Indian Journal of Fundamental and Applied Life Sciences ISSN: 2231– 6345 (Online)
An Open Access, Online International Journal Available at http://www.cibtech.org/jls.htm
2015 Vol. 5 (1) January-March, pp. 60-64/Azadeaskari et al.
Research Article

A COMPARISON OF EFFICACY AND SIDE-EFFECTS OF TWO METHODS OF VAGINAL MISOPROSTOL ADMINISTRATION IN THE FIRST TRIMESTER OF PREGNANCY TERMINATION FOR PATIENTS OF BANDARABAS HOSPITAL LOCATED IN IRAN

***Azadeaskari, Minoorajaee and Azinalavi**
Persian Gulf Fertility and Infertility Research Center, Hormozgan University of Medical Sciences
**Author for Correspondence*

ABSTRACT
Over the last two decades, medical methods have been conducted for abortion induction; these methods are more effective and practical alternatives for surgical methods. Non- surgical methods increase women's choice for treatment and decreasing its side-effects. Moreover, sometime surgical methods are not provided for women or they are impossible medically. The present paper aims to compare efficacy and side effects of two methods of vaginal misoprostol administration in the first trimester of pregnancy termination. Patients of Bandarabas hospital located in Iran are considered as the case study of the investigation. Research results indicate that no significant difference has been observed between the two studied groups; however, regarding the better results in the group receiving 400 mg of misoprostol per 6 h., misoprostol regime is suggested to treat the patients of the mentioned group.

Keywords: *Efficacy, Misoprostol Vaginal Administration, Pregnancy*

INTRODUCTION
In their article, Lin and colleagues has introduced a combination of misoprostol and mifepristone as the best selection to terminate the second trimester of pregnancy, this method has the most effects in the shortest period of time. However, if mifepristone is not available, using misoprostol alone will be a good alternative. According to this article, using 400 mg of vaginal misoprostol every 3 to 6 hours is the best regime to terminate the second trimester of pregnancy. Doses higher than 800 mg of vaginal misoprostol lead to more side-effects especially diarrhea.

In their study, Vitner and colleagues used dose of 400 mg of misoprostol every 6 hours at the gestational age between 13 to 24 weeks, and they indicated that misoprostol was a safe and effective way to terminate pregnancy.

Fekih and colleagues compared misoprostol and mifepristone in the first trimester of pregnancy termination. In this study, 252 patients were categorized into two groups to receive 200gm of oral misoprostol, and then 400 mg of oral misoprostol (group 1) or 800 mg of sublingual misoprostol every 4 h for a maximum of 3 doses (group 2). Mean of hemoglobin decrease in group 1 was significantly higher than that of group 2. There were no differences between two groups regarding other factors. According to this study, misoprostol hadadvantage over mifepristone in order to terminate the first trimester of pregnancy.

Chaudhuri and colleagues compared two regimes of 400 mg every 6 h for a maximum of 4 doses and 400 mg every 12 h for a maximum of 4 doses to end the second trimester of pregnancy. In the first group, mean of time duration for abortion (12.59 h) was significantly shorter than that of the second group (16.41 h) ($P < 0.001$). Moreover, percentage of successful abortions in the first group (56.52%) in 12 hours was higher than that of the second group (25.80%) ($P=0.00005$). Incidence of side effects in both groups did not have a significant difference. The study indicated that the regime of 400 mg of misoprostol every 6 h was more successful in relation with the second trimester of pregnancy termination.

Brouns and colleagues compared doses of 200 mg and 400 mg of misoprostol every 4 h in relation with the second trimester of pregnancy termination. Their study indicated that time of performing abortion in the group receiving 200 mg was more than that of the group receiving 400 mg of misoprostol. Therefore, the regime ofreceiving 400 mg every 4 h was suggested.

Some studies suggest new combining treatments for the first trimester of abortion. For instance, Samuel and colleagues introduced Dilapan-S and misoprostol combination as a successful method for the early first trimester termination of abortion. Anyhow, this was a pilot study and needed more investigation in this field.

Majority of studies that have compared using misoprostol with surgical operation have concluded that misoprostol percentage of success is equal to that of surgical operation. Moreover, in comparison with surgical operation, it has fewer side effects with less significance. For instance, Prasad and colleagues indicated that not only success of single dose of vaginal misoprostol was comparable with surgical operation but also it had fewer side effects.

