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Effect of Diclofenac Versus Misoprostol on Pain Perception during Intrauterine Contraceptive Device Insertion

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ABSTRACT

Background: The intrauterine device (IUD) is one of the most contraceptive methods with highly effective and safe use. However, insertion through a narrow cervix may be technically difficult and painful.

Objective: This study was performed to compare the effect of vaginal misoprostol and intramuscular diclofenac sodium in decreasing pain and facilitating IUCD insertion.

Patients and Methods: A randomized double-blind controlled trial in Zagazig University Hospital during the period from December 2019 to November 2020. It included sixty-four women who want to insert an IUD. They were classified into four groups on a randomized basis, the first group received two tablets (400 mcg) of misoprostol in the posterior fornix of the vagina 2 hours before IUD insertion and the second group received diclofenac sodium 75 mg ampule intramuscular 2 hours before IUD insertion. The third group received two tablets (400 mcg) of misoprostol in the posterior fornix of the vagina and diclofenac sodium 75 mg ampule intramuscular 2 hours before IUD insertion while the fourth group received placebo. Pain during insertion and difficulty in IUCD insertion were evaluated.

Results: Misoprostol significantly facilitated the insertion of IUD insertion whereas diclofenac sodium lowered the average pain score for all steps of IUD insertion. Side effects were higher in the misoprostol group.

Conclusion: 400 mcg of vaginal misoprostol 2 hours before IUD insertion facilitates the introduction and IM injection of 75 mg diclofenac sodium 2 hours before IUD insertion reduced the pain perception.

Keywords: IUD, Cervical stenosis, Misoprostol, Diclofenac sodium.

INTRODUCTION

The intrauterine device (IUD) is one of the most effective contraceptive methods available in addition to one of the safest long-acting reversible contraception (LARC) [(1)]. Its effectiveness refers to its low rate of unintended pregnancy that is expected due to independent use of adult females [(2)]. Despite that, the incidence of its exercise is only 7.6% of adult females in developed countries and 14.5% in developing nations. This can be attributed to worry for the difficulty of insertion, pain for the woman during insertion, and an increased risk of infection [(3)].

Cervical stenosis is the narrowing of the passageway through the cervix or even its complete closure [(4)]. It considers as a factor associated with the difficulty sounding of the cervical canal or even failure to insert IUD [(5)]. The mechanical means to overcome anatomic cervical stenosis and scarring during insertion of IUD by grasping the cervix with a tenaculum and the additional use of a dilator. These techniques are usually associated with increased anxiety, pain, or even failure [(6)].

Misoprostol is an inexpensive prostaglandin E1 analog, which is associated with few side effects. It is an effective method for treatment of incomplete and missed abortion as well as prevention, and treatment of postpartum hemorrhage. It is also used in the induction of provocative abortion as well as for labor induction [(7)]. Several studies have shown the benefit of misoprostol as a cervical ripening agent in nonpregnant women [(8)].

Diclofenac sodium is a nonsteroidal agent with marked analgesic, anti-inflammatory properties. It is an inhibitor of prostaglandin synthetase. It has been used in obstetrics and gynecology to control acute and chronic postoperative and menstrual pain as well as pain related to medical abortions, menorrhagia and it is administrated as tocolytics in preterm labor [(9)].

This study aimed to compare the effect of vaginal misoprostol and intramuscular diclofenac sodium in decreasing pain and facilitating IUCD insertion.

PATIENTS & METHODS

The current study was a randomized double-blind controlled trial. It included sixty-four women undergoing Cu T 380A IUCD insertion who came to the family planning clinic in Obstetrics and Gynecology Department in Zagazig University Hospitals during the period from December 2019 to November 2020.

Ethical approval:

Written informed consent was obtained from all participants and **the study was accepted by the Research Ethics Committee of the Faculty of Medicine, Zagazig University.**

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The study was carried out on experiments involving human subjects in compliance with the Code of Ethics of the World Medical Association (Declaration Helsinki).

