

Role of Misoprostol for therapeutic termination of pregnancy from 10 -28 weeks of gestation

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Abstract

Objective: To assess efficacy, safety and cost effectiveness of misoprostol (prostaglandin E1 analogue) for termination of pregnancy.

Methods: A descriptive study was conducted from March 2003 to December 2004, at Fauji Foundation Hospital Rawalpindi. A total of 200 patients, at 10-28 weeks of gestation, requiring termination of pregnancy were included. Each woman received first dose of 400µg of misoprostol vaginally. Second dose of 400 µg of misoprostol was administered after 4 hours, according to the cervical dilatation, softening and uterine contractions. Oxytocin infusion was started after six hours of administration of first dose of Misoprostol, depending upon the uterine contractility. The process of abortion was monitored to assess the outcome measures.

Results: Successful abortion was seen in 137 (68%) patients, with induction to delivery interval of 12.2 hours. In 40 (20%) patients surgical evacuation was performed. Out of 40 patients, 27 (13.5%) underwent surgical evacuation due to incomplete abortion and 13 (6.5%) for excessive per-vaginal bleeding. A total of 23 (12%) patients had failure of method for induction of abortion and needed either repeat dose of misoprostol after 24 hours or other methods of induction (besides misoprostol). Side effects included nausea, vomiting, diarrhoea and fever. Mean hospital stay for induction of abortion was 31 hours.

Conclusion: Misoprostol is safe, efficacious and a cost effective drug for induction of the first and the second trimester abortions (JPMA 57:129;2007).

Introduction

Termination of pregnancy for various, maternal as well as foetal conditions, is a common obstetrical problem. Induction of abortion needs meticulous and effective care, as do women in labour with childbirth. The rate of maternal mortality and morbidity increases significantly by surgical methods for termination of pregnancy as compared to medical methods.

The options for first and second trimester cervical ripening and labour induction are numerous and varied.¹ Prostaglandins have emerged as the agents of choice for induction of labour in pregnancies complicated by intra-uterine foetal deaths or gross foetal malformations.² Initially PGF_{2a} was used for induction of abortion.³ In current practice, misoprostol, an orally active, stable prostaglandin (PGE₁) analogue has entered its clinical use in Obstetrics and Gynaecology on a wide scale, though without having been registered for such use. It is a gastric cytoprotective agent that has been marketed in US since 1988 for the prevention of peptic ulcers. Misoprostol is not FDA approved as a pregnancy category drug, however FDA recognizes that in certain circumstances, off label uses of approved product is appropriate, rational and accepted.⁴ According to American College of Obstetricians and Gynaecologists (ACOG), misoprostol has been used too frequently and so effectively that it has become the treatment of choice "for ripening of cervix prior to induction of labour among pregnant women".⁵

Consequently misoprostol has become an important drug in obstetrical practice.⁶ It is useful for elective medical abortions,⁷⁻⁸ cervical priming before surgical abortions^{9,10} and evacuation of the uterus in case of embryonic foetal death.^{11,12}

Therefore, the main objective of this study was to assess the role of prostaglandin E1 analogue (misoprostol), being an efficacious and safe agent, as are other conventional prostaglandins. Moreover high cost of conventional prostaglandins still remains an important factor in poor resource settings.

Subjects and Methods

This study was conducted at Fauji Foundation Hospital, Rawalpindi from March 2003 to December 2004. A total of 200 patients, having had medical indications for termination of pregnancy were included. Inclusion Criteria were, patients with medical indications for therapeutic abortions (un-controlled hypertension, diabetes mellitus, cardiac diseases and renal diseases), patients with obstetrical indications (severe oligohydramnios and anhydramnios), and patients with foetal indications (structural foetal anomalies, genetic disorders and chromosomal anomalies).

The exclusion criteria were patients hypersensitive to prostaglandins having bleeding disorders and patients with uterine malformation like bicornuate uterus or uterus didelphys.

