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Efficacy of Misoprostol only and Mifepristone with Misoprostol in Non-viable First Trimester Termination of Pregnancy

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Abstract:
Objective: To compare the effectiveness, success rate and induction to abortion interval between administration of misoprostol only and mifepristone with misoprostol in first trimester abortions (6-12 weeks). **Methods*:*** This randomized clinical trial was conducted on 100 women with non-viable first trimester pregnancy need termination; divided two groups each consisting of 50 women. Group-I received only misoprostol; 600 mcg initial vaginal insertion followed by 200 mcg sublingually every 8 hour until abortion was completed. Women in Group-II received mifepristone 200 mg orally and after 12 hours tab misoprostol 400 mcg sublingually. **Results:** The success rate in Group-I was 90 %, whereas in Group-II it was 98 %. The mean of induction-abortion interval in Group-I was 28.13±3.1 hours where as in Group-II which was significantly less 17.28±2.04 hours (p<0.001). There was significant difference in the mean blood loss also, 95.12±7.12 ml in Group-I and 74.52±4.12 ml in Group-II. Also in Group-II lesser misoprostol dose was required. **Conclusion:** Pretreatment with mifepristone significantly reduces the need for curettage, the induction-abortion interval and the misoprostol dose along with minimal blood loss.

Indexing words: Misoprostol, Mifepristone, First trimester, Abortion, Induction-abortion interval (IAI)

Introduction:

The word abortion derives from Latin aboriri that means 'to miscarry.' Abortion is defined as the spontaneous or induced termination of pregnancy before fetal viability. The National Centre for Health Statistics, Centre for Disease Control and Prevention, and World Health Organization (WHO) defines abortion as pregnancy termination before 20 weeks of gestation or a fetus weighing <500 grams[1]. Most common cause of first trimester abortions is incomplete abortion, blighted ovum, and missed abortion.

Medical methods of abortion have been proved to be safe and effective[2]. The most effective regimens rely on the antiprogestin, mifepristone, which binds to progesterone receptors resulting in necrosis and detachment of placenta. It also softens the cervix and causes mild uterine contractions. It sensitizes the uterus to the action of prostaglandin which is given 1–2 days later, like synthetic prostaglandin E1 analogue, misoprostol, which binds to myometrial cells causing strong myometrial contractions and causes cervical softening and dilatation. This leads to expulsion of fetus from the uterus[3].

The effects of medical methods of abortion are similar to those associated with spontaneous abortion and include uterine cramping and prolonged menstrual-like bleeding. Bleeding occurs 9 days on an average but can last up to 45 days in rare cases[4].

The present study was undertaken to compare the effectiveness of simultaneous administration of mifepristone and misoprostol versus misoprostol alone in first trimester abortion.

Methods:

This was a randomized clinical trial carried out at the Department of Obstetrics and Gynaecology, Combined Military Hospital, Rangpur, during the period between January 2019 and June 2019. Ethic approval was obtained from Ethical Committee of Combined Military Hospital, Rangpur Cantonment. All patients with first trimester abortion prepared for medical termination. Information about the study was available to patient during consenting. The author had discussed the procedures with patients and they accepted and consented. Detailed history was taken, clinical examination including gynecological examination and

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ultrasonography was performed. 100 patients with first trimester abortion including incomplete abortion, missed abortion, blighted ovum were divided into two groups:

Group-I: 50 patient with first trimester abortion received only misoprostol; 600 mcg initial vaginal insertion followed by 200 mcg sublingually every 8 hours until abortion was completed.

Group-II: 50 patient with first trimester abortion received mifepristone 200 mg orally and after 12 hours tab misoprostol 400 mcg sublingually.

Inclusion criteria were: (1) women aged more than 18 Years (2) singleton pregnancy (3) women with incomplete abortion or blighted ovum or missed abortion (4) willing to follow the study protocol and provide informed consent and (5) willing to undergo required follow-up and surgical management when indicated. The exclusion criteria were women with (1) H/o previous three or more cesarian section (2) multiple pregnancy (3) contraindications to mifepristone and misoprostol like chronic or acute adrenal, hepatic or renal failure (4) cardiovascular disease, (5) poorly controlled seizure disorder (6) on anticoagulant therapy, known clotting defect (7) hemoglobin less than 8 gm/dl and (8) known or suspected pelvic infection. Women who fulfilled the criteria for the trial were interviewed and given an explanation of the trial. An informed written consent was obtained. A pelvic ultrasound examination was performed to confirm the abortion and to exclude multiple pregnancies. The side effects including nausea, vomiting, diarrhea and fever were recorded. The blood pressure, pulse, temperature and frequency of uterine contractions are monitored. After abortion, the products of gestation (fetus and placenta) were examined to see whether the abortion was complete. After fetal expulsion if placenta is not expelled then surgical evacuation under general anesthesia was performed. Rh antibody was given to Rh negative mothers. The amount of blood loss during abortion was assessed clinically and recorded. The number of doses of misoprostol required were calculated and recorded. Collection of patients data and statistical analysis were done by SPSS version 22.

