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Efficacy of misoprostol in reducing the time and easiness the insertion of Levonorgestrel-releasing intrauterine device; Randomized controlled trial

Abstract

Background: intrauterine devices (IUDs) have gained significant popularity as a prevalent form of reversible contraception. Levonorgestrel-releasing intrauterine devices (LNG-IUDs) have been found to be safe and cost-effective over an extended period. Furthermore, their efficacy is comparable to that of tubal sterilization.

Aim: The aim of our study to reveled the effect of vaginal misoprostol on timing and the easiness of insertion of (LNG-IUDs) in previous cesarean sections women.

Materials and method: One-hundred and eighty patients with a previous cesarean section attending for Mirena LNG-IUD insertion. This Randomized controlled trial set in Outpatient clinic in Department of Obstetrics and Gynecology, Faculty of Medicine, Helwan University Hospital at BADR city from March 2021 to March 2022. The current research assessed the effectiveness of 400mcg vaginal misoprostol 6 hours before LNG-IUD insertion in women who had only had a cesarean section before.

Results: one hundred- eighty patients included in our Randomized control trial. Our results; There was statistically insignificant terms of anticipated pain, Pain after 20 min and satisfaction p-value>0.05.While, we found a statistically significant difference in Ease of insertion, Pain at insertion and Insertion time <0.001. Moreover, there was no statistically significant nausea, vomiting, shivering, fever, and need additional analgesia p-value>0.05.

Conclusion: misoprostol is safe and effective in insertion the LNG-IUD because of the significant result in reduction of pain, timing and easiness of insertion.

Keywords: misoprostol, intrauterine device (IUD), satisfaction, vas

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Introduction

In present reproductive health practices, intrauterine devices (IUDs) have gained significant popularity as a prevalent form of reversible contraception.[1] Levonorgestrel-releasing intrauterine devices (LNG-IUDs) have been found to be safe and cost-effective over an extended period. Furthermore, their efficacy is comparable to that of tubal sterilization.[2] Furthermore, it is worth noting that the LNG-IUD, often known as Mirena®, offers advantages beyond contraception.[3] These include its efficacy in addressing conditions such as menorrhagia, and dysmenorrhea. The prevalence of intrauterine devices (IUDs) among women of reproductive age globally varies between 8% and 15%. Over the past decade, there has been a notable rise in the utilization of intrauterine devices (IUDs) among women aged 18 to 45 years in the Netherlands, with the prevalence increasing from 3% to 8%.[4] The difficulties associated with the insertion of intrauterine devices (IUDs) have been documented as follows: an 8.8% incidence of insertion failure ranging from 2.8% to 11.5%, cervical perforation occurring in 0.2% of cases, syncope in 0.2% of cases, and expulsion in 5.8% of cases.[5] There appears to be a higher incidence of insertion failures and cervical complications in women who have not undergone vaginal delivery. Factors such as cervical stenosis, an underdeveloped or undersized cervix, and a notably tilted posture of the uterus (either forward or backward) have been identified as potential contributors to challenges encountered during the insertion of an intrauterine device (IUD) into the cervical canal, and in some cases, may even result in the inability to insert the IUD successfully.[6] The use of prophylactic nonsteroidal anti-inflammatory medicines (NSAIDs) before intrauterine device (IUD) implantation has been recommended as a strategy to alleviate pain experienced during the procedure. This approach has been widely adopted in the Netherlands for a considerable period of time.[7] Nevertheless, in a comprehensive randomized controlled experiment that compared the administration of prophylactic 400 mg ibuprofen to a placebo prior to the placement of an intrauterine device (IUD), little alleviation of discomfort was observed.[8] Misoprostol is a pharmaceutical drug that is considered to be cost-effective. It is constituted of a prostaglandin E1-analogue. This substance causes uterine contractions, facilitates cervical dilation, and augments uterine tone. The findings of the study suggest that the use of misoprostol before hysteroscopy and dilatation and curettage operations has been linked to improved cervical dilatation and a lower occurrence of cervical laceration. Nevertheless, it is crucial to acknowledge that the use of misoprostol has been linked to certain detrimental consequences, including fever, shivering, moderate diarrhea, nausea, and vomiting.[9]

The aim of our study to reveled the effect of misoprostol on timing and the easiness of insertion of (LNG-IUDs); Randomized controlled trial.