The included patients were randomly divided into four equal groups of 16 cases each. **Group (1)**; Patients received two tablets (400 mcg) of misoprostol in the posterior fornix of the vagina 2 hours before IUD insertion. **Group (2)**: Patients received diclofenac sodium 75 mg ampule intramuscular 2 hours before IUD insertion. **Group (3)**: Patients received two tablets (400 mcg) of misoprostol in the posterior fornix of the vagina and diclofenac sodium 75 mg ampule intramuscular 2 hours before IUD insertion and **Group (4)**: Patients received placebo.

Inclusion criteria: Women above 18 years of age who want to insert an IUD and participate in this research.

Exclusion criteria: Positive pregnancy test, pelvic inflammatory disease or active cervical infection, uterine or cervical anomaly, cervical or uterine fibroid, unexplained vaginal bleeding, suggested gynecologic malignancy, and allergy to misoprostol or diclofenac sodium.

Methodology:

The selected patients were subjected to complete history taking including personal, obstetric, menstrual, and medical history. History of allergy to misoprostol or diclofenac sodium was asked about.

IUCD was inserted from the third to the fifth day of the menstrual cycle.

General, abdominal and vaginal examination was carried out to exclude genital infections or masses.

A pregnancy test was performed and those with a positive test were excluded.

Statistical analysis

Analysis of data was done using Statistical Program for Social Science version 20 (SPSS Inc., Chicago, IL, USA). Quantitative variables were described in the form of mean and standard deviation. Qualitative variables were described as number and percent. To compare parametric quantitative variables between two groups, the Student t-test was performed. Qualitative variables were compared using the Chi-square (X^2) test or Fisher's exact test when frequencies were below five.

Pearson correlation coefficients were used to assess the association between two normally distributed variables. When a variable was not normally distributed, Man Whitney test for comparing two non-Parametric variables. Kruskal Wallis test for comparing more than two non-Parametric variables. Spearman's correlation P-value < 0.05 is considered significant coefficients were used to assess the association between two variables which are not normally distributed.

RESULTS

Table 1 showed that there was no statistically significant difference between all groups according to age or BMI.

Table 2 showed that there was no significant difference between the studied groups according to the previous mode of delivery or history of genital infection.

Table 3 showed that there was no statistically significant difference between the 4 studied groups as regards the difficulty of IUD insertion. There was a statistically significant difference between (misoprostol diclofenac and placebo) and (Misoprostol and Placebo) groups as regards the difficulty of IUD insertion.

Table 4 showed that there was no statistically significant difference between the 4 studied groups as regard pain. There was a statistically significant difference between misoprostol diclofenac and placebo groups as regards pain.

Table 5 showed that the side effects in IUD insertion were nausea and vomiting in 37.5% and syncopal attack in 6.3% among the misoprostol group. In the diclofenac group, only gastritis in 18.7% of patients without nausea and vomiting. Among the misoprostol declophenac group, the syncopal attack reached 6.3%, and gastritis was presented in 12.5% while nausea and vomiting were presented in 18.7% of patients.

Table (1): Comparison between the different studied groups according to demographic data

	Misoprostol (n = 16)	Diclofenac (n = 16)	Misoprostol diclofenac (n = 16)	Placebo (n = 16)	F	P-value
Age (years)						
Min. – Max.	18.0 – 38.0	19.0 – 39.0	18.0 – 38.0	19.0 – 33.0	0.047	0.986
Mean ± SD.	26.63 ± 6.08	26.0 ± 6.44	26.37 ± 6.14	26.61 ± 4.0		
Median (IQR)	26.0 (21.0 – 30.5)	24.0 (21.0 – 29.0)	27.0 (21.0 – 30.5)	27.50 (24.0 – 29.0)		
BMI (kg/m^2)						
Min. – Max.	21.40 – 33.80	20.80 – 34.0	20.30 – 33.70	20.20 – 34.20	0.161	0.922
Mean ± SD.	27.19 ± 3.86	26.32 ± 3.58	26.60 ± 3.92	26.70 ± 4.34		
Median (IQR)	27.80 (23.7 – 29.9)	25.80 (23.7 – 29.0)	27.40 (23.3 – 29.5)	26.80(22.9 – 30.5)		

