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Safety, Efficacy and Acceptability of Oral misoprostol in the Management of Incomplete Abortion:–A Prospective Observational Study

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Abstract: To investigate the safety, efficacy, and acceptability of oral misoprostol of different doses for treatment of incomplete abortion according to the uterine size. A prospective observational study. Chittagong Medical College Hospital, Surgiscope Hospital Private Limited,Adhunik Hospital Private limited. March 2015-July 2017. Two hundred ten women with a clinical diagnosis ofincomplete abortion and a uterine size <14 weeks. A total of 210 women were randomized selected for the study, after clinical examination and proper counseling due to excessive bleeding (32patient) and 23 patient were disagreedue to other reasons to take the misoprostol, so 55 patient were excluded from the study and then 155 patient wererecruited for this study takeeither a singledose of 600 micrograms of oral misoprostol or multiple dose of misoprostol 600microgram 3 hourly for three times in a single day. After clinical diagnosisof incomplete abortion either spontaneous or induced, was confirmed by ultrasonography. single dose regimen were adopted when uterine height was less than 10 weeks and multiple dose were adopted when uterine height were within 10 -14 weeks. All the patient were treated as outdoor patient with oral antibiotic for 7 days, clinically assessed for completion and some need ultrasonography at 7-day follow up. If it was still incomplete, very minute amount of product of conception, then woman was offered for expectant management with oral contraceptives pill. During next period it was completely flushed out. Most of the time it was confirmed by ultrasonography of an additional 1-month follows up. Success rate was very high in both arms: single dose of misoprostol is 82.85% and failure rate -17.14%, in multiple dose success rate is 82.70%, and failure rate is 15.29%. Difference arenot so significant in both dose schedule. Most adverse effects were pain, although the mean pain score was almost same. Another complication was also observed that 22.31 % patient were suffering from slight irregular per vaginal bleeding since complete evacuation.All the womenwere very satisfied with misoprostol either of the dose and a higher proportion of women in the misoprostol treatment said that they would recommend the treatment to a friend (85% versus 70%, $P < 0.001$). Misoprostol is an effective drug for the treatment of incomplete abortion at uterine size of <14 weeks. The acceptabilityof misoprostol appears higher. There are so many practicaladvantages of misoprostol in low-resource settings like Bangladesh misoprostol should be more widely available for treatment ofincomplete abortion in the developing country.

Keywords: Incomplete abortion, misoprostol.

INTRODUCTION

Incomplete abortion isa common eventsin women of reproductive age with an incidence of 10-20%. Traditionally surgical evacuation of uterus was the gold standard for the management of incomplete abortion [1]. Now a days medical management is the revolution in the field of incomplete abortion, using a suitable dose of prostaglandin analogue -is a safe and effective alternative with high efficacy and patients acceptability [2]. Whatever the type of abortion is either spontaneous or induced every women seek care at health facilities. Not surprisingly, that these women make up a major part of the obstetric morbidity and mortality[3]so safe, effective,acceptable, and affordable means of treating incompleteabortion is therefore a priority, especially inlow-resource settings.Until

