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Sublingual Misoprostol Prior To Intra Uterine Contraceptive Device Insertion In Women With Previous Cesarean Section Who Had Never Delivered Vaginally

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ABSTRACT

Background: One of the reversible effective contraceptives is intrauterine contraceptive devices (IUCDs).
However, the expensive cost in certain contexts and the fear of discomfort during insertion restrict its usage. Lack of training, concern of inflicting pain during the operation, and problems during the procedure that may result in insertion failure are among the barriers to its usage for healthcare professionals.

Aim of the work: to see how effective sublingual misoprostol before IUCD insertion was in reducing discomfort, complications, and facilitating IUCD insertion in women who had previously undergone CS but had never delivered vaginally.

Patients and methods: The research was conducted at Bab ALsharia University Hospital's Department of Obstetrics & gynecology in a double-blind randomised controlled experiment. In this research, 600 participants were enrolled.

Results: In terms of insertion difficulties, there was a statistically significant difference between the two groups.
The insertion of an IUD was easier in the misoprostol group than in the placebo group. There were statistically significant differences between the two groups in terms of pain score, with the misoprostol collection having a lower discomfort score (5.73 1.34) than the placebo group (6.49 0.93), with a p-value of 0.001.

Conclusion: Our findings revealed that 200 ug sublingual misoprostol given 1 hours before IUD insertion in individuals who had a previous caesarean section (but no previous vaginal birth) simplified IUD installation and reduced the incidence of failure (primary outcome measure).

Keywords: *Misoprostol ; Intrauterine Contraceptive Device; Lscs; Pain; Easy.*

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INTRODUCTION

Intrauterine devices (IUDS) are considered the most common form of long acting reversible contraceptives (LARC) used worldwide within the first year, the total incidence of undesired pregnancy was less than 1%, with a decreasing failure rate in following years.[1]

They have fewer side effects compared to hormonal methods. [1]

require no attention, and with a quick restoration to the target level of fertility Although IUD insertion is generally a successful operation, nulliparous women and those who have never given birth vaginally have a greater risk of failure and problematic insertion. As a consequence, many health-care professionals continue to deny women who have never given birth vaginally access to IUDs. [2]

Based on the off-label use of misoprostol for cervical ripening in labour induction, medical evacuation of missed and incomplete abortions, and cervical preparation before other gynecologic procedures, some clinicians prescribed misoprostol, a prostaglandin analogue, to these women before IUD insertion in a trial to improve IUD insertion success. [3]

Connective tissue makes up the majority of the cervix, although collagen fibres also include fibronectin and elastin.

The internal os has the greatest elastin-to-collagen ratio. From the interior os to the exterior os of the cervix, both elastin and smooth muscle diminish. [4]

Misoprostol, also known as prostaglandin El (PGE1) analogue, is a synthetic prostaglandin that has been used to treat stomach ulcers. It may be given for cervical ripening which can be induced orally, vaginally, rectal, or sublingually. during vaginal birth and medical abortion induction. [5]

Misoprostol given sublingually has been found to be more efficacious than oral misoprostol for cervical priming and to be similarly effective as vaginal misoprostol.[6&7]

This study aimed to calculate the benefits of sublingual misoprostol before IUCD placement in women who had previously undergone CS but had never given birth vaginally in terms of reducing pain, complication and facilitating IUCD insertion.

PATIENTS AND METHODS

The research was a randomised controlled experiment with double blinding. carried out at The Department of Obstetrics at Bab ALsharia University Hospital. 600 patients were included in this study.

The sample size and power analysis was calculated using Epi-Info software statistical package created by World Health organization and center for Disease Control and Prevention, Atlanta, Georgia, USA version 2002.

The criteria used for sample size calculation were as follows: 95% confidence limit, 80% power of the study and expected outcome in in favorable treatment group 90% compared to least favorable treatment group is 60%.

