ON EFFICACY AND ACCEPTABILITY OF EARLY MEDICAL ABORTION BY MIFEPRISTONE WITH ORAL OR VAGINAL MISOPROSTOL

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ABSTRACT

BACKGROUND

Unsafe abortion is a major public health problem. Globally, 20 million unsafe abortions take place each year and account for 13% of all maternal deaths. According to WHO, 56% of abortions in developing countries are still unsafe even though medical abortion methods have been in use for more than a decade.

The main objective of the present study is to compare the efficacy, acceptability, side effects and factors affecting outcome of early medical abortion with oral and vaginal misoprostol after oral mifepristone in inducing early medical abortion up to 49 days.

MATERIALS AND METHODS

It was an interventional study (non-RCT) conducted on women requesting termination of early pregnancy at the outpatient department of family planning unit with ultrasound confirmed intrauterine gestation of ≤ 49 days allocated into two groups. Mifepristone 200 mg was administered on Day 1 followed by 400 mg of oral misoprostol for Group I and 800 mg of vaginal misoprostol for Group II. They were reviewed on Day 14 by ultrasound for completion of abortion and Hb. If abortion was incomplete or bleeding was excessive, curettage was done.

RESULTS

The two groups were comparable with respect to age, parity and gestational age, socio-economic status and level of education. There was no significant difference in the complete abortion rates for oral (91.1%) and vaginal (92.0%). Mean induction abortion interval was 4.29 hours for oral and 3.5 hours for vaginal ($p = 0.023$). History of previous abortion was found to be a strong predictor of failure of early medical abortion ($p = 0.007$). Nausea (24%), vomiting (13%) and fatigue (50%) were more in the oral group. Mean duration of bleeding was 9.4 days in oral and 8.2 days in vaginal group ($p = 0.000$). Method satisfaction was more among oral group (92.2%) compared to 85.1% in vaginal, but not statistically significant ($p > 0.05$).

CONCLUSION

Medical abortion with 200 mg of mifepristone in combination with 400 mg misoprostol orally or 800 mg vaginally after 48 hours was found to be safe, simple, effective, non-invasive and acceptable method.

KEYWORDS

Induction Abortion Interval, Mifepristone, Misoprostol.

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BACKGROUND

Unsafe abortion is a major public health problem in developing countries. Globally, 20 million unsafe abortions take place each year and account for 13% of all maternal deaths.⁽¹⁾

The incidence of induced abortions is not definitely known, because estimates of illegal abortions are generally unreliable. This has led to the liberalisation of abortion laws and search for newer methods.

Medical abortion offers great potential for improving abortion access and safety. The drugs used were mainly mifepristone (RU 486), a potent antiprogesterin in combination with prostaglandin E₁ analogue misoprostol.

It has been in use for over a decade and research is ongoing since its inception. But still in 2012, WHO and the Guttmacher Institute reported that 56% of abortions in developing countries were unsafe.⁽²⁾

Mifepristone 200 mg was found to be as effective as 600 mg in multicentre trials by WHO.⁽³⁾ Studies have also shown that vaginal administration of misoprostol after pre-treatment with mifepristone resulted in higher complete abortion compared to oral dose.⁽⁴⁾ The present study was undertaken to compare the efficacy, acceptability, side effects and factors affecting outcome of early medical abortion with oral and vaginal misoprostol after oral mifepristone in inducing medical abortion up to 49 days. Increasing access to safe abortion services is the most effective way of preventing unsafe abortions.⁽⁵⁾

MATERIALS AND METHODS

This interventional study (non-RCT) was conducted on women requesting termination of early pregnancy ≤ 49 days in the outpatient department of family planning unit for a period of one year. Women seeking MTP with USG confirmed intrauterine pregnancy; < 35 years and who were able to come for one to three follow-ups were selected for the study.

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Women with suspected/ confirmed ectopic pregnancy, IUCD, hypersensitivity to drugs with medical complications and previous scar on uterus were excluded.

Based on a pilot study, the mean induction abortion interval for the Group I (Oral) was 4.01 ± 2.7 and in the Group II (Vaginal) was 3.12 ± 1.2 . The following formula was used to estimate the minimum sample size.

$$= \frac{2\sigma^2(Z_{1-\alpha/2} + Z_{1-\beta})^2}{d^2}$$

$$\sigma^2 = \frac{\sigma_1^2 + \sigma_2^2}{2}$$

σ_1 = Standard deviation of the first sample
 σ_2 = Standard deviation of the second sample
 $d = \mu_1 - \mu_2$
 = Observed difference between the mean values of the two samples

Substituting the Values

Standard deviation in Group I	1.2
Standard deviation in Group II	2.7
Mean difference	0.89
Effect size	0.46
Alpha error (%)	5
Power (1-beta) %	80
1 or 2 sided	2
Required minimum sample size per group	87

Ethical committee approval was obtained. After getting an informed written consent, patients satisfying inclusion criteria were allocated alternately into Group I (Oral) and Group II (Vaginal). They were counselled regarding procedure characterisation like cost, efficacy, safety, number of visits and probable need of a surgical abortion.