Ozerkan and colleagues compared low dose and high dose of misoprostol for the second trimester of pregnancy termination. The study consisted of 60 patients , and it indicated that in comparison with normal doses, dose of 1400 mg of vaginal misoprostol in the second trimester shortened the time needed for abortion and also did not have more side effects.

Main Body

Annually, around 46 million abortions are performed in the world and half of abortions are performed illegally. According to definition of WHO, illegal abortions are unsafe. According to report of WHO, annually, unsafe abortions lead to death of 70 to 80 thousand women. Medical and surgical methods are used to safely terminate the first trimester of pregnancy; however, using these methods has decreased as a result of their high risks and costs.

For instance, curettage brings about infection for 0.1 to 4.7 percent of patients. Moreover, it might cause side effects such as uterine rapture, intrauterine adhesions, trauma to the cervix, bleeding, and risks associated with anesthesia. With regard tohigh risk of abortion via surgical methods, using medical treatment of prostaglandin is suggested. Recently, it is observed that medical treatment with misoprostol could be an effective and safe treatment for ending the first trimester of pregnancy. Misoprostol is a prostaglandin E1 analogue which is easily usably orally or through vagina.

Misoprostol is cheap and could be kept at the room temperature. Experimentally, it is used to prepare cervix and induce labor in order to perform abortion in the first and second trimester of pregnancy. Misoprostel does not have serious- long lasting side effects, and its side-effects rarely occur. Nausea, fever and chill, cramps, skin rashes, diarrhea, and vaginal bleeding are its common side effects. Many studies have been conducted to determine the desirable dose and administration method of it (oral or vaginal), however, its ideal dose and regime is not still determined. Consequently, a study is needed to recognize effective dose and method of administration that arrive at the desired result with the least side effects.

Research Hypotheses

1. Using vaginal misoprostol through shorter intervals and with lower dose results in complete abortion.
2. Using vaginal misoprostol through shorter intervals and with lower dose results in decrease of dilation cases and required curettage for abortion in the first trimester of pregnancy.
3. Using vaginal misoprostol through shorter intervals and with lower dose results in decrease of time needed for abortion in the first trimester of pregnancy.
4. In comparison with using vaginal misoprostol through longer intervals, using vaginal misoprostol through shorter intervals does not increase its side effects.

MATERIALS AND METHODS

Methodology

The present study is a double-blind, randomized clinical trial. The case study encompasses all pregnant women from beginning of their pregnancy up to the end of week 14 of pregnancy. The mentioned patients have referred to Bandarabas Shariaty hospital from the beginning of plan up to the time of completing sample sizein order to terminate pregnancy as a result of fetal death or a medical reason. The sample size is determined by a calculating formula and considering a=0.05, β= 0.2, P1= 0.55, and P2= 0.87 in order to compare two groups with each other. Success ratio in two groups is similar to each other. Sample size

for each group equals 41 people. Patients were categorized in the first and second groups randomly and alternatively.

Exclusion criteria of the study included factors of corioamionitis, prostaglandin sensitivity, history of heart disease, respiratory; hepatic; and kidney problem, description of uterine pathology, suspicion of ectopic pregnancy, mole, and symptoms of uterine infection or sepsis.

1. The first group includes all patients having the above factors from 20th of December 2009 up to the date of completing sample size (41 cases). The patients receive 800 mg of vaginal misoprostol every 12 to 48 hours (ma maximum of 4 days). Lack of abortion or an incomplete abortion after 48 hours is called treatment failure and the patient should tolerate D&C operation. Percentage of incidence of side effects including fever and chill, nausea, abdominal cramp, skin rashes, and diarrhea are determined in this group.
2. The second group includes all patients having the above factors from 20th of December 2009 up to the date of completing sample size (41 cases). The patients receive 400 mg of vaginal misoprostol every 6 to 48 hours (ma maximum of 4 days). Lack of abortion or an incomplete abortion after 48 hours is called treatment failure based on clinical examination and ultrasound treatment and the patient should tolerate D&C operation. Percentage of incidence of side effects is determined in this group as well.

Tablets of vaginal misoprostol were previously moistened with one or two drops of normal saline and were inserted into the posterior fornix of the vagina. Data were analyzed by SPSS20 software, chi- square test, Fisher's exact test, and independent t-test.

RESULTS AND DISCUSSION

In this study, patients were randomly categorized into two groups with 41 members. The first group was given four tablets of misoprostol (800 mg) every 12 h, and the second group was given two tablets of misoprostol (400 mg) every 6 h.

