Original Article

Efficacy and safety of misoprostol in missed miscarriage in terms of blood loss

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Objectives: To determine the efficacy and safety of misoprostol in missed miscarriage

Methodology: This descriptive study was were conducted at Department of Obstetrics and Gynecology, MCH Centre, Unit I, Pakistan Institute of Medical Sciences, Islamabad, Pakistan from July 2010 to June 2011. Seventy women of missed miscarriage were recruited from 19-45 years age group. First dose of misoprostol 800µg was given vaginally in OPD and patients were followed on 3rd and 8th day to see complete evacuation. Second dose of 800µg misoprostol was given on 3rd day, if needed. Hemoglobin (Hb) was checked on 1st and 8th day. Patients who had fall in Hb of more than 2 gm from base line were labeled as group in which drug was unsafe.

Results: Mean age of the study population was 28.00±5.001 year. Majority (45.7%) were from 26-30 years age group. Efficacy rate was 68.6% (n=48), while 31.4% (n=22) had to undergo surgical evacuation. Surgical intervention was needed in 17.6% of primi-gravid patients as compared to 35.9% of multi-gravid patients ($p<0.05$). Misoprostol was safe in 61 (87.1%) patients, while remaining 9 patients showed Hb level fall more than 2 g/dl. Only two patients needed blood transfusion.

Conclusion: Although the study duration was short and number of patients was small, yet the results show high efficacy and safety of misoprostol in cases of missed miscarriage. (Rawal Med J 2014;39:314-318).

Key words: Misoprostol, missed abortion, vaginal bleeding.

INTRODUCTION

Although the gold standard treatment of missed miscarriage is surgical uterine evacuation, its relative cost and need for operation theater with special equipment and anesthesia training is a problem in low resource countries like Pakistan. Misoprostol is now emerging as low cost method for treatment of miscarriage, in areas where mifepristone is unavailable, and has an effect on reducing the demand of beds, staff and wards. Training of manual vacuum aspiration (MVA) is time-consuming and costly at all the provincial and rural levels; more over providers face difficulty of maintaining an adequate stock of MVA equipment and supplies. That's why dilatation and curettage, with its higher rate of complications in untrained hands, continues to be practiced. Misoprostol might improve post-abortion care when resources are limited and surgical treatment is unavailable.

Petersen et al obtained 78% efficacy by using misoprostol on OPD basis and failed medical treatment at least results in cervical ripening and thus helped in subsequent surgical evacuation. Expectant management is successful in 65% patient within 2 to 6 weeks but problem is its long and tiring effect and high failure rate and risk of high unplanned admission rate. Adverse effect of misoprostol is heavier and prolonged vaginal bleeding. The decrease in Hb was more frequent in women who were treated with misoprostol than who received surgical evacuation, ye. Other minor side effects are diarrhea, nausea, vomiting and shivering, which are much less often seen if drug route is given through vaginal route. Zwierzchowska et al reported efficacy rate of misoprostol as 88% with 800ug by day 2 and heavy bleeding requiring hospitalization was rare, thus rendering misoprostol as effective and safe treatment of missed miscarriage. Aim of this study was to determine the success of misoprostol in patients with missed miscarriage when it is used on OPD basis and to evaluate its safety in terms of blood loss.

METHODOLOGY

This descriptive study was performed at Department of Obstetrics and Gynecology, MCH Centre, Pakistan Institute of Medical Sciences, Islamabad, Pakistan on OPD basis for one year starting from July 2010 to June 2011 on 70 patients diagnosed as missed miscarriage. Gestational age taken was up to 13 weeks. Patients with multiple pregnancy, heavy bleeding, sepsis, and anemia were excluded from study. Clotting factors were checked in all patients to rule out clotting problems. Liver functions were checked only on basis of history and patients with liver dysfunctions were excluded from the study. Informed consent was taken from all patients. Patient age, gravidity, parity, previous history of abortions, gestational age, base line Hb level, hospital number and contact number were recorded.

