

## Pain Control of Medical Abortion with Misoprostol in the First Trimester of Pregnancy

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### Abstract

**Background:** Abortion is the most common subjects of obstetric which has applied two methods including surgical and medical approaches. Pain is the most common complication of medical abortion and pain relief is one the most important items in these patients.

**Objectives:** Evaluated the effect of three non-steroidal anti-inflammatory drugs in pain reduction of medical abortion in less than 14 weeks gestation with forensics declaration.

**Methods:** This study was a retrospective cohort in 66 pregnant women with less than 14 weeks gestation referred to Yas hospital for medical abortion that were assigned to three groups based on sedative drugs: A) Mefenamic acid capsules 250 mg, B) Diclofenac tablets 100 mg and C) Ibuprofen tablets 400 mg. The standardized visual assessment scale was assessed before and after drug administration that presented in medical records of patients.

**Results:** Comparison of visual assessment scale means before and after using of three non-steroidal anti-inflammatory drugs demonstrated that all three drugs lead to pain relief after the abortion that was significant statistically (P value=0.001). There was a significant difference in termination time of pregnancy between three groups, (P value= 0.016). In the case of hemoglobin drop, diclofenac lead to the lowest hemoglobin drop (P value=0.004). The amount of receiving narcotic among three groups revealed the significant difference (P value=0.000). There were not significant differences in pain relief (P value=0.327) and demographic data between three groups.

**Conclusion:** It was indicated that the three NSAIDs drugs, had a significant effect on the management of pain, diclofenac expended less termination time of pregnancy, narcotic drug usage and also hemoglobin drop than other groups.

**What does this study add?** Non-steroidal anti-inflammatory drugs are effective in pain management of medical abortion and some of them are preferred to others. Diclofenac can reduce abortion time and also hemoglobin drop after abortion and additional dose of other narcotics too.

**Keywords:** Medical abortion; First trimester of pregnancy; Pain management

### Introduction

Abortion is the most common subjects of obstetric which is applied two methods including surgical and medical approaches [1]. Experience of the surgeon and also the gestational age are the crucial factors in method selection of abortion. For the medical method a variety of medicines are used and misoprostol has a high priority for abortion induction [2]. Misoprostol is the analogs of the E1 prostaglandin that is consumed in three forms such as oral, vaginal and rectal [3,4]. Vaginal protocol has better abortion results and its blood level remains longer than the oral form [5]. Medical abortion benefits lacking of implications reported for surgical methods and it can be applied outpatient which is affordable in costs and time as well. Regarding to abortion in first-trimester, the pain can indicate intensively followed by prescription of prostaglandin and its analogs [6]. A group of women have severe and intolerable abortion pain however the pain can control easily in medical abortion during first and second-trimester of the pregnancy. In US the abortion rate is estimated approximately 1.1 million in 2011 and 2.8 -2.9% of 15-44 years old women have applied abortion worldwide each year between 2003 and 2008 [7,8]. It is estimated that 43% of American women experience at least one abortion in the childbearing age [9]. then high prevalence of worldwide abortion and pain control as the main complication of medical abortion, the pain control is emphasized through different studies [10,11]. The priority of ibuprofen has been

considered in several studies and mefenamic acid is considered as a leading drug for treating dysmenorrhea and menstrual cramps [12,13]. Diclofenac has been reported to be effective on the musculoskeletal pain [14]. In this study it was tried to evaluate the effect of Mefenamic acid capsules 250mg, Diclofenac tablets 100 mg and Ibuprofen tablets 400 mg in pain relief among women less than 14 weeks gestation who underwent medical abortion with misoprostol.

### Materials and Methods

This study was a retrospective cohort in which 66 pregnant women with less than 14 weeks gestation referring to Yas hospital for medical abortion from 2013 to 2014 and received sedative agent for pain management during the medical abortion, Data was collected from

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medical records of Pregnant women. Women divided in three groups: A) Mefenamic acid capsules 250 mg, B) Diclofenac tablets 100 mg and C) Ibuprofen tablets 400 mg. The frequency of sedative agents was once in 4-6 hours.

Standardized Visual assessment scale (VAS) (scoring 1 to 10) evaluated for all patients before and after sedative taking that presented in medical records and finally the data was analyzed by SPSS 20 software. Based on the objectives in order to assess comparisons among three groups independent T-test and one-way ANOVA test were applied. In some cases mentioned sedatives didn't reduce the pain sufficiently so a narcotic drug called meperidine was used as well.