On Day 1, both groups received 200 mg of mifepristone. They were also observed in OP and allowed to go home. If abortion had not occurred in 48 hours, Group I was given 400 mg (2 tablets) of misoprostol orally. Group II received 800 mg (4 tablets) of misoprostol vaginally. Women were observed for 4 hours. They were asked to keep record of onset of bleeding, time of expulsion of products and any side effects noted. They were given a telephone number to contact when concerned.

All the women were reviewed on Day 14 with repeat USG and Hb estimation. They were enquired about the degree of satisfaction, whether they will use it for a second time if needed and whether they would suggest it to their friends.

Outcome was measured as complete abortion (requiring no surgical intervention), incomplete abortion (clinical and USG evidence), missed abortion and ongoing pregnancy. Success was defined as expulsion of products of conception with no need for surgical intervention. Induction abortion interval was defined as the time interval in hours from the administration of misoprostol to the passing of products of conception.

Quantitative variables were analysed by 't' test and qualitative variable by χ^2 test. $P < 0.05$ was taken as significant.

RESULTS

Table I. Demographic Profile of Both Groups

Age in Years	Group I		Group II		Total	
	No.	%	No.	%	No.	%
< 20	6	5.89	3	2.97	9	4.43
21-25	49	48.04	36	35.64	85	41.87
26-30	30	29.41	34	33.66	64	31.52
31-35	17	16.67	28	27.72	45	22.16

Table Ia. Distribution according to Age

$$\chi^2 = 0.1154; p > 0.05$$

Table Ia. Distribution According to Age

In the present study majority of patients come under 21-25yr age group (41.87%) followed by the 26-30yrs age group (31.52%). In <20 age group it was 5.89 % in Group I and 2.97% in Group II and in 31-38yrs age group it was 16.67% in Group I and 27.72% in Group II. Both groups are comparable with respect to age.

Parity	Group I		Group II		Total	
	No.	%	No.	%	No.	%
Primi	4	3.92	6	5.94	10	4.93
Para 1	70	68.63	59	58.41	129	63.55
Para 2	28	27.45	36	35.64	64	31.53
Total	102	100	101	100	203	100

Table Ib. Distribution according to Parity

$$\chi^2 = 0.311; p > 0.05$$

Table Ib. Distribution According to Parity

Multipara constituted 96.08% cases in Group I and 94.05 cases in Group II whereas primis constituted 3.92% and 5.94% in Group I & II respectively. Both groups were found to be comparable after applying the Chi-square test.

Gestational Age in Days	Group I		Group II		Total	
	No.	%	No.	%	No.	%
35-42	65	63.72	55	54.45	120	59.12
43-49	37	36.27	46	45.54	83	40.88
Total	102	100	101	100	203	100

Table Ic. Distribution according to Gestational Age

$$\chi^2 = 1.8; p > 0.05$$

Table Ic. Distribution According to Gestational Age

Both groups are comparable with respect to gestational age.

76.3% were residing in urban area and 23.3% in rural area. 79.8% were from middle socioeconomic group. 91.6% had high school or higher level of education. 86.2% were housewives. 92.6% were married. 98% induced abortions were on social grounds. 91.6% had complete abortion. Check curettage was done for 8.3% with incomplete abortion. There were no cases of missed abortion or continuing pregnancy. Complete abortion was 91.1% for Group I oral and 92% for Group II vaginal ($P=0.816$) showing both routes were equally effective.

Induction Abortion Interval	Group I		Group II		Total	
	No.	%	No.	%	No.	%
≤ 4 hrs.	80	78.43	91	90.09	171	84.24
> 4 hrs.	22	21.57	10	9.90	32	15.76

Table II. Comparison of Induction-Abortion Interval between the Two Groups

Table II Comparison of induction- abortion interval between the two groups.

Induction Abortion Interval	Mean	SD	't' Value	P Value
Group I	4.29	2.5	2.52	0.01 S
Group II	3.5	1.6		

Table III. Mean Induction Abortion Interval**Table III Mean Induction Abortion Interval**

The mean induction abortion interval was 4.29 hours for oral group and 3.5 hours for vaginal groups. 78.4% in oral group

Age in Years	Group I		Group II		Total		χ^2	P Value
	No.	%	No.	%	No.	%		
Nausea	25	24.51	8	7.92	33	16.26	7.41	< 0.05 S
Vomiting	14	13.73	5	4.95	19	9.36	3.8	< 0.05 S
Diarrhoea	6	5.88	3	2.97	9	4.43	0.34	> 0.05 NS
Abdominal Pain	88	83.27	83	82.18	171	84.24	0.64	> 0.05 NS
Fatigue	51	50	34	33.66	85	41.87	5.56	< 0.05 S

Table IV. Comparison of Side Effects Profile**Table IV. Comparison of Side Effect Profile**

Statistically established differences were noted in the occurrence of nausea, vomiting and fatigue between the two groups. Among the major side effect nausea (24%), vomiting (13.7%) and fatigue (50%) were significantly more in oral group.

