following failed IUD insertion attempts in eight patients. IUD insertion was successful in all eight following the use of 400 μg of misoprostol vaginally on the day before the insertion. Further studies are needed to determine if the benefit of using misoprostol in this specific clinical setting outweighs the risk of side effects.

CONCLUSION

Cervical preparation with misoprostol does not increase the ease of IUD insertion, and its use increases unpleasant side effects and may increase pain with insertion. Nevertheless, the practice is still widespread. The dictum "First, do no harm" should be remembered when planning and performing an IUD insertion. Research evidence clearly suggests that the routine use of misoprostol in this setting should be abandoned.

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