Table number 1 indicates a comparison between demographic characteristics of both of the groups. According to the information of the table, two groups were equal regarding the basic specifications at the beginning of treatment (P >0.005).

Table 1: A comparison between basic specifications of two studied groups

Variables	Group 1	Group 2	P Value
Age	28/34 ± 7/09	28/07 ± 5/53	0/849
Gravid	2/56 ± 1/28	3/10 ± 2/14	0/174
Abortion	0/44 ± 0/63	0/49 ± 0/89	0/777
Alive fetus	1/02 ± 1/03	1/51 ± 1/39	0/077
Dead fetus	0/12 ± 0/33	0/1 ± 0/62	0/221
Gestational age (day)	54/66 ± 13/65	59/27 ± 16/27	0/168
Baseline Hemoglobin	11/76 ± 0/92	11/59 ± 1/33	0/497

Table 2: A comparison between two groups regarding missed abortion, EP history, legal abortion, and blighted ovum

Variables	Group 1(frequency and percentage)	Group 2(frequency and percentage)	P value
Missed abortion	(%78) 32	(%58/5) 24	0/058
History of EP	(%2/4)1	(%0) 0	*0/500
Legal abortion	(%4/9) 2	(%9/8) 4	*0/338
Blighted ovum	(%4/9) 2	(%7/3) 3	*0/500

In the above tables, quantitative values are compared based on independent t-test, and qualitative values are compared based on chi-square test. Moreover, Fisher's exact test is used in the needed cases.

- Using vaginal misoprostol through shorter intervals and with lower dose results in complete abortion

In the first group, 19 patients (46.3%) had complete abortion, 15 patients (36.6%) had incomplete abortion, and 7 patients (17.1%) did not have abortion. In the second group, these values equaled 21 (51.2%), 13(31.7%), and 7(17.1%) respectively. Results of chi-square test indicated that no significant difference was observed between two groups regarding how the abortion was done.

- Using vaginal misoprostol through shorter intervals and with lower dose results in decrease of dilation cases and required curettage for abortion in the first trimester of pregnancy.

22 patients (53.7%) in the first group and 20 patients (48.8%) in the second group tolerated D & C operation. Based on chi-square test, the difference between two groups was not significant statistically (P= 0.413).

- Using vaginal misoprostol through shorter intervals and with lower dose results in decrease of time needed for abortion in the first trimester of pregnancy.

The average time needed for abortion in the first group equaled 25/84 ∓ 16.24, and in the second group equaled 21/19 ∓ 15.74. According to independent-t test, this difference is not significant statistically (P= 0.364).

- In comparison with using vaginal misoprostol through longer intervals, using vaginal misoprostol through shorter intervals does not increase its side effects.

11 patients (26.8%) in the first group and 8 patients (19.5%) in the second group suffered from side effects of using misoprostol. Chi-square test indicated that regarding side effects, two groups were similar to each other statistically (P=0.301). Table number 3 compared side effects incidence in each of the groups. Based on chi-square test and independent t-test, table 3 indicated that there was no significant difference between the groups statistically.

Table 3: A comparison between side effects of two studied groups

Variables	Group 1	Group 2	P value
Fever	(%2/4) 1	(%0) 0	*0/5
Nausea	(%14/6) 6	(%17/1) 7	0/762
Cramp	(%4/9) 2	(%0) 0	*0/247
Severe vaginal bleeding	(%9/8) 4	(%4/9) 2	*0/338
Hemoglobin dropping	(%0) 0	(%2/4) 1	*0/5
Mild diarrhea	(%2/4) 1	(%0) 0	*0/5
Dizziness	(%2/4) 1	(%0) 0	*0/5
Vomiting	(%2/4) 1	(%0) 0	*0/5

Fisher's Exact Test

Conclusion

In the present paper, regarding status of abortion (complete, incomplete failed abortion), no difference was observed between the two groups. Moreover, the need for D & C operation was equal in both groups. Among half of the patients, complete abortion was done via medical treatment of misoprostol. Chaudhuri's and colleagues' study indicated a higher percentage for the dose of 400 mg of misoprostol per 6 h (56/52%) for a period of 24 hours. According to the same study, complete abortion for the dose of 400 mg of misoprostol every 12 h for a period of 24 hours had a very low percentage and was reported around 25.80%. Although the mentioned study was done on abortion in the second trimester of pregnancy, comparing its results with the present paper indicated advantage of 400 mg dose of misoprostol per 6 h, and 800 mg per 12 h over 400 mg per 12 h .In the present paper, after beginning treatment, patients were observed for 48 h in order to abort intrauterine pregnancy. If it was possible to observe patients for a longer period of time, the possibility of complete abortion would increase. Since many of the patients were from rural area, it was not possible to observe their condition for a longer period of time.