Patients and method

One-hundred and eighty patients with a previous cesarean section attending for Mirena LNG-IUD insertion. This Randomized controlled trial set in Outpatient clinic in Department of Obstetrics and Gynecology, Faculty of Medicine, Helwan University Hospital at BADR city from March 2021 to March 2022.

Study population

Inclusion exclusion criteria

We included women from 20 to 45 years old, previous cesarean , No vaginal delivery, Negative pregnancy test, No history or current pelvic inflammatory disease, No contraindication to LNG-IUD insertion (Gynecological malignancy, Undiagnosed abnormal vaginal bleeding) and No allergy to misoprostol or contraindication for the use of it.

We excluded women (20-45) years old, delivered by more than two CS, Previous Vaginal Delivery, Positive pregnancy test, any signs of pelvic inflammatory infection, Uterine anomaly, any contraindication to LNG-IUD insertion (Gynecological malignancy, Undiagnosed abnormal vaginal bleeding) and Allergy to misoprostol or patients are contraindicated to the administration of misoprostol.

Group 1: (misoprostol group): received 400 µg misoprostol vaginally 6 hours before LNG-IUD insertion. while women are menstruating, starting from the fifth to the tenth day of the menstrual cycle.

Group 2: (A placebo control group): we used YAZ (contraceptive tablets) white placebo tablets which are equal in shape, weight, and color to the misoprostol tablet and has placebo proven efficacy with no active substances vaginally 6 hours before LNG-IUD insertion. while women are menstruating, starting from the fifth to the tenth day of the menstrual cycle.

Intervention

A comprehensive assessment of the patient's medical background was conducted, including obstetric, menstrual, and medical history. The three types of examinations that will be discussed are general, abdominal, and pelvic. All female participants have counseling sessions regarding the various types of intrauterine devices (IUDs) and the positive and negative aspects associated explicitly with levonorgestrel-releasing IUDs (LNG-IUDs). Additionally, they have been provided with comprehensive information about the methods employed in the study. After conducting a complete medical interview, as well as performing an examination of the abdomen and pelvis to exclude the presence of genital infections or abnormal growths, we proceeded to conduct a transvaginal ultrasound on the patient. This procedure aimed to validate the findings of the physical examination and rule out any abnormalities or disorders in the uterus or pelvic region that could hinder the safe insertion of an intrauterine device (IUD).

Additionally, the ultrasound was utilized to assess the dimensions and orientation of the uterus. The levonorgestrel-releasing intrauterine device (LNG-IUD) (Mirena®) was inserted following the manufacturer's prescribed standard protocol during the menstrual phase, specifically between the fifth and tenth day of the menstrual cycle. During the day of LNG-IUD placement, the clinic nurse conducted a pregnancy test on each participant's urine. The participants assumed the lithotomy position for six hours before the implantation of the LNG-IUD. Two tablets of Misotac (SIGMA Pharmaceutical Industries, Egypt) containing 400 mg of misoprostol, the investigational medicine, or two white YAZ (Bayer HealthCare Pharmaceuticals contraceptive pills), the inert substance, were placed into the posterior vaginal fornix to the maximum depth achievable. The participants have been informed that they can return to their residences and return after six hours to receive the LNG-IUD placement.

IUD insertion

The speculum was placed into the vaginal canal, followed by application of the povidone-iodine solution to clean the cervix. A unicuspid vulsellum was employed to secure the front lip of the cervix to stabilize the uterus. Subsequently, a uterine sound was introduced to assess the dimensions and orientation of the uterus. The LNG-IUD (Mirena®, Bayer HealthCare Pharmaceuticals) was prepared using a non-contact technique before insertion to ensure sterility. A transvaginal ultrasonography was conducted to assess the intrauterine device's positioning within the uterine cavity subsequent to the removal of its threads, resulting in a residual length of 3 centimetres. The echogenicity of the arms of the LNG IUD is limited to its proximal and distal ends.