recently, the treatment for incomplete abortion hasusually been surgery of some kind- evacuation and curettage ,dilatation and curettage, and manual vacuum aspiration (MVA). Though these treatments are effective, they require specialised equipmentand skills. Furthermore, the woman are prone to more dangers on a surgical procedure[4]trauma, perforations,infections, bleeding due to instrumentation, and hazards of anaesthesia, even then some women also lost their uterus in their early life for complication of surgical procedure. For surgical intervention patient need hospital admission and it will more costly than medical treatment, for these reasons, determiningan effective nonsurgical approach for the treatment of incomplete abortion is the priority of choice. Many studieshave indicated that the uterotonic andcervical ripening properties of the prostaglandin E1 analogue-misoprostol make it a safe and highly effective method ofevacuating the uterus in cases of incomplete abortion [5]. Allresearch on misoprostol for this indication to date, however, has taken place either in developed or middle-income countriesor of developing countries.Misoprostol is a prostaglandin E-1analogue that has a low cost and longer life stability at room temperature could make it an ideal treatmentin low-resource settings, as well as lower education community, should it prove safe andeffective in such locales [6]. The present study was designed to fillan important relationship in the research by testing misoprostol forincomplete abortion at different hospital with an urban and ruralcatchment area in a low-income country.This study evaluate the safety efficacy of the regimen of misoprostol in the treatment of incomplete abortion.The 600 micrograms dose and oral route of misoprostoladministration were chosen on the basis of two earlier dosefindingstudies conducted in Thailand and Vietnam. Anda further recent large study in Kampala, Uganda which achieved the highest success rates by using 600 microgram 3 hourly for three times.While somestudies of misoprostol for incomplete abortion have employedthe vaginal route of administration [7], the majority ofsuch studies have employed the oral route [7-9]. Furthermore, there are women who find vaginal administrationmore invasive and less acceptable than oral use, and thereis an unconfirmed possibility that this route may be associatedwith greater rates of infection.[10] Given that the studies citedabove suggest that excellent results can be achieved with oraladministration as well, we chose to employ this route here.This study evaluate the safety efficacy of the regimen of different dose of misoprostol in the treatment of incomplete abortion.

MATERIALS AND METHODS

This was an open randomily selected study to compare the efficacy, safety, and acceptability of different doses of oral misoprostol for treatment of incomplete abortion. A total of 210 women in the in different hospital in Chittagong city who werediagnosed with incomplete abortion between the study period March 2015-July 2017.out of these 210 patient 55 patient was excluded for excessive bleeding and anxiety and refuse to take medical management so 155 patient were finally recruitedfor our study protocol.Women with missed abortion at or below 14 weeks gestation confirmed by history clinical examination and ultrasonography were proposed the regimen for misoprostol if they were hamodynamically stable.

Inclusion criteria

An eligible incomplete abortion was suitable for this study when all of the following criteriawere met:

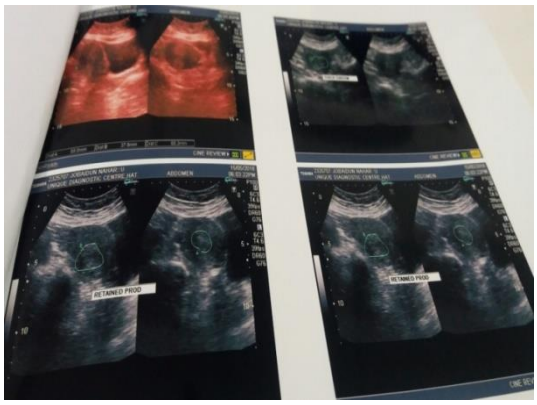
- Past or present history of bleeding during this pregnancy.
- Cervical os open by visual/digital inspection.
- Uterine size of not greater than 14 weeks by bimannual examination and ultrasonography of lower abdomen.
- Woman in generally in haemodynamicallystable .
- Woman willing to return for follow up.

Exclusion criteria

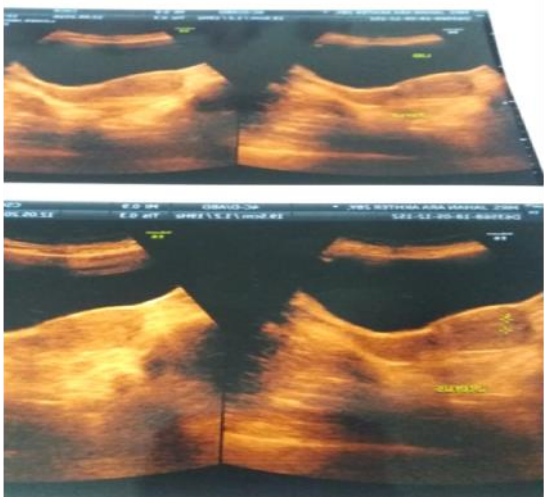
Women were excluded if they had active pervaginal bleeding, haemodynamicaly unstable, known case of bronchial asthma, cardiac diseases signs of severe infection(foul-smelling discharge, fever > 39^0C, or pulse > 110/minute)or a known allergy to misoprostol.