All patients received first dose misoprostol 800µg, in form of 4 tablets of 200µg each, into posterior fornix of vagina. They were observed for one hour in day care area for any immediate side effect or hypersensitivity reaction before sending home. Patients who suffered from heavy bleeding or any symptomatic bleeding were advised to report in hospital emergency. All study patients were advised to take oral NSAIDs to relieve pain, if needed. Antibiotics were not prescribed to any patient. Fever and shivering, which are common side effect of drug were explained to them and they were prescribed 1gm paracetamol tablet, as per need. All patients were followed in OPD on 3rd day and evaluated clinically and ultrasonographically for any retained product of conception (RPOC).

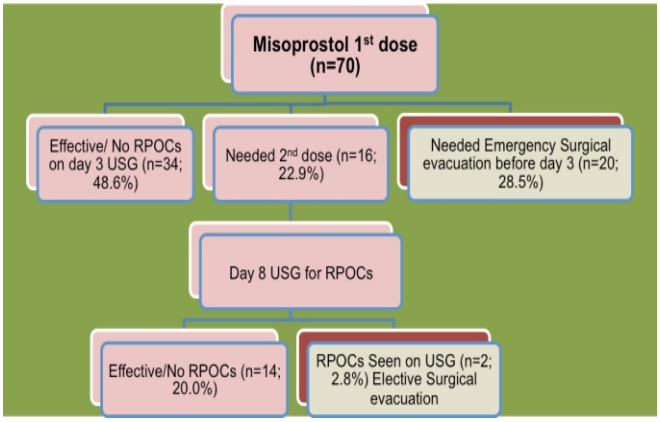
Patients who still showed RPOC were given repeat dose of 800µg misoprostol and sent home, again with the similar advice. All patients were again seen in OPD on 8th day for clinical examination and ultrasound for RPOC. If RPOC were present then, they were underwent surgical evacuation on that day or next morning on elective list. Patients who presented in emergency for heavy bleeding underwent surgical evacuation on that day, irrespective of their day of treatment. Hemoglobin of all patients was repeated on 8th day to see any fall from base line.

All data were entered into SPSS version 10 for statistical analysis. Frequencies and percentages were calculated for categorical data like efficacy and safety rate of misoprostol, gravidity of patients, need for surgical evacuation, first dose or second dose response, effect of previous abortion on efficacy and safety, effect of gestational age on efficacy and safety of misoprostol.

RESULTS

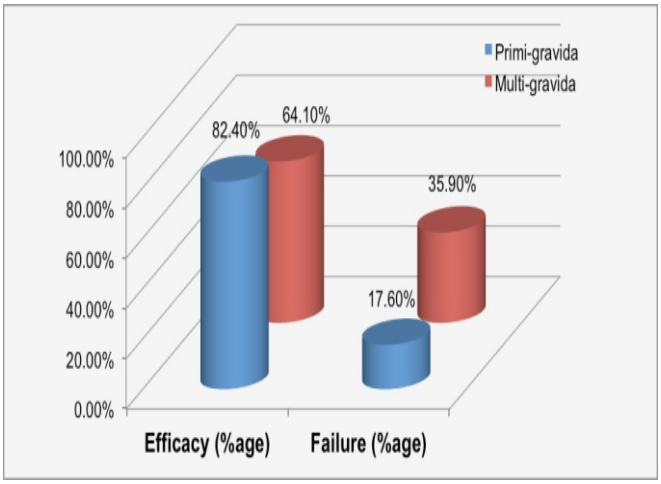
Mean age of the study population was 28 years. Majority (71.4%) was between 21 to 30 years age. Out of 70 patients, 75.7% (n=53) were multi-gravida. Mean gestational age at presentation was 11.10±1.704 weeks. Study protocol is shown in Fig. 1.

Fig. 1. Schema of study protocol.



Misoprostol was successful in 34 patients with first dose and 14 with second dose (overall success rate 48/70; 68.6%). Remaining 22 patients (31.4%) needed surgical evacuation. Effect of gravidity of patient was significant, as there were only 3 failure (17.6%) out of total 17 primi-gravid patients and 19 failures (35.9%) out of total 53 multi-gravid ones ($p<0.05$). Average duration of complete evacuation or emergency surgical evacuation for RPOCs after 1st dose was 2.35 days (2.04). Only 2 patients went up to 8 days; both underwent elective surgical evacuation. Collectively, misoprostol was effective in 68.6% (n=48) patients and non-effective in 31.4% (n=22). First dose affectivity was more pronounced (48.6%) as compared to 2nd dose (20.0%) (Fig. 2).