Table (2): Comparison between the different studied groups according to the previous mode of delivery and history of genital infection

	Misoprostol (n = 16)		Diclofenac (n = 16)		Misoprostol diclofenac (n = 16)		Placebo (n = 16)		χ^2	P-value
	No.	%	No.	%	No.	%	No.	%		
Previous Mode of delivery										
NVD	2	12.5	3	18.7	2	12.5	2	12.5	0.387	^{MC}p= 0.942
CS	14	87.5	13	81.3	14	87.5	14	87.5		
History of Genital infection										
No	7	43.7	9	56.3	6	37.5	8	50.0	1.255	0.739
Yes	9	56.3	7	43.7	10	62.5	8	50.0		

Table (3): Comparison between the different studied groups according to the difficulty of IUD insertion

Difficulty of IUD insertion	Misoprostol (n = 16)		Diclofenac (n = 16)		Misoprostol diclofenac (n = 16)		Placebo (n = 16)		χ^2	p-valua
	No.	%	No.	%	No.	%	No.	%	19.81	0.07078
Easy	6	37.5	1	6.3	6	37.5	1	6.3		
Extremely easy	2	12.5	1	6.3	2	12.5	1	6.3		
Moderate	6	37.5	7	43.7	7	43.7	4	25.0		
Difficult	1	6.3	4	25.0	1	6.3	6	37.5		
Extremely difficult	1	6.3	3	18.7	0	0.0	4	25.0		
Sig.bet.grps	$^{MC}p_1$= 0.147, $^{MC}p_2$=0.898, $^{MC}p_3$= 0.0463, $^{MC}p_4$= 0.0689, $^{MC}p_5$= 0.851, $^{MC}p_6$= 0.0153*									

Table (4): Comparison between the different studied groups according to pain

Pain	Misoprostol (n = 16)		Diclofenac (n = 16)		Misoprostol diclofenac (n = 16)		Placebo (n = 16)		χ^2	P-value
	No.	%	No.	%	No.	%	No.	%	12.96	0.1646
No	3	18.7	6	37.5	5	31.3	1	6.3		
Mild	6	37.5	4	25.0	5	31.3	2	12.5		
Moderate	4	25.0	5	31.7	4	25.0	6	37.5		
High	3	18.7	1	6.3	2	12.5	7	43.7		
Sig.bet.grps	$^{MC}p_1$= 0.473, $^{MC}p_2$= 0.851, $^{MC}p_3$= 0.172, $^{MC}p_4$= 0.885, $^{MC}p_5$=0.0316*, $^{MC}p_6$= 0.0678									

Table (5): Comparison between the different studied groups according to the side effects of IUD insertion

The side effects of IUD insertion in both groups	Misoprostol (n = 16)		Diclofenac (n = 16)		Misoprostol diclofenac (n = 16)		Placebo (n = 16)		χ^2	P-value
	No.	%	No.	%	No.	%	No.	%	20.9	0.013
Non	9	56.3	13	81.3	10	62.5	16	100.0		
Syncobal attack	1	6.3	0	0.0	1	6.3	0	0.0		
Gastritis	0	0.0	3	18.7	2	12.5	0	0.0		
Nausea & vomiting	6	37.5	0	0.0	3	18.7	0	0.0		
Sig.bet.grps	$^{MC}p_1$= 0.0133*, $^{MC}p_2$= 0.383, $^{MC}p_3$=0.0113*, $^{MC}p_4$=0.204, $^{FE}p_5$= 0.0688, $^{MC}p_6$= 0.061									