There was not a significant difference between two groups regarding the time needed for abortion. It equaled 26 h in the first group, and 21 h in the second group. The time difference (over 4 hours) between two groups indicated that if the study had been done with a larger sample size, the difference might have been significant. In his study, Chaudihuri determined 12.5 and 16.5 hours of abortion for the two studied groups. In this study, the advantage was also for treating regime of 400 mg per 6 h. The studies indicated more efficacy of misoprostol in higher doses.

Studies on higher doses of misoprostol such as Ozerkan's and colleagues' study compared 1400 mg of misoprostol with normal doses of it. The result indicated that higher doses could shorten the time needed for abortion without having more side effects.

According to the present paper, nausea was the most common side effect of using misoprostol. Totally, incidence of side effects in the first group equaled 25 percent and in the second group equaled 20 percent. However, another study indicated that no significant difference was observed between different doses regarding side effects of using misoprostol. Generally, studies showed that misoprostol was a useful treatment for the first and second trimester of pregnancy termination. Moreover, its effects could be compared with that of surgical treatment. Side effects of misiprostol treatment were less than that of surgical treatment.

This research indicated that there was no difference between doses of 800 mg of misoprostol every 12 h up to 3 days, and 400 mg every 6 h up to 48 hours regarding side effects and efficacy. Although no difference was observed between two groups of misoprostole treating regime, the regime of 400 mg every 6 h for a period of 48 hours had advantages over other regimes from perspective of efficacy ,fewer side effects and the time needed for abortion. Therefore, this treatment was suggested for patients requesting the first trimester of pregnancy termination.

REFERENCES

Brouns JF, Van Wely M, Burger MP and Van Wijngaarden WJ (2010). Comparison of two dose regimens of misoprostol for second-trimester pregnancy termination. *Contraception* **82**(3) 266-75, Epub 2010/08/14.

Chaudhuri S, Banerjee PK, Mundle M and Mitra SN (2010). A comparison of two regimens of misoprostol for second trimester medical termination of pregnancy: a randomized trial. *Tropical Doctor* **40**(3) 144-8, Epub 2010/06/18.

Fekih M, Fathallah K, Ben Regaya L, Bouguizane S, Chaieb A and Bibi M *et al.*, (2010). Sublingual misoprostol for first trimester termination of pregnancy. *International Journal of Gynaecology and Obstetrics: the Official Organ of the International Federation of Gynaecology and Obstetrics* **109**(1) 67-70, Epub 2010/01/08.

Lin CJ, Chien SC and Chen CP (2011). The use of misoprostol in termination of second-trimester pregnancy. *Taiwanese Journal of Obstetrics & Gynecology* **50**(3) 275-82.

Ozerkan K, Ocakoglu G, Rehimli S, Uncu G and Develioglu O (2009). A comparison of low-dose and high-dose protocols of vaginal misoprostol for second trimester termination of pregnancy. *Clinical and Experimental Obstetrics & Gynecology* **36**(4) 45-7, Epub 2010/01/28.

Prasad S, Kumar A and Divya A (2009). Early termination of pregnancy by single-dose 800 microg misoprostol compared with surgical evacuation. *Fertility and Sterility* **91**(1) 28-31, Epub 2008/02/26.

Samuel MI and Parsons JH (2009). Hygroscopic dilator (Dilapan-S) and misoprostol combination for the early first-trimester termination of pregnancy: a pilot study. The journal of family planning and reproductive health care / Faculty of Family Planning & Reproductive Health Care, *Royal College of Obstetricians & Gynaecologists* **35**(1) 45-7, Epub 2009/01/08.

Vitner D, Deutsch M, Paz Y, Khatib N, Baltiter T and Rosenberg S *et al.*, (2011). Association between gestational age and induction-to-abortion interval in mid-trimester pregnancy termination using misoprostol. *European Journal of Obstetrics, Gynecology, and Reproductive Biology* **156**(2) 140-3, Epub 2011/04/22.