COMPARISON OF RECTALLY ADMINISTERED MISOPROSTOL AND OXYTOCIN INFUSION FOR MANAGEMENT OF 3RD STAGE OF LABOUR IN 2ND TRIMESTER PREGNANCY LOSS

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ABSTARCT

Misoprostol and oxytocin are two common medications used to prevent PPH and other pregnancy related complications, particularly in pregnancy loss. Both of these drugs can be administered through different routes and have different effectiveness. So this study was done to compare the effectiveness of these drugs.

Objective: To compare the outcome of rectally administered misoprostol and oxytocin infusion for management of 3rd stage of labour in 2nd trimester pregnancy loss.

Material & Methods: The randomized control trial was conducted at department of Obstetrics and Gynaecology, Lady Willingdon Hospital, Lahore. Then patients were randomly divided into two groups by using lottery method. In group A, 600 μg tablets of misoprostol was used rectally at the time of delivery of foetus. In group B, 20 IU of oxytocin was given I/V infusion at the time of delivery of foetus. For comparison independent sample t-test was used to compare blood loss in both study groups. P-value<0.05 was taken as significant.

Results: In our study the mean age of the patients was 27.35±6.35 years and the mean gestational age was 18.21±3.95 weeks, the mean blood loss was 369.28±87.26 ml. Retained placenta was observed in 48(17.1%) patients and the PPH was found in 15% patients. Statistically there is significant difference was observed between the study groups and retained placenta of the patients i.e. p-value=0.011.

Conclusion: The results of our study concluded that the use of misoprostol is an effective and feasible drug in blood loss, PPH and Retained placenta as compared to oxytocin drug in the managmenet of 3rd stage of labour in 2nd trimester pregnancy loss.

Keywords: Excessive blood loss, PPH, Misoprostol, Oxytocin, Retained Placenta, Pregnancy loss

INTRODUCTION

Second trimester pregnancy loss either spontaneous or induced due to medical indication or malformed foetus may result in prolonged third stage of labour and it has an association with retained placenta in 9% - 20% of cases as compare to term pregnancy in which risk of retained placenta is minimal (0.5-3%).[1]

Because of ineffective contraction of myometrium especially that part directly in contact with placenta, results in retained placenta and additional role might be played by presence of inhibitory factors those can prevent contraction of placenta before and after the labour (nitrous oxide or Progesterone).[2]

Retention of placenta may be associated with complications in mother, resulting in morbidity and at times maternal death when we are considering under developed countries where resources for appropriate obstetric cares are limited.[3] In relation to pregnancy, postpartum haemorrhage (PPH) is another complication and one of the leading causes of mortality and morbidity.[4]

530,000 women every year die due to complications related childbirth and pregnancy. 98% of these cases occur in the developing countries.[5]

The management of 3rd stage of labour in 2nd trimester pregnancy loss could reach a better outcome in regard to low risk of placental retention and duration of delivery. Prostaglandins shows higher rate of expulsion of placenta without manual removal and lower time for delivery of placenta as compare to oxytocin.[6]

A study reported the using misoprostol by rectal route resulted in significantly reduction of retention of placenta (n=3, 7.5%) when it was compared to other group where oxytocin was used (n=10, 25%), p=0.034.[6]

Another study reported a contradictive statement, in which the incidence of PPH was 12% in the misoprostol 200ug given per rectally and 10% in the oxytocin group (P>0.05), mean blood was 436.6±214.04 in misoprostol groups and 415.06±227.2 in oxytocin group and retained placenta was noted in 6% of misoprostol and 8% of oxytocin group patients.[8]

Rationale of this study is to compare retained placenta, post-expulsion blood loss and frequency of PPH with rectally administered misoprostol versus oxytocin infusion for management of labour in 2nd trimester pregnancy loss.

There is no local study available on our own population and in international study. In literature review it has been observed that there is controversy as in rectally administered misoprostol as compared to oxytocin in terms of blood loss and incidence or prevention of PPH while retention of placenta is not widely reported in the literature. If misoprostol has a better effect than oxytocin then we may implement the use of rectally administered misoprostol.

Third stage of labour is the period starting from birth of a foetus till the placenta is expelled and this is also named as involution stage. Delivery of placental starts when the placenta separates from the wall of the uterus. On an average it takes 10-12 minutes for the placenta to be expelled after the foetus is delivered and if this time exceeds longer than 3o minutes than risk of retention is a concern in 3% of all vaginal deliveries. Foetus can be born with the intact membranes if during the labour, sac is not ruptured. It is named as "delivery en caul".[9, 10]

Expulsion of placenta can be an active event or it can be managed as per situation. Most of the time strategy is to allow the placenta to be delivered as physiological phenomenon without giving medication. Active way management is manual traction of placenta in experienced hand while giving uterotonic drug within a minute of delivery of the foetus. Massage of the fundus every 15 minutes after placental expulsion is over and continue up to two hours is passive way of management to avoid retention. In a joint statement, World Health International organizations and federations of gynaecology and obstetrics, strongly recommends active management of placental removal to avoid PPH in third stage of labour and similar guidelines mentioned by the International Confederation of Midwives.[11, 12]

Operational Definitions:

Second trimester pregnancy loss: It's defined as if pregnancy with maternal or fetal indications likes fetal death, congenital anomaly for pregnancy termination between 13 to 28 weeks.