Women who met the above requirements were randomly assigned to one of the two study regimens according o their uterine size. Single dose regimen (600microgram) were selected upto 10 weeks of uterine height, and another regimen- 600 microgram 3 hourly for 3 times in a single day where uterine height upto 14 weeks. Either of the regimen prophylactic antibiotics was given for 7 days.Each women was advised to return to the hospital 7 daysafter treatment. If the abortion was found to be complete clinically and bimannual examination showed height of the uterus was smaller than the initial size with closed cervix and with or without slight vaginal bleeding. All the patient were advised for routine ultrasonography for determination of treatment success,

Ultrasonography findings



A. Before Evacuation



B. After Evacuation

Complete expulsion was defined as an absence of intrauterine echogenic structures measuring less than 15 mm in antero posterior diameter, incomplete expulsion was definedas open cervical os with associated bleeding found on bimannual examination following passess of mass per vagina or presence of intrauterine echogenic structure measuring more than 15 mm in antero posterior diameterin ultrasound. Failed expulsion was defined as no passess of any product of conception per vagina within 24 hours of strating of treatment.If the abortion was still incomplete; the woman was offered thechoice between an additional follow-up visit in 1 week withno further intervention during this period or immediate surgicalevacuation. If after the additional week of follow up theabortion was still not complete, the woman underwent MVA and take as a failure case. The primary outcome was the achievement of completeuterine evacuation after initial treatment (either of the selected doses of misoprostol).

The incidence of adverse effects from the treatmentswas assessed by observation after administration ofmisoprostol by interviewing of the women wereasked to report on the adverse effects they had experienced- pain, nausea, vomiting,diarrhea, hyperthermia and vaginal bleeding was assessed.The presenceof infection at follow up was assessed clinically.This study was originally conceived as a feasible study foremploying an approach to uterine evacuation which hadproved successful in a major urban area in Chittagong and a periurban area. As such, the sample size of 155 women, 75 and 80 patient in each study arm, was meant to ensure a sufficientnumber of participants to allow the benefits and drawbacksand the adverse effect of the approach to present themselves fully.After complete evacuation al the patient were advised for oral contraceptives pill and ask for a follow up visit after one month.

RESULTS

Overall, between these two years of study period, 155 women were randomly selected into the two different schedule of misoprostol dose. A significantlylarger percentage of women in the misoprostolgroup were (85versus 70%; P value= 0.006) and hadspontaneous rather than induced abortions.

Datawere analysed using SPSS statistical software and descriptively. Count and percentage were calculated for categorical variables and mean ±SD for quantitative variables .Chi-square tests was used for categoricaldata, and t tests were used for continuous data. The mainanalysis of the data included success rates defined as thepercentage of women receiving each regimen who experienceda complete abortion without recourse to additional intervention, frequency of particular adverse effects, andacceptability.

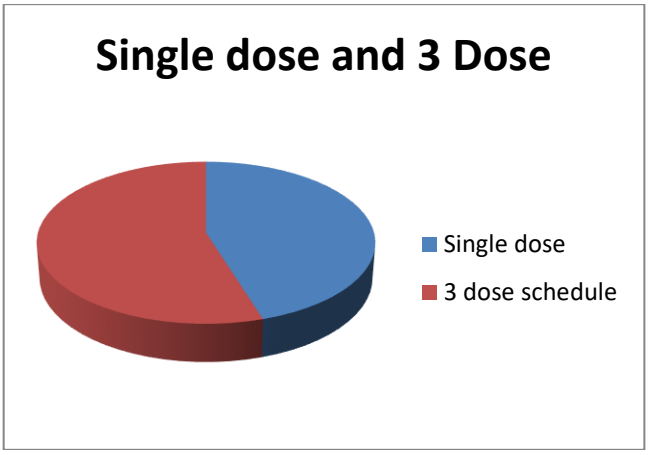


Fig-1: Dose schedule of misoprostol

Figure shows that 70(45.16%) women were for single dose regimen who have less than 10 weeks of uterine size and 85 (54.83%) were for three dose schedule those who have uterine size10-14 weeks.

