ORIGINAL ARTICLE

Umbilical Vein Injection of Misoprostol Vs Syntocinon in normal saline for the Treatment of Retained Placenta: Randomized Control Trial

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ABSTRACT

Background: The third stage of labour may be complicated by retained placenta (RP), which should be managed promptly because it may cause severe bleeding and infection, with a potentially fatal outcome.
Aim: To compare the effectiveness of intraumbilical Oxytocin Vs misoprostol in patients with retained placenta to avoid manual removal of placenta.
Study design: Randomized controlled trial.
Setting: This study was conducted in the Dept. of Obs & Gynae JPMC, Karachi.
Duration of study: Six months from 25th, February 2011 to 24th August, 2011.
Methods: Total 60 patients were selected for study. The inclusion criteria were: gestational age ≥37 weeks, vaginal delivery and failure of the placenta to separate within 30 minutes after delivery of the infant despite active management of the third stage of labour. Sixty women with retained placentas were eligible for inclusion. Informed consent was taken and the patients were randomly allocated into two groups by envelope method to receive umbilical vein injection of either 800mcg misoprostol dissolved in 30ml of normal saline (misoprostol group) or 50units oxytocin in 30ml of normal saline (Oxytocin group). The SPSS version 10.0 was applied, p-value <0.005 was considered significant.
Results: There were no significant differences between the misoprostol and oxytocin groups in terms of maternal mean age, parity, or gestational age. After intra umbilical vein injection, delivery of the placenta occurred in 83.33% of women in the misoprostol group and in 60% of women in the oxytocin group, which was a statistically significant difference between the two groups($p< 0.005$).Time interval between injection and delivery of placenta was also shorter in misoprostol group as compare to oxytocin group ($p< 0.005$).
Conclusion: Misoprostol (800mcg) dissolved in 30ml normal saline, administered through intraumbilical route significantly reduces the need for manual removal for retained placenta under general anesthesia compared with 50iu injection of oxytocin in normal saline through similar route.
Keywords: Retained placenta, manual removal of placenta, syntocinon, misoprostol.

INTRODUCTION

Postpartum hemorrhage(PPH) is a major cause of maternal morbidity and mortality all over the world[1]. Retained placenta affects 0.5% to 3% of women following delivery and is a major cause of PPH, maternal morbidity and mortality.[2] Reducing the time of delivery of placenta through active management of third stage of labor can prevent uterine atony and PPH[3]. No consensus exists regarding the normal length of the third stage of labour, or the time at which the placenta should be termed "retained" and intervention should be started[4]. The intrapartum guidelines published by the National Institute for Health and Clinical Excellence suggest intervention when the placenta has not been delivered within 30 minutes after birth with active management of the third stage of labour, or within 60 minutes after birth with physiological management of the third stage of labour[5]. The current standard management for RP is manual removal of the placenta (MROP), which usually requires general or regional anesthesia in hospital setting. MROP is an invasive procedure that may lead to serious complications such as hemorrhage, infection, and genital tract trauma.[6] A simple and safe alternative treatment for RP that can be administered at birth place and reduces the need for MROP could be of major benefit to women worldwide[7].

Alternative to MROP, non-operative methods such as umbilical vein injection of saline plus oxytocin or prostaglandin to achieve expulsion of the placenta have been reported[8]. Intraumbilical vein oxytocin reaches the placental bed in high concentration that stimulates the uterine contractions, thus decreasing the placental attachment site and the resulting hematoma accelerates the process of placental separation. Prostaglandins may be an alternative treatment particularly in developing countries. Such medical care can facilitate the expulsion of retained

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placenta and be a safer alternative to surgery[9]. Misoprostol is an analogue of prostaglandin E1 that act at myometrial receptor and initiating a cascade of events including a change in calcium concentration that initiates myometrial contraction leading to expulsion of the uterine contents[10].

Many studies are reported in literature regarding use of syntocinon for RP with conflicting results. Similarly Misoprostol has also been used in different studies through different routes. The results of preliminary published trials suggest that administration of prostaglandins such as misoprostol may result in delivery of the placenta and reduced volume of blood loss in women with RP. However very limited studies are available to compare the efficacy of misoprostol versus oxytocin through intra umbilical route to treat retained placenta. This study evaluated the effectiveness of umbilical vein injection of misoprostol dissolved in normal saline versus oxytocin in normal saline for the treatment of RP.