Duration of Bleeding in Days	Mean	SD	't' Value	P Value
Group I	9.38	2.5	3.49	< 0.000 S
Group II	8.2	1.87		

Table V. Mean duration of Bleeding**Table V Mean duration of Bleeding**

Mean duration of bleeding was significantly less in Group II compare Group I (P=0.000). Mean Hb drop was not clinically significant between two groups. The average duration of bleeding was 9.37 ± 2.5 days with oral group and 8.28 ± 1.8 in vaginal group which was similar other studies.^{3,4}

Acceptance	Group I		Group II		χ^2	P Value
	No.	%	No.	%		
Satisfied	94	92.2	86	85.1	2.4	> 0.05
Will use the same method	92	90.2	86	85.1	1.2	
Will suggest to friends	92	90.2	86	85.1	1.2	

Table VI. Distribution according to Level of Acceptance**Table VI. Distribution According to Level of Acceptance**

Method satisfaction was more among oral group 92.2% compared to 85% vaginal. Acceptance is further reflected by the fact that 90% of oral group and 85% in vaginal group were willing to accept to the method again and if needed the same % would suggest it to their friends.

DISCUSSION

In our study mean age was 26.2 which is comparable to other studies.^{6,7} There was no association of complete abortion rate with gestational age or parity. In a WHO Multi national study of 2219 women with gestational age < 63 days parity

had induction abortion interval ≤ 4 hours compared to 90% in vaginal group. Factors affecting induction abortion interval was studied. There was no statistically significant association with age, parity and gestational age. In both groups those with a history of previous abortion had a failure rate of 33.3% (P=0.000 and P=0.007 respectively in oral and vaginal groups)

significantly affected the percentage of complete abortion³. Complete abortion was 91.1% for Group I oral and 92% for Group II vaginal (P=0.816) showing both routes were equally effective. Similar efficacy in oral and vaginal routes were noted in studies by Peyron et al⁹ and Nitya et al⁶. Schaff et al in randomized trial have found the complete abortion with oral group to be 95% as against 99% in the vaginal groups.¹⁰ The mean induction abortion interval was 4.29 hours for oral group and 3.5 hours for vaginal groups. 78.4% in oral group had induction abortion interval ≤ 4 hours compared to 90% in vaginal group which is comparable to the study by el Refaey et al⁴. Shorter induction abortion interval in vaginal group may be because of the long lasting and continuously increasing uterine contractility of vaginal misoprostol.¹¹ In both groups those with a history of previous abortion had a failure rate of 33.3% (P=0.000 and P=0.007 respectively in oral and vaginal groups). Premila et al in a study of factors affecting outcome of early medical abortion with review of 4132 consecutive cases of have found out that those who had a previous abortion were more likely to have a failed medical abortion (OR = 2.09)⁸. The average duration of bleeding was 9.37 ± 2.5 days with oral group and 8.28 ± 1.8 in vaginal group. This was similar to studies by el Refaey et al⁴. WHO studies showed 11-12 days bleeding³. Among the major side effect nausea (24%), vomiting (13.7%) and fatigue (50%) were significantly more in oral group. Studies by Schaff et al¹⁰ and el-Refay⁴ also showed increased vomiting in oral group compared to vaginal. The latter study⁴ also note fatigue as a major side effects in both groups (67% in oral and 70% in vaginal). There were no major adverse events in this study as in others studies.^{4,9}

Method satisfaction was more among oral group 92.2% compared to 85% vaginal. Acceptance is further reflected by the fact that 90% of oral group and 85% in vaginal group were willing to accept to the method again and if needed the same % would suggest it to their friends. Similar acceptability rates were seen in studies by Schaff et al¹⁰ whereas Winikoff et al¹² evaluated acceptability of Mifepristone and Misoprostol regimen and found that it was highly acceptable and 96% would recommend it to others and 91% would choose it again.

CONCLUSION

It is evident from the present study that both oral and vaginal routes of misoprostol had similar efficacy in early pregnancy termination up to 49 days. Medical abortion can be safely propagated and can replace surgical abortion in the coming years in view of its efficacy and acceptability as shown in the present study. Moreover, women can exercise their choice of the method which will ensure the acceptability and thus decreasing unsafe abortions and related morbidity.

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