Based on the above stated parameters, the sample size was determined to be N>33 for each study group. The sample size will be increased to 35 for each group to increase validity of results

The inclusion criteria**:** age (18–35 years), any parity, and no vaginal delivery history, no prior IUD insertion history, and no contraindications to IUD insertion

The exclusion criteria**:** history of IUD implantation contraindication, history of prior IUD insertion previous cervical surgeries, allergy to misoprostol, dysfunctional uterine bleeding and positive pregnancy test in suspected cases.(cases with amenorrhea or DUB)

All patients in this study were exposed to the following :

History taking: Including the personal history, parity, obstetric and contraceptive history menstrual history, medical history, previous gynecologic operations

Clinical examination: Vaginal and Cusco examination to exclude vaginitis or any active infection or cervical pathology, abdominal examination to exclude presence of masses and bimanual examination.

Investigational studies: Radiological investigation: Ultrasound to determine the uterus's location and rule out uterine contraindications such as an abnormal uterine cavity.

Laboratory investigations**:** Pregnancy test in suspected cases with amenorrhea or DUB. All patients signed a fully informed written permission after meeting the presence standards and deliberating and approving the IUD as a means of contraception.

After counselling and agreement on the use of an IUD as a method of birth control, the patients were split into two groups at random.

By means of a locked wrapper technique, the clinician was unaware of the misoprostol or placebo randomization, in which each woman received an envelope containing the tablet (misoprostol 200 microgram) or placebo. (folic acid 0.5 mg) and instructed to take it sublingually for 15–20 minutes before returning one hour later to have her IUD inserted.

The following technique was done: Women are placed in the lithotomy position, a sterile Cusco's speculum is used to expose the vaginal and cervix, a vulsellum is used to grasp the cervix, uterine sounds are inserted to assess cervical dilatation, uterine direction, and uterine cavity length, and a vulsellum is used to grasp the cervix. and a copper IUD is prepared (In a T-shaped IUD, the stem and the arms of the T should be identified, with the proximal end in the internal os and the distal end in the fundal region within the endometrium).During the IUD implantation procedure, the woman's discomfort was evaluated using a subjective numeric rating scale of 0 to 10 that she reported herself.

The Numeric pain Rating Scale (NRS-11) is an 11-point scale for patient self-reporting of pain. It is for adults and children 10 years old or older**.** [8] **:**

0: No pain, 1–3: Mild pain, 4–6: Moderate pain, 7–10: Severe pain

Difficulty in IUD insertion was measured using five point scale: 1: very easy, 2: easy, 3: neutral, 4: difficult and 5: very difficult.

The following parameters were also studied: Misoprostol side effects within 48h of intake: nausea, vomiting, fever, pain and bleeding and failure of IUD insertion.

The primary outcome measures of this study were: Proportion of failed IUD insertions in misoprostol versus placebo group and difficulty of insertion of IUD in both groups

Secondary outcome measures were: Complications related to misoprostol (abdominal cramp, headache, nausea, diarrhea and fever) and Complications related to IUD insertion (uterine perforation, heavy bleeding, pain during insertion and syncope).

Statistical analysis: SPSS (Statistics Program for Social Science) statistical software, v. 15.2, Echosoft corp., USA, 2004, was used to analyse the data as follows: Quantitative data are described as mean, SD, and range, qualitative variables are described as no and percent, and analysis of variance (ANOVA) is used to compare more than two groups.

Epi-Info version 6 and SPSS for Windows version 8 were used to input, verify, and analyse data.

(SPSS Inc. , Chigaco, USA). Mann Whitney-U test: It is used for comparison between the 2 groups (successful and weaning) for the not normally distributed data.