MATERIAL & METHOD

This study was conducted in the department of Obstetrics & Gynaecology, Jinnah Postgraduate Medical Centre, and Karachi over the period of six months from 25th February 2011 to 24th August 2011. It was a randomized controlled trial. For selection of patient non-probability purposive sampling technique was used. Only those women were selected for the study who had term pregnancies (≥37 weeks) delivering vaginally at JPMC, hemodynamically stable and prolongation of third stage of labour >30min.The women who were excluded from the study were those who had twin pregnancies, premature delivery (<37 weeks), blood loss > 500ml, and high risk pregnancies like hypertension, diabetes & previous caesarean section. Informed consent was taken and the patients were randomly allocated into two groups by envelope method. The women were blinded to the group allocation, but the investigator who administered the injection was not. Data was collected using a specially designed questionnaire, including the obstetric history, vital signs, obstetric and vaginal examination findings. In oxytocin group patients received injection 50 I.U oxytocin in 30ml normal saline ,while misoprostol group were given 800mcg misoprostol in 30ml normal saline injected in umbilical vein via an NG feeding tube.

Umbilical vein injection was performed according to the Piping's method, as follows. The cord was cut, and a size 10 paediatric nasogastric tube was advanced into the umbilical vein. If resistance was felt, the catheter was retracted 1–2cm and then advanced further if possible. If the catheter could not be advanced further without using force, the injection was administered through the catheter at that time. The cord was occluded by finger pressure around the catheter during injection. If spontaneous delivery of the placenta did not occur, delivery by gentle cord traction was attempted at 15 and 30 minutes after injection. The time from umbilical vein injection to delivery of the placenta was recorded. If placental delivery failed to occur within 30 minutes after the injection, or significant bleeding occurred, MROP was performed under general anesthesia. The volume of blood loss from the time of umbilical vein injection to delivery of the placenta was measured by placing a pad under the patient's buttocks. The pad weighed 45g before use, and was weighed after delivery of the placenta using a dedicated electronic scale. The blood loss was recorded in ml.

Adverse effects after misoprostol administration such as shivering, fever, dizziness, vomiting, flushes, nausea, abdominal pain, and headache were recorded. Patients were observed for 1 hr for the expulsion of placenta. All women in both treatment arms were followed up for 24 hours postpartum. Vital signs (blood pressure, pulse rate, temperature, and respiratory rate), uterine fundal height, abnormal vaginal bleeding, and abdominal pain were recorded. Tonics, analgesics, and antibiotics were prescribed before discharge if needed.

The whole data was analyzed on computer based program SPSS version 10.0. Descriptive statistics were used to present demographic status of the participants. Mean and standard deviation was calculated for continuous variables like age, parity. Percentage and frequencies were calculated for categorical variables like success versus failure of placental spontaneous expulsion. Chi Square test was used to compare effectiveness between both groups. $p \leq 0.005$ was taken as significant.

RESULTS

Sixty women fulfilling the inclusion criteria were included in this study. Thirty women were included in each group. There were no significant differences between the misoprostol and oxytocin groups in terms of maternal mean age, parity, or gestational age. After intra umbilical vein injection, delivery of the placenta occurred in 83.33% of women in the misoprostol group and in 60% of women in the oxytocin group, which was a statistically significant difference between the two groups($p< 0.005$).Time interval between injection and delivery of placenta was also shorter in misoprostol group as compare to oxytocin group($p< 0.005$).. The median vaginal blood loss from the time of injection until delivery of the placenta was significantly less ($p<0.005$) the misoprostol group (100ml) than in the oxytocin group (210ml).

Table I: Comparison of demographic characteristic between misoprostol and oxytocin group .

Variables	Misoprostol group(n=30)	Oxytocin group (n=30)	p-value
Age (years)	22.42 ± 3.58	23.11± 3.18	p> 0.005(NS*)
Gestational age(weeks)	39.02 ± 1.10	38.82 ± 4.12	p> 0.005(NS*)
Parity	1.4±1.22	1.9±0.93	p> 0.005(NS*)

Note: For patient characteristics, data are expressed as means(SD – standard deviation ,NS * - not significant)

Table II: Comparisons of outcome between the misoprostol and oxytocin groups

Variables	Misoprostol group(n = 30)	Oxytocin group (n=30)	p-value
Expulsion of placenta	25(83.33%)	18(60%)	p< 0.005
Need for MROP	5(16.66%)	12(40%)	p< 0.005
Blood loss(ml)	110 ml	210 ml	p< 0.005
Mean time(min) from Injection to placenta delivery	8.50±1.23	15.55±284	p< 0.005

Note: For primary outcome measures, data are expressed as number/percentages(n=number of patients.