Patients, fulfilling the criteria were admitted in the labour ward of the hospital. Complete history was taken and physical examination was performed. Ultrasonographic examination was conducted to confirm the gestational age of the foetus, placental localization and uterine abnormalities. The study was approved by, the Institutional Ethics Committee of the hospital. After taking informed consent of the patients, 400µg of misoprostol was administered vaginally, followed by second dose of 400ug of misoprostol after 4 hours, according to cervical softening, dilatation and uterine contractions. Oxytocin infusion was started after 6 hours of first dose administration, at a rate of 2 mIU/min with increments of 1mIU/min after every 30 minutes, to a maximum of 8 mIU/min. Vigilant monitoring of the process of abortion was done to avoid any complications.

The primary outcome measure was the mean time interval from induction to abortion. Other outcome variables included, need for surgical evacuation and successful abortion rate. Successful abortion rate was defined as complete abortion within 24 hours of initiation of induction of abortion. Surgical evacuation was needed in patients who had incomplete expulsion of products of conception or excessive bleeding with retained products of conception in the uterus, threatening the life of patient. Surgical evacuation was performed under conscious sedation.

If expulsion was deemed to be complete on clinical grounds, no further intervention was undertaken and 10 IU of oxytocin was administered, intravenously. Patients, who had complete abortion and did not exhibit any kind of complications, were discharged after 24 hours.

The failure of method was declared if no cervical change was found after 24hours of first dose of misoprostol administration. Then according to clinical scenario, either another repeat dose of 400 µg of misoprostol was repeated next day or PGF2a was administered extra-amniotically. In women, who had previous two or three lower uterine segment scars, if induction of abortion failed, hysterotomy was performed.

Complications included, pyrexia, nausea, vomiting, diarrhoea and excessive vaginal bleeding. Pyrexia was defined as temperature of >38.2°C or 100.4°F. Excessive per vaginal bleeding was evident by symptoms and signs of hypovolaemic shock. Uterine rupture was diagnosed on clinical grounds.

Results

A total of 24 (12%) patients were primipara, 113

(56.5%) had parity of 2-4 and 63 (31.5%) were grand-multiparous.

A total of 196 (98%) patients had singleton pregnancy and 4 (2%) had twin pregnancy. Out of 200 patients, 181(90.5%) had no uterine scar prior to induction, 9 (4.5%) had previous one lower segment caesarean section (LSCS), 8 (4.0%) had previous 2 LSCS and 2 (1%) patients had previous 3 LSCS.

Termination of pregnancy was required by 115 (57.5%) women due to missed abortion, 5 (2.5%) for blighted ovum, 8 (4%) for chorio-amnionitis after septic induced abortion, 14 (7%) due to medical disorders and 46 (23%) women had structural foetal anomalies. Ten (5%) patients were diagnosed as having foetuses with thalassaemia major (on chorionic villus sampling) and 2 (1%) patients due to intake of teratogenic and chemotherapeutic agents.

Mean gestational age for induction of abortion was 17.14 weeks. In 101(50.50%) cases, maximum dose of misoprostol required, was 800µg with 88 (44%) requiring 400µg and (5.5%) patients needed 1200µg.

Out of 200 patients, 163 (81.5%) were given oxytocin infusion for induction of abortion, whereas 37 (18.5%) did not need augmentation.

Induction to abortion interval in our study was 12.23 hours. Successful abortion rate was 68%. In 40 (20%) patients surgical evacuation was performed. Of these, 27 (13.5%) had incomplete abortion and 13 (6.5%) excessive per-vaginal bleeding, threatening the life of the patient. Failure of induction of abortion was encountered in 23 (12%) cases who needed either repeat dose of misoprostol after 24 hours or other methods after 24 hours.

During the study, two patients had to undergo hysterotomy due to failure of induction with misoprostol. They had two or more uterine scars previously, due to lower segment Caesarean section. One woman had uterine rupture with previous two lower uterine scars due to caesarean section before termination of pregnancy with misoprostol. None of the patients died due to any complications. Minor complications like vomiting and fever were found in 7 (3.5%) and 6 (3%) patients respectively. Thirteen (6.5%) patients had excessive per-vaginal bleeding during induction of abortion and needed immediate surgical interventions. Pain during vaginal administration of misoprostol was complained by 58 (29%) women. The average hospital stay for induction of abortion was 31 hours.