Table-I

Dose	Success	Percentage	Failure	Percentage
Single dose n=70	58	82.85	12	17.14
Three dose n=85	72	82.70	13	15.29

This table shows that in single dose study success rate was 58(82.85%) and failure rate was 12(17.14%). In three dose schedule success rate were 72(82.70%) and failure rate were 13(15.29%).

Table-II: Demographic characteristics of the patient (n= 155)

Age	17- 33 yrs	
Mean age	21.84±5.59	
Education	Number	Percentage (%)
upto SSC	116	74.83
More than SSC	39	25.16
Parity		
Primipara	69	44.51
Para 2-4	57	36.77
Para >4	29	18.70
Mode of abortion		
Spontaneous	114	73.54
Induced	51	32.90

This table shows demographic variables including age, education status, parity, and mode of abortion. In this study mean age was 21.84±5.59%, regarding education level 116 (74.83%) were upto SSC pass and 39 (25.16%) were more than SSC to masters degree holders. About parity –primi patient were 69(36.66%), having para upto 4 were 57(36.77%) and para more than 4 were 29(18.70%). This table also shows the mode of abortion. Here abortion occurs

spontaneously were114 (73.54%) and induced abortion was 51(32.90%).

Table-III: Adverse effect of misprostolol

Side effect	Number of patient	Percentage
Abdominal pain	144	92.90
Vaginal bleeding	127	81.93
Nausea	21	13.54
Vomitting	9	5.8
Diarrhoea	17	10.96
Hypersensitivity reaction	7	4.51

This table shows 144(92.90%) women were experienced abdominal pain, and 127 (81.93%) developed vaginal bleeding but it was little in amount. Nausea was experienced by 21 (13.54%) women, vomiting were experienced by 9 (5.8%) anddiarrhoea were experienced by 17(10.96 %) of women. Seven women were developed hypersensitivity reaction after 3-4 hours of strating the treatments but with prompt management and they recovered quickly.

After 7 days follow up none return with complication and then all women were advised for next follow up visit after one month. All of them resume normal menses 28- 35 days after complete evacuation.

DISCUSSION

Misoprostol, a prostaglandin analogue, is approved by FDA for abortions.However it has been used successfully in the medical treatment of incomplete abortion various trials have been conducted to study its efficacy versus surgical evacuation [11] but in my study we use only misoprostol.

In this study, both dose schedule of oral misoprostol accordind to the uterine size were very effectivein treating the incomplete abortion. Although women in themisoprostol arm of three dose schedule experienced more adverse effects, but they didn't find these adverse effects difficult to tolerate, in comparison with women in the single dose arm, they also experienced lower levels of pain.Kelly Blanchard, surasakTaneepanichrirojana showed two regimen of misoprostol for treatment of incomplete abortion [12]. Our study have similarity with this study, protocol and success rate almost same.Women in the three dosemisoprostol arm experienced a significantly higher success rate like other studies.

Perhaps in consequence, patients' feelings about adverse effects present a mixed picture: while a higher percentage of women in the misoprostol group found that adverse effects were 'easily tolerable' [13]. When women were questioned about satisfaction with their treatment, a clearer picture emerges. Women were significantly more likely to report being 'very satisfied' with misoprostol in either of the dose, and larger proportions of women in informed that they would choose the treatmentagain and would recommend it to a friend.