The duration of the LNG-IUD implantation procedure, including the time from insertion to removal of the speculum, as well as any immediate complications such as vasovagal reaction, uterine perforation, or insertion failure, were recorded both immediately after the insertion process and five minutes after that. The participant selected the specific point on the Visual Analogue Scale (VAS) sheet that corresponded to the level of discomfort she was experiencing. At the same time, the research assistant provided assistance by holding the sheet for her. The participants were requested to evaluate their degree of discomfort during the surgical procedure using a Visual Analogue Scale (VAS) ranging from 0 (indicating absence of pain) to 10 (representing the most severe pain). The Visual Analogue Scale (VAS) is a linear measurement tool commonly utilized in clinical settings. It typically consists of a line, approximately 10 centimetres in length, with the phrases "no pain" and "the most intense pain imaginable" positioned at opposite ends. The individual places a mark on the designated line to indicate the subjective assessment of their pain intensity. While it is possible to represent a line using either a horizontal or vertical orientation, the preference frequently leans towards horizontal lines. The horizontal visual analog scale (VAS) was employed. If the pain level of women was five or more significant, they were administered a single intramuscular injection of 75 mg/3 ml diclofenac sodium (Voltaren, Novartis, Basel, Switzerland). The study involved an assessment of the rate of failure in the insertion of the LNG-IUD, as well as the evaluation of the difficulty score associated with the procedure. The difficulty score was determined by the gynecologist performing the insertion, who rated the level of discomfort experienced by the patient on a scale ranging from 0 to 10. Before the administration of the LNG-IUD, an inquiry was made on the potential adverse effects of misoprostol experienced by the patient, including abdominal pains, nausea, and vomiting. This was performed. The negative impacts of LNG-IUD insertion, including as hemorrhage and uterine perforation, were recorded in our data.

Sample size: For the primary outcome of pain with LNG-IUD insertion, evidence from the family planning literature suggests a 1.5 difference on the scale is clinically meaningful. We aimed to detect a 1.5 difference in VAS pain scores between the two study groups with a standard deviation of 2 with a power of 90% and $\alpha = 0.05$ (2-tailed), So the sample size was 130 patients (91 patients per group). The sample size and power analysis were calculated using Epi-Info software statistical package.[9]

Statistics

The collected data were analyzed using SPSS software (SPSS; version., 28). Continuous variables were presented as mean ± standard deviation (SD), while Categorical variables were presented as number and percentage. We used Chi-square ($\chi 2$) test or Fisher exact test (when

the expected frequency was <5) to analyze categorical variables and Student t-test to compare continuous variables. P value less than 0.05 was considered statistically significant.

Results

We approached 202 women to participate in the study. We excluded 22 of them; 10 did not meet inclusion criteria, 7 declined participations, and 5 failed insertions. One hundred eighty were included in the final analysis (Table 1).

Table 1 Demographic data of the studied groups

Variable		Misoprostol (90)	Placebo (90)	P-value
Age		33.3+5.2	34.1+4.9	0.3
BMI		29.7+4.1	29.4+3.8	0.6
Residence	Urban	35(38%)	38(42.2%)	0.6
	Rural	55(62%)	52(57.8%)	
Education level	Low	13(14.4%)	11(12.2%)	0.3
	Medium	24(26.6%)	16(17.8%)	
	High	53(59%)	63(70%)	
Parity	P1	29 (32.2%)	31(34.4%)	0.7
	P2	61 (67.8%)	59(65.6%)	
Previous abortion	Yes	53(58.9%)	48(53.3%)	0.5
	No	37(41.1%)	42(46.7%)	
Duration from last pregnancy		3.8+2.8	3.9+2.9	0.8
Position of uterus	AVF	66(73.3%)	71(78.8%)	0.4
	RVF	24(26.6%)	19(21.1%)	

There was no statistical significance according to demographic data of the included women p-value >0.05 (Table 2).

