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Combination of Vaginal Misoprostol and Intramuscular Diclofenac Sodium Prior to Intra Uterine Contraceptive Device Insertion in Women with Stenosed Cervix

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ABSTRACT

Background: The intra uterine device (IUD) is one of the most contraceptive method with highly effective and safe used. However, insertion through a narrow cervix may be technically difficult and painful. **Objective:** This study was performed to assess the effect of combination of vaginal misoprostol with intramuscular diclofenac sodium in decreasing pain and facilitating IUD insertion in women with cervical stenosis. **Patients and Methods**: A randomized double-blind controlled trial in Zagazig University Hospital during the period from December 2019 to November 2020. 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, 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 and 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 of pain score all steps of IUD insertion. Side effects were higher in the misoprostol group. **Conclusion**: The administration of 400 mcg of vaginal misoprostol and IM injection of 75 mg diclofenac sodium 2 hours before IUD insertion in women with stenosed cervix facilitate the IUCD insertion, decrease failure of insertion and reduce pain sensation during IUCD insertion.

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]. In spite of 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 narrowing of the passageway through the cervix or completely closed [4]. It considers as a factor associated with difficult sounding of the cervical canal or

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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 analogue, which is associated with few side effects, is an effective method for treatment of incomplete and missed abortion, prevention and treatment of postpartum hemorrhage and 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 pain, menstrual pain, pain related to medical abortions, menorrhagia and administrated as tocolytics in preterm labor [9].

The aim of this study was to assess the effect of combination of vaginal misoprostol with intramuscular diclofenac sodium in decreasing pain and facilitating IUD insertion in women with cervical stenosis.

PATIENTS & METHODS

The current study was randomized double-blind controlled trial. Included sixty-four women undergoing Cu T 380A IUCD insertion came to 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. Study has been carried out on experiments involving human subjects in compliance with the Code of Ethics of the World Medical Association (Declaration Helsinki).**

The included subjects 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, **Group (4)**; Patients received placebo.

Inclusion criteria: Women above 18 years of age who want to insert an IUD and to participate in this research and they have already cervical stenosis or had a history of cervical stenosis, such as delivery by cesarean section, history of cervical surgical manipulation and inflammation of the cervix. **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.

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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.

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. In order to compare parametric quantitative variables between two groups, Student t test was performed. Qualitative variables were compared using 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 groups according to age or BMI.

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

Figure 1 showed that This there was no statistically significant difference between the 4 studied groups as regard difficulty of IUD insertion. There was statistically significant difference between (misoprostol diclofenac and placebo) and (Misoprostol and Placebo) groups as regard difficulty of IUD insertion.

Figure 2 showed that there was no statistically significant difference between the 4 studied groups as regard pain. There was statistically significant difference between misoprostol diclofenac and placebo groups as regard pain.

Table 3 showed that the side effects in IUD insertion were nausea and vomiting in 37.5% and syncopal attack in 6.3% in the misoprostol group, in the diclofenac group only gastritis in 18.7% of patients but nausea and vomiting in 18.7%, syncopal attack in 6.3% and gastritis in 12.5% of patients in the misoprostol diclofenac group.

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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
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 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
	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		

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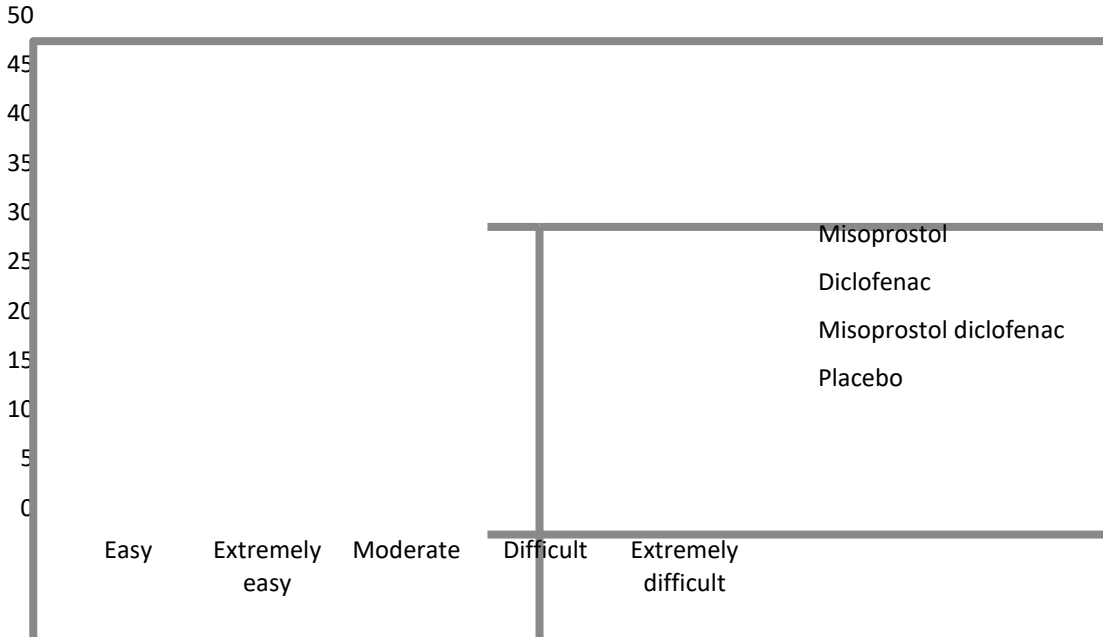