Two expert perinatologists measured the retained products of conception using Acuson SEQUIA 512 after one week of termination of pregnancy. Inter-observer reliability was 87%. Hemoglobin was assessed using Symbex, K-800, made in Japan, 12 hours after abortion.

Ibuprofen was provided from Arya pharmaceutical company. Diclofenac and misoprostol was purchased from Sobhan pharmaceutical company and mefenamic acid was produced by Raha pharmaceutical company. All companies had certificate from Iranian Ministry of Health and Medical Education.

Inclusion criteria: pregnant women with less than 14 weeks gestation referred to Yas hospital for medical abortion, abortion had to be indicated based on forensics declaration.

Exclusion criteria: history of chronic medical diseases including cardiovascular, thyroid, renal, and liver diseases.

Ethics: The project that was approved by ethic committee of Tehran University of Medical Sciences as medical doctor dissertation of one of the authors.

## Results

Totally 66 participants assayed in this study. The mean age of the patients was  $28.86 \pm 6.45$  years. The mean gestational age was  $9.2 \pm$

2.5 weeks and the mean of BMI was  $24.39 \pm 3.71$  kg/m<sup>2</sup>. Demographic information is presented in the (Table 1).

One-way ANOVA test revealed hemoglobin drop indicated a statistically significant difference among three groups (P value=0.004). In this regard Mefenamic acid had the most hemoglobin drop with the mean of 1.49 mg/dl and diclofenac with the mean of 0.77 mg/dl had the least hemoglobin drop 12 hours after abortion. The mean of misoprostol usage to terminate the pregnancy was 1050 microgram and in three groups of Diclofenac, Ibuprofen and Mefenamic acid recipients, it was 900, 1400 and 1000 mg in order which their difference was statistically significant (P value=0.017). Termination time of the pregnancy was the next variable that differed significantly among three groups (P value=0.016). Although the amount of sedative receiving among three groups revealed significant difference (P value=0.000), the comparison was not attributable due to different taking dosages (dosage for each drug was mentioned previously). Comparison of VAS means before and after sedative receiving demonstrated all three drugs lead to significant statistically pain relief (P value=0.001). The means of VAS decrement for Diclofenac, Ibuprofen and Mefenamic acid taking groups were 2.23, 1.68 and 2.63 respectively (Table 2). Thus the most decrement was reported for Mefenamic acid taking group and the least decrement was recorded for Ibuprofen taking group. However, this difference wasn't statistically significant (P value=0.327).

The comparison between the amounts of sedative taking according to age, gravidity and gestational age among three groups of the participants indicated the dosage of Mefenamic acid was related with mother age (P value= 0.011) and gravidity (P value= 0.002) and Ibuprofen dosage was related with gravidity (P value= 0.035). Among all 66 patients, 10 patients (15.2%) had fever, 19 patients (28.8%) had nausea, 18 patients (27.3%) had diarrhea, 28 patients (42.4%) suffered from cramps and 10 patients (15.2%) complained about epigastric pain. The information about patients' complains are presented in the (Table 3).

Comarison between the means of clinical imparments determined that diarrhea and pelvic pain had significant differences among three groups (P value=0.001 and 0.000 respectively).

Value	Diclofenac	Ibuprofen	Mefenamic Acid	P value
Age(year)	29.5909	29.3333	27.6500	0.591
Height(meter)	1.6053	1.6418	1.5986	0.127
Weight(kg)	67.4474	64.4545	59.9545	0.081
Gravidity(mean)	2.6364	2.5455	2.0909	0.321
Live birth(mean)	1.1818	1.2727	0.8636	0.340
History of cs* (mean)	0.3636	0.5000	0.1905	0.265
Still birth(mean)	0.0909	0.09	0.1364	0.891
Misoprostol administration (microgram)	900.0000	1400.0000	1000.0000	0.017
Narcotic usage (mg)	247.6190	1018.1818	700.0000	0.000
VAS** Before NSAID administration	8.3158	7.1818	8.0000	0.120
VAS** After NSAID administration	6.0789	5.5000	5.3636	0.612
Gestational age(week)	8.5455	8.5455	9.6364	0.313
Abortion Number(mean)	0.4091	0.2273	.3182	0.566
BMI(kg/m <sup>2</sup> )	26.0890	23.9982	23.2672	0.064
Retained products of conception (mm)	12.8250	16.7111	10.3333	0.304
Termination Time(hours)	5.9524	15.9545	8.5455	0.016
Hb*** Before abortion(mg/dl)	12.5091	12.5091	12.3818	0.022
Hb*** After abortion(mg/dl)	11.0909	11.0909	10.8864	0.827
Reduction Hb*** (mg/dl)	-0.7727	-1.4182	-1.4955	0.004