There have been at least 15 previous studies of misoprostol for treatment of incomplete abortion [12–20]. In comparison with this our study only conducted with different dose of oral misiprostol Of these, however, only two [6,20] were conducted in low-income countries that is similar to our study.Some portion ofboth studies weretook place in the larger tertiaryhospital. This is the first trial of oral misoprostol for the treatment of incomplete abortion at a lower level health facility in a developing country.Its findings generally parallel those of the one previous study conducted in East Africa.[6] In this study, misoprostol was successful in evacuating the uterus in 99% of cases and in our study it is almost 85%. This is an extremely high success rate, but it is not out of line with those previously reported. Ten ofthe 15 earlier studies[6,7,10,13–15,17–20] showed rates of at least90%; two report 100% success, albeit with very low numbersof incomplete abortion cases [13,17]. There is, furthermore, somereason to believe that as practitioners become more familiarwith this method and as the base of experience grows, successrates are improving: while four of the five studies that reportrates lower than 90% were conducted in 2001 or earlier, eight of the ten showing rates of 90% and above took place between2001 and 2005. The two previous studies of this methodconducted in the developing world, which included samplesof 160 and 300 women, report rates of 96 and 95% (weightedaverage), respectively. Together with the current study, thisrecord strongly suggests that misoprostol is an effectivetreatment for incomplete abortion, in both developed anddeveloping countries [14].

Shwekerela *et al.* showed his study some were lost of follow-up, which is unusual in our study, none of the 155 women who participated was lost to follow up. By comparison, in the previous study of misoprostol for incomplete abortion conducted in East Africa [15], one-third of women inthe misoprostol arm did not return for their next scheduledvisit. However, the other similar trials which have been conductedeither in a developing

country20 or in sub-SaharanAfrica [16-18] had lost to follow up. Clearly, it is possible for dedicated staff to ensure maximize their effort.

The fact that this study was conductedin a large city with a transient and relatively anonymouspopulation may have given it an advantage in this respect. The main strength of this study is that, as noted above, it isthe first to be conducted at a lower level health facility Ina developing country. A case could be made that it is in suchfacilities—or in facilities even lower down in the health systemhierarchy, that most cases of incomplete abortion with potentially serious consequences are likely to present. Themain supportive tools of this study are that, as ultrasound was used to diagnose incomplete abortion, the study populationmay have included women with inevitable or even alreadycompleted abortions. While this is true, it is also true thatthe study, as conducted, accurately reflects 'real-world' conditions [19].

It is unlikely that any healthcare facility in a lowincomecountry, particularly one in a smaller city or rural area,is going to have the resources to verify incomplete abortionstatus through ultrasound for all presenting women. In suchcases, a facility is likely to do exactly what was done in thisstudy, that is, presumptively treat all women who appear tohave an incomplete abortion as if they do have one. Thecurrent study shows that, in such real-world circumstances, misoprostol can be as effective an incomplete abortion treatmentwhatever the dose schedule.

This study demonstrates that use of misoprostol for treatingincomplete abortion is effective and feasible at theregional hospital level in Chittagong, Bangladesh. Although other similartrials will need to be conducted to fully establish misoprostol'svalue in such settings, this study strongly suggests that misoprostolmay prove a valuable treatment at secondary healthcarefacilities. Full exploitation of misoprostol for thisindication might make an important impact on reducingmaternal death in rural areas of developing countries.Additionally, the next round of research shouldfocus on the feasibility of treating incomplete abortion withmisoprostol at the subregional level, where MVA is often notavailable and where misoprostol's low cost and ease of storageand use might make it especially valuable[20].

CONCLUSION

Oral misoprostol is a very effective alternative to surgical curettage as treatment of incomplete abortion. It should be employed more often in compliant patients, due to high patient's satisfaction with fewer side effects. So many further studies need to establish that oral route of misoprostol should be more widely used for the treatment of incomplete abortion in the developing country.

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