Retained Placenta: It was labelled if female would not spontaneously expel the placenta within six hours and there need for surgical evacuation of placenta during third stage of labor.

Mean blood loss: The volume of blood loss was measured by counting total number of soaked pads and weighing each soaked pad. Where 1ml=1gm till – 24 hours.

Post-partum hemorrhage (PPH): PPH was established by definition if volume of blood loss was ≥500ml. It was calculated as weight of soaked pads minus the weight of dry pads. Where 1gm=1ml within 24 hours. Weight of total pads was added.

Third stage of labour: It commences when the baby is delivered and ends when the placenta and membrane are delivered. Average duration is 30 minutes to 4 hours.

Hypothesis: There is a difference in frequency of retained placenta, PPH (if blood loss more than 500ml) and mean blood loss with rectal administration of misoprostol and oxytocin infusion for management of3rd stage of labour of 2nd trimester pregnancy loss.

MATERIAL AND METHODS

Study design: Randomized Controlled Trail

Setting: Department of Obstetrics and Gynaecology, Lady Willingdon Hospital (LWH), Lahore.

Duration of study: 6 month after Ethical approval of study

Sample size: Sample size of 280 females; 140 females in each group was calculated with power of test = 80%, level of significance 5% and taking expected percentage of retained placenta i.e. 39.56% with rectally administered misoprostol and 54.26% with oxytocin infusion.

Sampling technique: Non-probability, consecutive sampling and sample divided into two groups randomly.

Sample selection

Inclusion criteria: All pregnant woman between 13 and 28 weeks of gestation (on antenatal record or by ultrasound) admitted with spontaneous or induced 2nd trimester pregnancy termination (as per operational definition).

Exclusion criteria: Women with placenta Accrete, percreta (was assessed on USG and clinical examination)

Clinical chorioamnionitis (was assessed on clinical assessment) by signs and symptoms of pyrexia (fever>100ºF for >2 hours), increased TLC count>1100mm^3, abdominal tenderness and change in color of liquor.

Previous cesarean delivery or other significant uterine surgery.

Data collection procedure: Approval was taken from the ethical committee of the hospital, 280 Women fulfilling the criteria were taken from emergency department of Obstetrics & Gynaecology, LWH. After taking informed consent, their demographic profile including name, age, gestational age and parity was obtained.

Then patients randomly divided into two groups using lottery method. In group A, 600 µg tablets of misoprostol was used rectally at the time of delivery of fetus. In group B, 20 IU of oxytocin was given via I/V infusion at the time of delivery of fetus. The patients were managed expectantly with vaginal examination every hour until it was required to intervene or up to 6 hours when the curettage is schedule.

If patients do not expel placenta spontaneously up to 6 hours and require for uterine curettage for placental removal, then retained placenta was labelled and total amount of blood loss and PPH (if amount of blood loss more than 500ml) was recorded as per operational definition. All this input recorded on a predesigned Performa.

Data analysis procedure: The data was analysed through SPSS version 20. Descriptive statistics like age, gestational age and blood loss was presented as mean and standard deviation. Retained placenta and incidence of PPH was presented as Frequency and percentage. Chi-square test was applied to compare the frequency of retained placenta and incidence of PPH in both groups. Independent sample t-test was used to compare blood loss in both study groups. P-value ≤ 0.05 was taken as significant.

RESULTS

Table # 1: Descriptive statistics of age (years)

Age (years)	n	280
	Mean	27.35
	SD	6.25
	Minimum	18.00
	Maximum	40.00

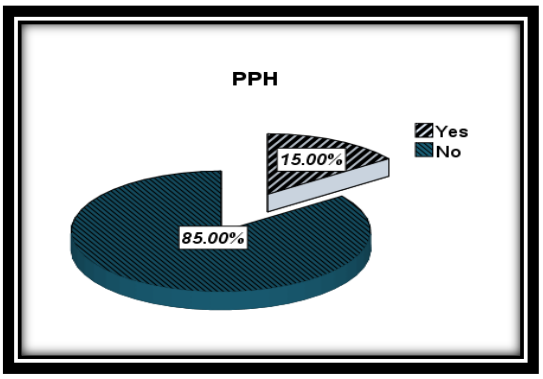

Fig # 1: Frequency distribution of PPH

Table # 2: Comparison of retained placenta both study groups

		Study Groups		Total
		Oxytocin	Misoprostol	
Retained placenta	Yes	32	16	48
	No	108	124	232
Total		140	140	280