Table 2 outcomes of the procedure

Variable	Misoprostol (90)	Placebo (90)	P-value
Ease of insertion	4.1+1.2	2.3+1.3	<0.001
Anticipated pain	6.4+1.8	6.1+1.9	0.3
Pain at insertion	3.1+1.2	4.2+1.8	<0.001
Pain after 20 min	2.0+0.9	1.8+1	0.2
Insertion time	4.2+1.1	5.5+1.4	<0.001
Satisfaction	79(87.8%)	37(41.1%)	0.002

There was statistically insignificant terms of anticipated pain, pain after 20 min and satisfaction p-value>0.05. While, we found a statistical significant difference in Ease of insertion, pain at insertion and Insertion time <0.001 (Table 3).

Table 3 adverse events of the participant

Variable	Misoprostol (90)	Placebo (90)	P-value
Nausea	11(4.8%)	21(9.4%)	0.1
Vomiting	3(1.6%)	8(4.7%)	0.2
Shivering	6(7.8%)	11(7.8%)	0.2
Fever	7(3.2%)	16(6.3%)	0.1
Need additional analgesia	21(31.3%)	32(41.9%)	0.2

There was no statistically significant nausea, vomiting, shivering, fever, and need additional analgesia p-value>0.05.

Discussion

We conducted this randomized control trial to maintain the efficacy of misoprostol 400 µg misoprostol vaginally 6 hours before LNG-IUD insertion comparing with the placebo. There was insignificant difference between misoprostol and placebo in the base line demographic data so well the adverse events of included patient. Misoprostol has the superiority in easiness if insertion, pain at insertion, timing of insertion and satisfaction on placebo. Both of them have the same effect on anticipated pain and pain after 20 min.

Misoprostol is a pharmaceutical drug that is considered to be cost-effective. It is constituted of a prostaglandin E1-analogue. This substance causes uterine contractions, facilitates cervical dilation, and augments uterine tone. The findings of the study suggest that the use of misoprostol before hysteroscopy and dilatation and curettage operations has been linked to improved cervical dilatation and a lower occurrence of cervical laceration. Nevertheless, it is crucial to acknowledge that the use of misoprostol has been linked to certain detrimental consequences, including fever, shivering, moderate diarrhea, nausea, and vomiting.[9]

Our results correlate with the outcomes of El-Gawad et al., who determined that administering misoprostol vaginally at a dosage of 400mcg three hours prior to intrauterine device (IUD) insertion had a significant impact on the ease of insertion and decreased the occurrence of pain during the procedure.[3] In a study conducted by El-Garhy et al., the authors examined the impact of administering 600mcg of sublingual misoprostol two hours prior to the insertion of Tcu 380. A study was conducted on a group of 120 women who had undergone a cesarean section but had not previously given birth vaginally. The purpose of the study was to examine the effects of an intrauterine device (IUD) installation in this specific population.[10] The findings of the study indicated that the administration of misoprostol before to intrauterine device (IUD) insertion resulted in a reduction in reported discomfort among patients. However, it was also observed that this intervention led to an increase in the occurrence of moderate side effects such as nausea, fever, and abdominal cramps prior to the insertion procedure.

In their study, Chaves et al.[11] examined the distinction between women who had experienced a prior vaginal birth and nulligravida, as well as women who had undergone a previous cesarean section (CS). The authors found that women with a history of vaginal birth reported lower levels of pain during the levonorgestrel intrauterine device (IUD) implantation procedure compared to nulligravida women and those who had undergone an elective cesarean delivery without any prior labor. In our research, it was observed that women who had previously undergone elective cesarean delivery and were administered vaginal misoprostol experienced a reduction in pain during the insertion of a levonorgestrel intrauterine device (IUD). This finding is supported by Abdalla et al, who also concluded that women who had only undergone elective cesarean delivery may derive advantages from the administration of 400 mcg of misoprostol vaginally prior to IUD insertion. However, it is important to note that these women may still encounter the drawbacks associated with misoprostol, such as adverse symptoms and increased waiting time.[3] Previous results the results disagreed with some studies which found that misoprostol was not useful to facilitate the insertion of IUDs. However, most of these previous studies have been carried out with nulliparous women, whereas in the present study, women were selected among those with elective cesarean sections.[6]

However, some articles have expressed contrary opinions regarding the findings of our randomized controlled trial (RCT). In this study, 43 women were administered sublingual 400 µg misoprostol, while 46 women received a placebo three hours prior to the prompt replacement of a second levonorgestrel-releasing intrauterine device (LNG-IUD).