DISCUSSION

Postpartum hemorrhage due to retained placenta remains a major cause of maternal morbidity and mortality in the developing countries. Manual removal of retained placenta is an element of basic Emergency Obstetric Care(EmOC) but it is difficult to apply at basic health setting. Therefore, an affordable medical solution which is applicable even in the basic health settings is seriously needed.

Regarding administration of uterotonic drugs via the umbilical vein, the World Health Organization recommends umbilical vein injection of a uterotonic drug as the first line of treatment for RP. However, this treatment is not routinely used, probably because of lack of a large randomized controlled trial and uncertainties regarding optimal drug and dosage regimens[11].

Many studies have been conducted regarding use of intra umbilical oxytocin in retained placenta with conflicting results. A Cochrane collaboration review found that umbilical vein injection of oxytocin is not effective for the treatment of RP[12]. Similarly another double-blind, placebo-controlled trial including women in the UK, Uganda, and Pakistan reported that umbilical vein injection of oxytocin had no clinically significant effect on the need for MROP[13].

Carroli & Bergel presented the Cochrane review on the use of Saline solution plus oxytocin versus saline solution. The meta analysis of which included 10 trials showed that there was significant reduction in the rate of manual removal of placenta with saline plus oxytocin compared with placebo[14]. Another trial by ivalingam & Surinder also showed reduction in the need for manual removal of placenta by the use of saline plus oxytocin compared with placebo**[15].**

Prostaglandins have strong uterotonic properties and have been used in the postpartum period since 1976 to treat uterine atony and established postpartum hemorrhage. Prostaglandins now are used as routine prophylactic agents in the third stage of labor. Bider investigated Saline solution plus prostaglandin F2 alpha injection into the umbilical vein versus saline solution. Saline plus prostaglandin showed a significant reduction in need for manual removal of placenta compared with placebo, while there was no evidence of difference in blood loss between the two groups[16]. Misoprostol is a synthetic prostaglandin E1 analogue and has the advantage of being thermo stable and inexpensive and has been widely used effectively in the management of postpartum hemorrhage placenta either alone or as an adjuvant to umbilical vein oxytocin. Misoprostol has also been used and reported effective for expulsion of retained placenta in different studies, where it has been compared with placebo and used through different routes[6,17].

In our study we have compared intraumblical misoprostol versus syntocinon for expulsion of placenta in cases of RP. Out of 30 women in Oxytocin group 50% had effective expulsion of placenta as compared to misoprostol group, where 83.33% of women achieved spontaneous placental expulsion. Similarly study conducted by Rany Harara concluded that in retained placenta ,success rate of spontaneous placental separation within 30 min after intraumbilical injection of uterotonics was higher with misoprostol when compared to oxytocin and ergometrine i.e., 80%, 73.08%, 62.96% respectively[18]. Injection to separation interval in our study was significantly shorter in misoprostol group as compare to syntocinin (p <0,005).Similarly in study conducted by Rany Harara injection-to-separation interval was significantly shortest in the misoprostol group than in the oxytocin and ergometrine groups (7.0±2.2min, 13.14±3.76min, 22.5±4.37min, respectively, P<0.001)[18].

Another three arm randomized controlled trial comparing 50 IU syntocinon versus 800mcg misoprostol versus 30ml normal saline performed at Princess Margaret Hospital concluded that misoprostol (800 mcg) dissolved in 30ml normal saline & administered by intraumbilical injection using

the Pipingas technique significantly reduces the need for manual removal for retained placenta[19]. Another study conducted by Van Beekhuizen HJ regarding role of misoprostol in retained placenta ,success rate was 40% and it was concluded that treatment with misoprostol was found to have no clinically significant beneficial effect among women with retained placenta.[17.] The probable reason for this difference is that although they used it in 800microgram dose but it was used through sub lingual use and they included all retained placenta after 28 weeks of gestation where response to uterotonics is less effective as compare to term (≥37 weeks) .

Nausea &vomiting like other prostaglandin related side effects, failed to reach statistical significance in our study. Similarly diarrhea, shivering and pyrexia were not commonly seen in our misoprostol group. Only one of our patient developed shivering and pyrexia in misoprostol group. Significantly high incidence of nausea &vomiting was also not reported in the WHO multicentre randomized trial[20].

CONCLUSION

Misoprostol (800mcg) dissolved in 30ml normal saline, administered through intraumbilical route significantly reduces the need for manual removal for retained placenta under general anesthesia compared with 50iu injection of oxytocin in normal saline through similar route.

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