RESULTS

There was no important change between misoprostol group and control group as regard number of previous cesarean sections (CS). Table (1)

Group	Misoprostol (n=300)		Placebo (n = 300)		X^2	P
	No	%	No	%		
1 CS	167	55.7	178	59.3	0.829	**0.364**
2 CS or more	**133**	**44.3**	**122**	**40.7**		

Table 1: Comparison of the two groups as regard number of previous cesarean sections (CS)

The proportion of failed insertion 2/300, (0.7%) in misoprostol group was statistically significantly lower than placebo group 11/300, (3.7%) p-value 0.012, table (2)

group	Misoprostol (n=300)		Placebo (n = 300)		X^2	p-value
	No	%	No	%	6.731	0.012*
Failed insertion	2	0.7	11	3.7		

Table 2: failed insertion in cases of misoprostol and placebo groups:

There was a statistically important change amid both groups regarding difficulty of insertion .The insertion of IUD in misoprostol group was easier than in placebo group. Table (3)

Difficulty of insertion	Misoprostol (n=300)	Placebo (n = 300)	t-test	P-value
Total	2.17 ± 0.81	2.92 ± 0.93	10.529	0.001*
1CS	1.98 ± 0.45	2.51 ± 0.58	12.503	0.001*
2CS or more	2.34 ± 0.68	3.25 ± 0.61	17.249	0.001*

Table 3: Difficulty of insertion in the studied groups

There were statistically significant differences between both groups as regard abdominal cramp, nausea and fever occurring more in misoprostol group before insertion of IUD. There were no statistically significant differences between both groups as regard headache and diarrhea table (4)

Side effect	Misoprostol (n=300)		Placebo (n = 300)		X^2	p-value
	No	%	No	%		
Abdominal cramp	78	26	34	11.3	21.249	0.001*
Headache	25	8.3	19	6.3	0.882	0.347
Nausea	23	7.7	10	3.3	5.419	0.020*
Diarrhea	6	2	2	0.7	2.031	0.155
Fever	8	2.7	0	0	6.072	0.014*

Table 4: Side effects following sublingual administration of misoprostol or placebo before insertion of IUD

Pain during insertion of IUD There was statistically important differences amid both collections concerning pain score with pain scoreless (5.73 ± 1.34) in misoprostol group, than placebo group (6.49 ± 0.93), p-value is 0.001. Table (5)

Groups	Misoprostol (n=300)	Placebo (n = 300)	t-test	P-value
Mean of pain score	5.73 ± 1.34	6.49 ± 0.93	8.072	0.001*

Table 5: Mean of Pain scores for studied group

DISCUSSION

The pill is allowed to melt beneath the tongue after sublingual delivery of misoprostol, and it typically melts and disappears within 10–20 minutes.

If the pill is taken too soon by accident, the impact will be similar to that of oral administration.

Sublingual misoprostol causes a faster rise in plasma levels than vaginal misoprostol, compared to oral delivery, a longer period of increased plasma concentrations of the active misoprostol free acid, and development of uterine contractility comparable to vaginal therapy according to pharmacokinetic uterine contractility in pregnant women is the subject of many research. [9]

Our study included 600 women candidates for IUD insertion. 300 women had received sublingual 200 µg misoprostol (group 1) and 300 women received the placebo (group 2) 1 hour prior to iucd insertion .Our study was conducted at Obstetrics and Gynecology Department, Bab AL sharia University Hospital to see whether taking sublingual misoprostol before inserting an IUD lowers the incidence of unsuccessful insertions and insertion-related problems. Misoprostol pretreatment decreased the frequency of unsuccessful insertions and problems after IUD insertion, according to the research. Furthermore, misoprostol reduced discomfort during insertion. The insertion difficulty was calculated based on the cervix's resistance.

When compared to untreated controls, misoprostol had a facilitating impact on IUD insertion, with substantially reduced Internal cervical os resistance and technically simpler insertions This should imply that the insertions were simpler and easier in general in cases of misoprostol group. There were 11 insertions “3.7%” in The control group failed owing to an extremely small cervix. In the misoprostol group, only two of the insertions (0.7 percent) failed; the estimated p value was 0.012. Pain during insertion was improved and significantly lower (P=0.001).There was a statistically important change amid both collections concerning difficulty of insertion. The insertion of IUD in misoprostol group was easier than in placebo group(P=0.001).