There was no observed impact on the ease of insertion or any pain experienced by the patients. Nevertheless, the misoprostol group noted a substantially greater incidence of adverse effects than the placebo group.[6] A multicenter randomized controlled trial (RCT) was undertaken to evaluate the potential efficacy of administering vaginal misoprostol prior to intrauterine device (IUD) installation in reducing the incidence of failed insertions and problems associated with the insertion process. A recent meta-analysis revealed that the administration of misoprostol prior to intrauterine device (IUD) insertion did not demonstrate a significant reduction in the occurrence of unsuccessful insertions or complications. Furthermore, the study findings indicate that the administration of misoprostol did not have an impact on the level of discomfort experienced during IUD insertion.[12] Additionally, the author of this study concluded that there was no evidence to support the use of misoprostol as a beneficial intervention prior to IUD insertion. Nevertheless, there exists a propensity for potential injury with respect to adverse reactions.

Strength points and limitation

We included in our study ninety patients in each group and use misoprostol prior six hours and included many adverse events. On the other hand, we need to make a large multicenter study with many doses and different time prior the administration.

Conclusion

Our study recommends misoprostol for insertion the LNG-IUD because of the significant result in reduction of pain, timing and easiness of insertion.

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None.

Conflicts of interest

All authors declare that they have no conflict of interests.

References

1. Aronsson A, Bygdeman M, Gemzell-Danielsson K. Effects of misoprostol on uterine contractility following different routes of administration. *Hum Reprod*. 2004;19(1):81–84.
2. Barcaite E, Bartusevicius A, Railaite DR, et al. Vaginal misoprostol for cervical priming before hysteroscopy in perimenopausal and postmenopausal women. *Int J Gynaecol Obstet*. 2005;91(2):141–145.
3. Abdellah MS, Abbas AM, Hegazy AM, et al. Vaginal misoprostol prior to intrauterine device insertion in women delivered only by elective cesarean section: a randomized double-blind clinical trial. *Contraception*. 2017;95(6):538–543.
4. Espey E, Singh RH, Leeman L, et al. Misoprostol for intrauterine device insertion in nulliparous women: a randomized controlled trial. *Am J Obstet Gynecol*. 2014;210(3):208.e1–5.
5. Buhling KJ, Zite NB, Lotke P, et al. Worldwide use of intrauterine contraception: a review. *Contraception*. 2014;89(3):162–173.
6. Dijkhuizen K, Dekkers OM, Holleboom CAG, et al. Vaginal misoprostol prior to insertion of an intrauterine device: an RCT. *Hum Reprod*. 2011;26(2):323–329.
7. Hubacher D, Reyes V, Lillo S, et al. Pain from copper intrauterine device insertion: randomized trial of prophylactic ibuprofen. *Am J Obstet Gynecol*. 2006;195(5):1272–1277.
8. Heikinheimo O, Inki P, Kunz M, et al. 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(6):481–486.
9. Ashour ASA, El Sharkawy M, Ali AS, et al. Comparative efficacy of vaginal misoprostol vs vaginal dinoprostone administered 3 hours prior to copper T380A intrauterine device insertion in nulliparous women: a randomized controlled trial. *J Pediatr Adolesc Gynecol*. 2020;33(5):559–565.
10. Ibrahim ZM, Sayed Ahmed WA. Sublingual misoprostol prior to insertion of a T380A intrauterine device in women with no previous vaginal delivery. *Eur J Contracept Reprod Health Care*. 2013;18(4):300–308.
11. Chaves IA, Baêta T, Dolabella GB, et al. Pain scores at the insertion of the 52 MG levonorgestrel-releasing intrauterine system among nulligravidas and parous women. *Eur J Contracept Reprod Health Care*. 2021;26(5):399–403.
12. Saad AEHS, Soliman EEDA, Negm OML. Role of vaginal misoprostol before intrauterine device insertion. 2022;35(1):240–244.