DISCUSSION

The present study assessed the demographic characteristics of the participants and revealed that there is a non-significant difference between the studied groups as regards the demographic data. In the present study, we found that the misoprostol and the misoprostol diclofenac groups showed a significantly higher number of easy IUD insertions, while the misoprostol diclofenac group showed a significant lower extremely difficult insertion in comparison to other groups (P-value 0.070**).** In agreement with our results, **Abo Gharam *et al.*** [10] found that 400 micrograms of misoprostol 2 hours vaginally before IUCD insertion facilitates its insertion in comparison to IM administration of 75 mg of diclofenac sodium, 2-hours before IUCD insertion, and also **Mohammed *et al.*** [11] found that 400 micrograms of sublingual misoprostol 2 hours before IUCD insertion reduces the number of failed insertions and pain during insertion. Contrary to our finding, **Dijkhuizen *et al.*** [12] showed that no benefit for use misoprostol before IUD insertion. However, there is a tendency for possible harm regarding side effects. In addition, **Heikinheimo *et al.*** [13] found that sublingual misoprostol did not have a significant effect on the ease of insertion in subjects having repeat insertion of the LNG-IUS.

Sääv *et al.* [14] demonstrated that misoprostol facilitates insertion of an IUD, and reduces the number of difficult and failed attempts of insertions in women with a narrow cervical canal. **Dijkhuizen *et al.*** [12] study did not show a positive effect of administration of misoprostol. Misoprostol may affect cervical dilatation; however, this does not lead to easier insertions or lower pain scores. IUD insertion in nulliparous women who used sublingual 400 micrograms misoprostol and 100 mg diclofenac were significantly easier than in women who used 100 mg diclofenac alone (1 h before IUD insertion). However, no difference in dilatation of the cervix, as well as patient-scored pain estimation and the number of failed insertions were observed between the two groups.

In the current study, we found that there was a statistically significant difference between misoprostol diclofenac and placebo groups as regard pain. The present study shows that the administration of 75 mg of diclofenac sodium intramuscular, 2-hours before IUCD insertion reduces the sensations of the pain during IUD insertion in comparison to other groups (P-value 0.164). **Fouda *et al.*** [15] found a statistically significant decrease of pain scores during pretreatment with diclofenac potassium and lidocaine gel in parous women having copper IUD placement, but the reduction is not clinically relevant.

Espey *et al.* [16] found that 400 mcg of sublengual misoprostol 2-8 hours before insertion of an IUD for nulliparous women did not decrease pain or improve the ease of insertion of an IUD. Most women were willing to wait for a medication that decreases pain, indicating a need to pursue alternatives for pain control with IUD insertion. **Abo Gharam *et al.*** [10] found that there was an insignificant difference between misoprostol and diclofenac groups as regards pain score.

In the current work, we found that side effects during IUD insertion were nausea and vomiting in 37.5% and syncopal attack in 6.3% among the misoprostol group while in the diclofenac group only gastritis in 18.7% of patients. Nausea and vomiting reached 18.7% while the syncopal attacks represented 6.3% and gastritis was found among 12.5% of patients in the misoprostol diclofenac group (P-value 0.013).

In agreement with our results**, Abo Gharam *et al.*** [10] found that side effects in IUD insertion were nausea and vomiting in 36.7% and syncopal attack in 3.3% in the misoprostol group while in the diclofenac group only gastritis in 20% of patients. Inconsistent with our result **Maged *et al.*** [17] found that a higher number of women experienced nausea, vomiting, and cramps in the misoprostol group compared with the placebo group. The difference was statistically significant, however, only in women who experienced cramps. **Ibrahim and Ahmed** [18] investigated

whether sublingual misoprostol administered one hour before intrauterine device (IUD) insertion reduces failed insertions, insertion-related complications, and pain in parous women delivered only by elective cesarean section (CS).

They found that sublingual administration of misoprostol one hour before IUD insertion in parous women with no previous vaginal delivery does not facilitate the procedure and may cause undesirable side effects. Moreover, **Mohammed *et al.* (11)** found that abdominal cramps occurred in 22.3% of participants using misoprostol and in 54% using placebo. Nausea occurred in 69% of participants using misoprostol and in 1.5% using placebo.

Limitation: Large-scale, multicenter, randomized, and controlled studies are needed to assess and confirm these results.

CONCLUSIONS

This study depicts that the use of 400 mcg of misoprostol vaginally before IUD insertion facilitates the introduction and IM injection of 75 mg diclofenac sodium reduced the pain perception.

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