Discussion

Induction of abortion presents a significant problem, especially in mid-trimester as well as, in patients with an unfavourable cervix. The development of standardized commercially available prostaglandins has improved management, but cost of prostaglandins varies from one preparation to another. Therefore the identification of the most effective pre-induction agent is of great clinical importance in this era of cost containment.

Misoprostol used in this study was found to be efficacious. Moreover it is stable at room temperature and cheaper than other expensive conventional prostaglandins. Only few side effects of misoprostol were observed in our cases.

In this study the successful abortion rate was 68%. This figure is higher as reported earlier on by Munthali¹³ who reported a success rate of 83.6% with misoprostol, when compared with PGF_{2a}, for induction of abortion. Herobotya¹⁴ experienced complete abortion rates of 77.6% with 600ug dose of misoprostol and 72.4% with 800ug of misoprostol for second trimester termination. The success rate of 72-77% is comparable with 68.5% of this study.

In 2003, a group of experts met to develop consensus recommendation on dosage of misoprostol use.¹⁵ A dose of 800ug of misoprostol was used vaginally every 24 hours upto 2 doses, showing efficacy of 85-90%. A dose of 800ug of misoprostol was used vaginally, by Jain JK¹⁶⁻¹⁸ every 24 hours upto 3 doses, revealing an efficacy upto 68-93%.

A success rate of 85-90% was reported by Ghora.¹⁹ He concluded that endocervical administration of misoprostol appears to be effective and well tolerated with decreased side effects. In his study, induction to abortion interval for intra-cervical misoprostol, was 10.3 ± 4 hours, which is quite comparable with 12.23 hours, induction to abortion interval of this study.

A success rate of 74.1% was reported by Sirimai²⁰ who concluded that misoprostol alone could be used with caution, for induction of abortion especially in 2nd trimester. Scarred uterus is not a contraindication for the use of misoprostol.²¹ This study included 19 cases with previous uterine scars. Out of 19 patients, 16 patients had successful abortion within 24 hours, 2 patients needed more than 24 hours for expulsion and one patient needed Laparotomy, due to uterine rupture with previous scar. Few more studies will consolidate the use of misoprostol with greater safety in patients with previous uterine scar.

A study by Creinin²² compared the efficacy, acceptability and cost of medical versus surgical abortion and he concluded that surgical abortion requires zero to ten percent more personnel cost than medical abortion using methotrexate (MTX) and misoprostol.

The sublingual route of administration of misopros-

tol was used by Wagaarachchi et al.²³ with 200 mg of mifepristone with 400µg of misoprostol given sublingually at 6 weeks of gestation. There was 83% success rate in induction of abortion.

In another study, Wagaarachchi²⁴ used 200 mg of mifepristone and 800µg of misoprostol vaginally, at 10 weeks of gestation at a success rate of 84.1%. In his study 2.2% of patients needed surgical evacuation in comparison to this study, which showed surgical evacuation rate of 20%. This difference could be explained due to the use of misoprostol alone in our study as compared to the combined use of mifepristone and misoprostol in the study by Wagaarachchi.

A success rate of 52% was found in another study by Nielsen et al.²⁵ He conducted a prospective study and used 400mg of mifepristone, orally and 400µg of misoprostol, vaginally. In this study 6% of patients experienced severe vaginal bleeding during induction process that is comparable to the results of our study, having 6.5% of patients, with excessive vaginal bleeding.

In this study, one of the prostaglandin E1 analogue, misoprostol had been used, that is cheaper, as compared to other prostaglandins, available in Pakistan. A total of 68% of patients had successful complete abortion with misoprostol, did not need any surgical intervention and were discharged within 24 hours. This significantly decreased the financial burden on patients, hence assuring cost-effectiveness of the drug.

Conclusion

Misoprostol is safe, efficacious and cost effective drug for induction of the first and the second trimester abortions.

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