Misoprostol sublingual dosage before IUD implantation causes side effects were mainly abdominal cramps in 78 of cases "26%" of misoprostol group comparing with 34 cases of placebo group "11.3%" (The intended p worth was 0.001) and there were other side effects such as headache in 25 of cases of misoprostol group "8.3%" in placebo group 19 cases "6.3%"(p value was 0.347), nausea in 23 of cases of misoprostol "7.7%"while in placebo group 10 of cases "3.3%"(p value was 0.020), diarrhea in 6 cases of misoprostol group "2%"in placebo group only 2 cases "0.7%"(p value was 0.155) and the last side effect found was fever in 8 cases of misoprostol group "2.7%" and no cases was found in placebo group (p value was 0.014).

Except for stomach pains, nausea, and fever, there were no significant differences in side effects between the two groups. There were no important changes amid the two collections. regards complications related to IUD implantation syncope "p value=0.824", perforation "p value=0.317"and heavy bleeding "p value =0.244".

In terms of the degree of difficulty, the current findings are consistent with those reported by other writers and reduction of pain during insertion. [10&11]

Abdellah et al.2017 found that 400 µcg of vaginal misoprostol 3 h before insertion increases the success rate of insertion [69 (98.6%) vs. 61 (87.1%), P=0.009]. Pain and difficulty in insertion were also reduced. [12]

Another study found that 400 µcg of sublingual misoprostol 2 h before IUCD insertion decreases the number of failed insertions from six (4.6%) failed insertion in the placebo group to only one (0.8%) case in the misoprostol group (P=0.023)also Pain during insertion was improved and significantly lower (P<0.001). [11]

Bahamondes et al., 2015 also tried the pretreatment with 200 µcg of intravaginal misoprostol 10 and 4 h before IUCD insertion in patients with a history of failure to insert the loop during the first trial. He found that insertion failure was significantly better than that in the placebo group. The IUCD was successfully placed In 42 (87.5%) of the 48 women randomised to misoprostol and 26 (61.9%) of the 42 females allocated to placebo, correspondingly (P=0.0066).

1.41 was the relative risk of successful insertions. (absolute difference (8.2–43.0), with a 95 percent confidence range of 8.2–43.0. [13]

In a separate study including limited number of instances (eight) where IUD insertion failed owing to cervical stenosis, administering 400 cg of misoprostol vaginally resulted in successful insertion in all of the women involved, indicating that IUD implantation may be effective. and easier when misoprostol has been used previously. [10]

In one study published in the United States, 2211 doctors employed in the area of generative remedy were polled. Overall, 1905 (86%) of those surveyed said they had inserted IUCDs in nulligravidas, with 947 (42.7%) of those saying they had taken misoprostol previous to the operation, with the popular (n=515; 54%) thinking that using this drug makes the process much easier. [14]

However, other studies showed no improvement in discomfort during the operation or an increase in the probability of a successful insertion. [15]

Dijkhuizen et al., 2014 performed a 270-patient RCT to see whether pretreatment with vaginal misoprostol makes it easier to implant an IUD in nulliparous and multiparous women. They found no advantage to using misoprostol before IUD pullout. However, there is a risk of potential damage in terms of side effects. [16]

The administration of 400 ug of misoprostol orally 90 minutes before IUD implantation in 35 nulligravidas in a published clinical study showed no meaningful change in pain experienced by the women.

In that research, the misoprostol group had a higher degree of opposing indications, especially cramps and nausea. [17]

Heikinheimo et al., 2010 reported the findings of a double-blind RCT in which 43 women were given sublingual 400 cg misoprostol and 46 women were given a placebo 3 hours before a second LNG-IUD was replaced. [18]

There was no discernible impact on insertion ease or patient-reported discomfort.

However, the misoprostol group had substantially greater adverse effects than the placebo group. This may be because of the limited number of people that took part their study and the use of sublingual route with 3-h interval as sublingual misoprostol is more effective after 1 h

CONCLUSION

Our results showed that 200 ug sublingual misoprostol given 2 hours before IUD insertion in patients with previous cesarean section (with no prior vaginal delivery) facilitated the insertion of IUD and decreased the failure rate of insertion (primary outcome measure).

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