Fig. 2. Efficacy of misoprostol.



No significant effect of number of previous abortions was noted on efficacy of misoprostol and no significant effect of gestational age was noted on its efficacy (p>0.05). Mean of the base line Hb at presentation was 11.71±1.257 gm. Fall in Hb from baseline is shown in Table 1.

Table 1. Fall of hemoglobin.

	Base line Hb (g %)	Day 8 Hb (g %)	Drop in Hb (g %)
Minimum	9	6	0
Maximum	14.3	14	4
Mean	11.71	10.61	1.11

Safety of misoprostol was established in 87.1% (n=61). However, for 12.9% (n=9) patients it was not safe. Statistical analysis revealed that parity has no effect on safety profile of misoprostol. Likewise, gestational age has also no effect on misoprostol safety. Regarding safety of misoprostol, it was noted that two patients (2.8%) developed shock with fall of Hb more than 4 g/dl at day 8, rendering the results towards failure; these required blood transfusion. While, in 38 patients (54.2%) drug was safe because fall of hemoglobin was less than 1 g/dl. Also, the drug was safe in another 23 patients (32.8%) where the drop was not more than 2 g/dl.

DISCUSSION

More than 600 studies have been published on the use of misoprostol in obstetrics and gynecology that have involved well over 90,000 women.[9,10] Success rate of Misoprostol in case of missed miscarriage in our study was 68.6%, which is comparable to some studies. However, success rate was markedly low as compared to 84.1% by Wagaraachchi et al.[9] and 77.3% by Shankar et al.[10] It was probably because of inconsistent inclusion criteria, different dosing regimens and varying definitions of failed treatment. One very important reason for different results was that most of the studies showing more than 90% success rate of misoprostol did their research on incomplete miscarriage patients whereas, we conducted our study only on missed miscarriage cases.

We used the Misoprostol per-vaginum because most studies have shown that the vaginal route of administration is more effective and gives a higher complete miscarriage rate.[9] Self-reported heavy bleeding and an open cervical os on day 3 were two potential factors and useful indicators of treatment success after first dose of misoprostol. Nonetheless, a higher predictive value would be more desirable. Second, the short interval between the treatment and the follow-up visit could make prediction difficult. For instance, an open cervical os could indicate that the uterus has responded to the misoprostol treatment. It would also indicate that the expulsion may not be complete, or is in the process of occurring, or has just been completed. Data suggests that on day 3, an open os is more likely to be indicative of a positive uterine response and expulsion may have just been completed. However, this indicator may not be applicable for later dates.

In most studies, women go home after completing the misoprostol protocol even if products have not been passed and have been reassessed at 7-14 days. This assessment strategy increases the success rate of medical management considerably. Indeed, there is a crude correlation between success rate in various trials and time of assessment. The point to ponder for doctors offering medical management of first trimester miscarriage is that it is important to delay the clinical assessment of "failure" for at least seven days to prevent unnecessary surgical intervention.

Women with any previous pregnancy, especially term pregnancies whether ended by cesarean section or spontaneous delivery, are more likely to

require surgical intervention compared to primigravid women. Our study also showed the same results and is in agreement with several previously published reports.[7] However, some reports did not find any correlation between parity and the need for surgical intervention.

Miscarriage contributes disproportionately to maternal morbidity and mortality in much of the developing world. Hemoglobin fall was used in our study as measure for estimated blood loss and safety of drug which is practical but not very reliable method for this purpose. Misoprostol was found to be safe in 87.1% patient, as it is found in study where no patient needed blood transfusion. In Mexico City and Uganda, shifting from a practice of hospital-based D&C to clinic-based MVA and enhancing access to medical abortion had the best chance to minimize miscarriage-related morbidity and mortality.[7] The ideal medical regimen of management of miscarriage would be one that can be finished within a short and defined period of time. The clinically acceptable success rate should be around 90%. This is especially true for the management of miscarriage since expectant management may already result in a success rate of up to 50%.

CONCLUSION

Misoprostol was an effective and safe alternative to surgical choice, for treatment of missed miscarriage in patients especially where OPD treatment is opted.

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