Results:

There were no statistically significant differences between the two groups in age (Group I: mean 23.1± 4.16 years, range 17-36 years, median 24 years; Group II: mean 24.46±5.87 years, range 18-40 years, median 25 years; p=0.104), parity, H/O previous cesarian section and gestational age (Group I: mean 8.12±1.09 weeks; Group II: mean 8.22±1.18 weeks). Successful abortion was significantly higher in Group II compare to Group I. Total blood loss, induction-abortion interval and duration of bleeding significantly lower in Group II compare to Group I. Nausea, vomiting, diarrhoea were not significantly different in two groups.

Table 1: Comparison of patients characteristics between two groups (n=100)

Variables	Group I (n=50)	Group II (n=50)	p-value
Age (years)	23.14±4.1	24.46±5.8	0.104
ZParity- Primi	15(30.0%)	15(30.0%)	1.000
Multi	35(70.0%)	35(70.0%)	
H/O previous cesarean section	10(20.0%)	10(20.0%)	1.000
Gestational weeks	8.12±1.09	8.22±1.18	0.661
Successful abortion	45(90.0%)	49(98.0%)	0.0194*
Curettage needed	5(10.0%)	1(2.0%)	0.242
Induction abortion interval	28.13±3.14	17.28±2.04	<0.001*
Total blood loss	95.12±7.12	74.52±4.12	<0.001*
Duration of bleeding	1.34±0.21	1.12±0.11	<0.001*
Nausea	0(0.0%)	1(2.0%)	0.371
Vomiting	2(4.0%)	1(2.0%)	0.559
Fever	0(0.0%)	0(0.0%)	-
Diarrhoea	4(8.0%)	1(2.0%)	0.178
Blood transfusion	0(0.0%)	0(0.0%)	-
Analgesia	0(0.0%)	0(0.0%)	-

Group-I: First trimester abortion received only Misoprostol; 600 mcg initial vaginal insertions followed by 200 mcg sublingually every 8 hour until abortion was completed.

Group-II: First trimester abortion received Mifepristone 200 mg orally and after 12 hours Tab. Misoprostol, 400 mcg sublingually.

Discussion:

Medical method for termination of non-viable pregnancy is becoming popular now a days to avoid the risk of anesthesia, surgical injuries of cervix, uterus, other organs as well as the cases of uterine perforation (0.12-1.98%), blood transfusion (0.5%), necessity of repeating

surgical intervention (1%) and ongoing pregnancy due to failure of surgical intervention (0.2%)[5-8]. Medical methods of abortion have been proved safe and effective.

This trial compared the difference in IAI, dose of misoprostol required and amount of blood loss in first trimester abortions with misoprostol only and mifepristone plus misoprostol. There was no difference in the prevalence of gastrointestinal side effects between the two groups. Nearly all the women in our study aborted before 24 hours like other similar studies conducted by Elami et al[9], Dickinson et al[10] and Borgatta and Kapp[11]. Borgatta and Kapp[11] reported a success rate of 95% within 24 hour. In our study, the success rate was 90% in Group-I and 98% in Group-II (Table 1). The mean induction abortion interval in Group-I was 28.13±3.1 hour where as in Group-II which was significantly less 17.28±2.04 hour (p<0.001*). Modak et al[12] in a comparative study of sublingual and vaginal misoprostol in second trimester abortions reported a complete abortion at 24 hour of 79.41% (in sublingual group) and mean IAI of 12.28 h. Ngoc et al.[13] in their double blind study reported the mean IAI was statistically shorter for mifepristone plus misoprostol group compared to misoprostol only group (8.1 hour and 10.6 hour, respectively, with a p≤0.01). Dabash et al[14] in their study reported mean IAI of 10.4 ± 6.8 hour in mifepristone group and 20.6 ± 9.7 hour in misoprostol only group. Reduction in induction to abortion interval is likely to improve the acceptability of women[13]. Wildschut et al[15] in their review article on medical methods for mid- trimester termination of pregnancy suggested that mifepristone plus misoprostol is the most efficient regimen and 3-hourly intervals of misoprostol administration are more effective than 6-hourly intervals. Mifepristone enhances the action of misoprostol there by reducing the induction to abortion interval and dose of misoprostol .The mean dose of misoprostol required in Group-II was significantly lower compared to Group-I like in other similar studies[13].

We also observed that in Group-II the mean blood loss (74.52±4.12 ml) was less, probably due to shorter IAI. Hou et al[16] in their study reported a total abortion rate of 95–100% within 24 hour, mean IAI was shorter in parous women (6.3 ± 3.7 hour) and the mean blood loss 2 hour after expulsion of products of conception was 98.3 ± 76.2 ml. Nagaria et al[17] reported a success rate of 100%, and the mean IAI was significantly shorter and the mean dose of misoprostol required was less in the mifepristone pretreated group. Also the mean blood loss was slightly higher in the misoprostol only group. Garg et al[18] reported a success rate of 96% in the buccal group in the second trimester abortion.

Conclusion:

Outcome of the study is pretreatment with mifepristone significantly increases the success rate, reduces the induction abortion interval, dose of misoprostol required and blood loss compared to using only misoprostol, thus increasing the patient compliance and thereby reducing the rate of surgical intervention, morbidity and mortality.

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