\*cs=cesarian section

\*\*\* vas=Visual assessment scale

\*\*\* Hb=hemoglobin

**Table 1:** Demographic information for three groups of the participants.

Typet	Mean	Std. Deviation
Diclofenac	-2.23	1.53
Ibuprofen	-1.68	1.61
Mefenamic acid	-2.63	2.83

**Table 2:** The means of VAS decrement for three groups.

	Fever	Nausea	Diarrhea	Cramp	Epigastria	Pelvic Pain	
Diclofenac	18.2	22.7	45.5	40.9	13.6	9.1	Yes
	81.8	77.3	54.5	59.1	86.4	86.4	No
Ibuprofen	22.7	22.7	36.4	45.5	9.1	68.2	Yes
	77.3	77.3	63.6	54.5	90.9	22.7	No
Mefenamic acid	4.5	40.9	100	40.9	22.7	50	Yes
	95.5	59.1	100	59.1	77.3	50	No

**Table 3:** Percentage of complains among diclofenac, ibobrufen and mefenamic acid taking groups.

## Discussion

In this study the mean of 7.8 for VAS before the treatment demonstrated that the pain was a serious issue in medical abortion. In the case of hemoglobin drop among three groups, significant difference was observed and mefenamic acid caused the most hemoglobin drop (1.49 mg) while diclofenac taking lead to the least hemoglobin drop (0.77 mg). In the case of termination time of pregnancy, three groups revealed significant difference ( $P$  value=0.016), mefenamic acid, diclofenac, ibuprofen-taking groups recorded the mean of 8.5, 5.9, 15.95 hours in order for this indicator. Thus diclofenac can be a best medicine in medical abortion.

The priority of the utilized drugs in this study was mentioned previously. The study's results indicated that medical abortion caused pain that can be managed effectively by NSAIDs that their usage among previous medical abortion protocols was in association with disagreements due to probable interventions with misoprostol's function [15-18], were ignored and it doesn't seem they have significant difference for the management of medical abortion pain.

Avraham et al. indicated that pre-emptive effect of ibuprofen for medical abortion pain relief during a mifepristone and misoprostol regimen was statistically significant [19]. NSAIDs not only for medical abortion but also for spontaneous abortions have been studied. The effect of indomethacin, diclofenac, naproxen and ibuprofen before a spontaneous abortion have been evaluated by Daniel *et al.* that have demonstrated diclofenac and indomethacin specifically were associated with spontaneous abortions [20]. In a previous review by Murray *et al.* it was revealed that premedication with NSAIDs and playing music has improved pain control during surgical abortions remarkably [21]. However women are shown to be more satisfied with medical abortion rather than surgical abortion, as Di Carlo *et al.* has reported. They identified VAS scores for surgical and medical abortion  $7.9 \pm 1.0$  versus  $7.2 \pm 1.2$ ;  $p < 0.0001$  [22].

Para cervical blocking in association with local anesthesia has been used to pain relief but the effectiveness of this method is in consideration. Some studies have reported a remarkable pain relief and some haven't report a significant pain reduction. They have also mentioned that this method not only couldn't reduce the pain but it caused bradycardia and hypotension [23].

Generally a few studies on management of medical abortion have been approached and even these studies are not comparable according to heterogenous data. In a previous systematic study in 2011 in order to evaluate the studies with the objective of assessment of controlling pain caused by medical abortion in first and second-trimester of

pregnancy, among 363 studies only 10 surveys were included and as of analgesia regimens heterogeneity, meta analysis wasn't applicable [24]. In this study due to using different dosages of the drugs, significant statistical comparison of three drugs wasn't possible and it is strongly suggested that more studies with larger sample volume are needed so more accurate determination of different effects of these drugs can be achieved and prospective studies should be considered ideal analgesia regimens for pain control in the first trimester of pregnancy.

## Conclusion

In this study three groups of NSAIDs were surveyed for pain relief of medical abortion in first trimester including Diclofenac, Ibuprofen and Mefenamic acid, these drugs had a significant influence on pain management of patient with less than 14 weeks gestation, the effect of these three drugs in pain management were not significantly different. Although the results showed Diclofenac reduced the abortion time, extra narcotic and sedatives were needed less, hemoglobin drop and misoprostol were needed less too. Thus it seemed that Diclofenac can use as a first choice drug with higher priority with good effect on pain, termination time and hemoglobin drop after abortion.

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## Author Contributions

All authors contributed significantly towards the study.

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