Figure (1): Comparison between the different studied groups according to difficulty of IUD insertion

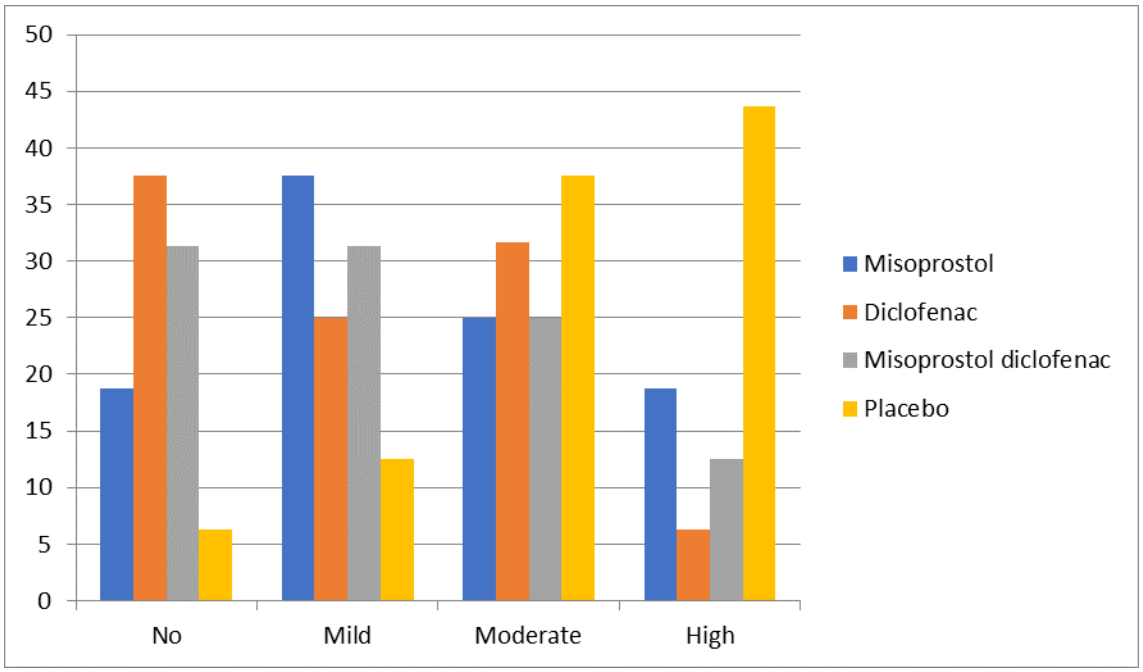

Figure (2): Comparison between the different studied groups according to pain

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Table (3): 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
	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 non-significant difference between the studied groups as regard demographic data. In the present study, we found that misoprostol group and misoprostol diclofenac group showed a significant higher number of easy IUD insertion, and misoprostol diclofenac group showed a significant lower extremely difficult insertion in comparison to other groups (p value 0.070**).** In agreement with our result **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 On the contrary to our finding, **Dijkhuizen et al. [12]** showed that conclusion: The study showed no benefit for use misoprostol prior to IUD insertion. However, there is a tendency of 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 might have an effect on 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 prior to IUD insertion). However, no difference in dilatation of the cervix, as well as patient-scored pain estimation and the number of failed insertions was observed between the two groups.

In the current study, we found that there was statistically significant difference between misoprostol diclofenac and placebo groups as regard pain, our study shows that administrated of 75 mg of diclofenac sodium intramuscular, 2-hours before IUCD insertion reduces the

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sensations of the pain during IUD insertion in comparison to other groups (p value 0.164). In a study by **Fouda et al.** [15] they found a statistically significant lowering of pain scores with pretreatment with diclofenac potassium and lidocaine gel in parous women having copper IUD placement, the reduction is not clinically relevant. **Espey et al.** [16] found that 400 mcg of buccal 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 to pain score.

In the current survey, we found that side effects in IUD insertion were nausea and vomiting in 37.5% and syncopal attack in 6.3% in the misoprostol group, in the diclofenac group only gastritis in 18.7% of patients but nausea and vomiting in 18.7%, syncopal attack in 6.3% and gastritis in 12.5% of patients in the misoprostol diclofenac group (p value 0.013). In agreement with our result **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 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 caesarean 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

The administration of 400 mcg of vaginal misoprostol and IM injection of 75 mg diclofenac sodium 2 hours before IUD insertion in women with stenosed cervix facilitate the IUCD insertion, decrease failure of insertion and reduce pain sensation during IUCD insertion.

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