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Original Article

Comparison of different regimes of misoprostol for the termination of early pregnancy failure

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ABSTRACT

Background: Nearly 20% of all confirmed pregnancies end in spontaneous abortion. Misoprostol's use in early pregnancy failure is varied and dose and route are not well established. The aim of this study was to compare the efficacy and the side effects of different regimes of misoprostol in causing expulsion of products of conception in early pregnancy failure.

Method: Women patients with an ultrasound diagnosis of early pregnancy failure, less than 12 weeks gestation were divided into two, Group-A: tab. Misoprostol 800 mcg 6 hourly vaginally, upto 3 doses. Group-B tablet misoprostol 600 mcg 6 hourly, sublingually for 3 doses. All observations were noted and statistical analyzed.

Results: Mean gestational age was 7.93 weeks. Mean induction abortion interval 18.183 h. Women patients with less than six weeks gestational age had least mean induction-abortion interval time, 15.75 ± 2.82 h in vaginal group but was highest in sublingual group 22 ± 2 h and 18.43 h in overall ($P = 0.02$). Though after 8 weeks, both routes were equally effective. Mean dose required in group-A was 20044 mcg and in group-B was 1564 mcg ($P < 0.001$). Efficacy of protocol was 88.89% in group-A and 92.85% in group-B.

Conclusion: Both regimes had comparable efficacy, acceptability (90%) and side effects. In women patients less than six weeks period of gestation, the vaginal (800 mcg) route was distinctly superior, in women patients with 6–8 weeks the sublingual (600 mcg) route was more advantageous. The correct dose must be used for the route chosen. The route of administration should be decided in accordance with the preference of the patient and the clinical situation.

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Introduction

Early pregnancy failure is common and represents a significant gynecological emergency workload. Nearly 20% of all confirmed pregnancies end in spontaneous abortion.[1] The conventional method of uterus evacuation by vacuum aspiration is associated with morbidity and mortality. The use of prostaglandins PGE2 vaginally had replaced the surgical methods due to their ease of administration, high effectiveness and fewer complication.[2] However, the high expense of the medicine and instability in room temperature were barriers to their use in developing countries. Misoprostol – a synthetic prostaglandin E_1 analog, is cheap, stable at room temperature and effective in inducing cervical ripening and uterine contractions.[3] However, the regimes for its use in early pregnancy failure are varied and not well established. Earlier clinical trials had shown vaginal misoprostol to be superior. Misoprostol given vaginally though took longer for onset and had a lower peak (peak concentration after 60 minuet it had a more sustained effect as compared to oral misoprostol). Thus, smaller doses were needed when misoprostol was used vaginally. Pharmacokinetics now shows that sublingual misoprostol has the shortest onset of action, the highest peak concentration and greatest bioavailability among the routes of administration.[4] As the bioavailability varies with each route, the correct dose must be used for the route chosen e.g. sublingual to oral or vaginal and route should not be changed without checking the dose. The aim of this study was to compare the efficacy and the side effects of different regimes of misoprostol in causing the complete expulsion of products of conception in early pregnancy failure.

Material and methods

This was a comparative; hospital based prospective study conducted from April 2012 to May 2013. Women patients with an ultrasound diagnosis of early pregnancy failure, singleton pregnancy, less than 12 weeks gestation, who had not experienced uterine cramping, no active bleeding (os closed on per vaginal examination) and were in a normal frame of mind to give consent and willing for a surgical evacuation in case of failure with medication or active bleeding, were included in the study.

The USG criteria used for diagnosis of early pregnancy failure (missed abortion) were-embryo with CRL greater than 7 mm with no cardiac activity or irregular gestational sac with mean sac diameter greater than 16 mm or a gestational sac more than 25 mm with no visible fetal pole.[5]

Sample size was calculated at 80% study power and alpha error of 0.05 assuming standard deviation for duration of induction to abortion interval of 5 h and minimum difference to be detected of 2 h. Thus sample size came to be 50 patients in each group which was enhanced 55 assuming 10% dropout rate.

Group allocation after counseling and informed written consent, the women patients were divided into two groups using coin tossing method and allocated for treatment with either regimes.

Group-A: In this group women patients were given vaginal – tablet misoprostol 800 mcg every 6 hourly upto 3 doses.

Group-B: In this group women patients were given sublingual-tablet misoprostol 600 mcg every 6 hourly for 3 doses. The dose was decreased to lessen the side effects.

Evaluation was done 6 h after 3rd dose of misoprostol, i.e. at 24 h. If the uterus was not felt empty on per vaginal examination and ultrasonography showed products of conception, then dilatation and evacuation was done and was considered a true drug failure.

Data analysis and processing: Collected data was entered into a computer using Epi Info Version 2000 and analyzed using Medcalc 14.0.0 version and Microsoft excel. Continuous data was presented as mean and standard deviation while non-continuous data was categorized and the percentage of each category was calculated. Chi-square was used to test for association. A P value less or equal to 0.05 was considered indicative of a significant factor effect.

Results

The mean age of women patients in the study was 24.18 ± 5.1 years. Majority of the women patients were educated up to primary level or less and 80% were from urban background. Due to the use of misoprostol at PHC and CHC, referrals to tertiary care center like ours for early pregnancy failure have decreased. 90% of the cases in both the groups belonged to middle and lower middle class Table 1.

71.81% women patients came with complaints of bleeding per vaginum. 28.18% women patients had come for routine checkup and USG had shown missed abortion. 9.09% women patients came with pain abdomen and 3.64% women patients came with brownish discharge. 79.09% of the women patients had fetal pole absent or irregular gestational sac in the ultrasonographic findings. The other finding was a blighted ovum seen 20.91%.

Mean gestational age was 7.93 ± 1.2 weeks. Mean induction abortion interval was similar in the two groups, 18.125 h in group-A and 18.241 h in group-B. Women patients with less than six weeks gestational age in group-A, had least mean

Table 1 – Maternal and gestational characteristics of the study population.

Variables	800 mcg	600 mcg
Maternal age (years)	24.57 (±5.1)	23.79 (±5.2)
Literacy primary or less	27 (49.99%)	27 (49.08%)
Primigravida	19 (35.18%)	21 (37.5%)
1 previous vaginal deliveries	24 (44.44%)	24 (42.86%)
2 or more previous vaginal deliveries	11 (20.38%)	11 (19.64%)
Presenting complaint – bleeding P/V	38 (70.37%)	41 (73.21%)
Gestational age (weeks)	7.905 (±1.2)	7.946 (±1.3)
Anembryonic sac	10 (18.52%)	13 (20.91%)

Maternal age and gestational age are expressed as the mean (SD). All other parameters are shown as number (percentages). No significant differences were observed between the two groups.