Chi value=6.43 p-value=0.011 (Significant)

Table # 3: Comparison of PPH both study groups

		Study Groups		Total
		Oxytocin	Misoprostol	
PPH	Yes	31	11	42
	No	109	129	238
Total		140	140	280

Chi value=11.20 p-value=0.001 (Significant)

Table # 4: Comparison of blood loss both study groups

		Study Groups	
		Oxytocin	Misoprostol
Blood loss (ml)	n	140	140
	Mean	430.59	311.98
	SD	63.12	67.60

T-value=15.17 p-value=0.000 (Significant)

In this present study total 280 cases participated. The mean age of the patients was 27.35±6.25 years with minimum and maximum ages of 18 & 40 years respectively. Table#1

The study results showed that the PPH was found in 15% patients and it was not found in 85% patients. Fig#1

In this study retained placenta was noted in 48 cases in which 32 were from oxytocin group and 16 were from misoprostol group, similarly retained placenta was not noted in 232 cases in which 108 were from oxytocin group and 124 were from misoprostol group. Statistically there is significant difference was observed between the study groups and retained placenta of the patients. i.e. p-value=0.011. Table#2

In this study, PPH was found in 42 cases out of which 31 were from oxytocin group and 11 were from misoprostol group. PPH was not found in 238 cases out of which 109 cases were from oxytocin group and 129 were from misoprostol group. Statistically, significant difference was observed between the study groups and PPH of the patients. i.e p-value=0.001. Table#3

In this study the mean blood loss in oxytocin group patients was 430±63.12 ml and the mean blood loss in misoprostol group patients was 311.98±67.60 ml. Statistically there is highly significant difference was

found between the study groups and the mean blood loss of the patients. i.e p-value=0.000. Table#4

DISCUSSION

This randomised control trial, carried at the department of Obstetric and Gynaecology, LWH, Lahore for the management of 3rd stage of labour in 2nd trimester pregnancy loss, was to compare the outcome of misoprostol administered via rectum versus oxytocin given via infusion.

The incidence of maternal mortality due to pregnancy related complications is significantly l lower in developed countries.[13] Use of misoprostol to manage and prevent postpartum haemorrhage is increasing over years.[14] World Health Organization (WHO) has enlisted it as essential medicines for the management of postpartum hemorrhage(PPH) in 2011.[15]

Results of our study mentioned PPH in 42 (15%) patients out of which 11 belonged to the misoprostol group while 31 belonged to the group which received oxytocin. Statistically, the difference observed between both groups was significant enough with the p-value = 0.001 as paired tTest while comparing PPH of the patients.

Oral misoprostol given after delivery in a study which was carried out at a rural set-up of India, involving 1620 women, has shown significantly better results than the placebo to reduce the rate of PPH. Additionallym the mean blood loss during the post partum period was also less. The side-effects of misoprotol can be more frequent than with placebo (shivering in 52.2% vs. 17.3% and fever in 4.2% vs. 1.1%, respectively).[16]

SM Parsons, et al showed in their study that misoprostol 800 ug if administered rectally is equally effective as the intramuscular oxytocin 10 IU in controlling post-partum hammorhage in the third stage of labour. Equivalent oral dose of misoprostol causes a lesser frequency of side-effects as compared to the rectal dose.[17]

In a randomised controlled trial in 514 women, that compared 800 ug misoprostol placed in rectum, intravenous infusion of 5 IU oxytocin and matching placebos, as effective approch in preventing PPH, when given immediately after delivery. Complication of fever was more in number in misoprostol group (18.7% vs. 0.8% with Pvalue <0.001). [18]

622 patints were compared in a double-blinded randomised trial with oral misoprostol (400 μg) versus intravenous oxytocin (5 IU) in the prevention of bleeding, showed shivering in misoprostol group (6.8%) however in all the cases, it was self-limiting. Fever occurred in 12.5% (39) women in the study group of misoprostol and 0.3% (1) woman in the oxytocin group (P=0.01). By intervening with mesoprostol there were limited to no blood transfusions required, did not endup into hysterectomies, or deaths in either group.[19]

In this present study, the average blood loss in each patient was 371.28±88.27 ml. The mean blood loss was 430±63.12 ml and 311.98±67.60 ml in the oxytocin group and in misoprostol group patients respectively. Statiscally the difference of blood loss was significant (p-value=0.000) with lesser amount of blood loss in patients given mesoprostol in comparison with oxytocin.

WHO concluded that 600 misoprostol given as oral medication is less effective in comparison to oxytocin given parentrally in decreasing hammorhage (measured blood loss greater than 1000 mL or use of additional uterotonics).[20]

CONCLUSION

Our study results concluded that the use of misoprostol is an effective and feasible drug in blood loss, PPH and Retained placenta as compared to oxytocin drug in the managment of 3rd stage of labour in 2nd trimester pregnancy loss.

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