CONTEMPORARY PERSPECTIVE STUDY

Sublingual Misoprostol versus Intramuscular Oxytocin in the Active Management of Third Stage of Labor

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Abstract

Objective: To compare the efficacy and safety of 400 µgm of sublingual misoprostol with 10 units of intramuscular oxytocin in active management of the third stage labor.

Methods: The study was carried on 200 women undergoing vaginal delivery who were randomized alternatively into two groups of 100 women each. Group 1 (misoprostol group) received 400 µgm misoprostol sublingually and group 2 (oxytocin group) received injection oxytocin 10 units intramuscularly immediately after the delivery of the baby. Primary outcomes measures were amount of blood loss and drop in hemoglobin level. Secondary outcomes were need for additional oxytocics, manual removal of placenta, operative intervention for PPH, and side effects of the drugs. The blood loss was measured by clinical estimation by weighing the linen, sponges and pads before and after the delivery. Duration of the third stage of labor, need for manual removal of placenta and the use of additional uterotonics, if required, were noted. One hour after the delivery, the women were asked about the side effects of the drugs like nausea, vomiting, headache, chest pain, fever, shivering, etc. Hemoglobin estimation was done at time of admission and 24 hours after the delivery. At the end of the study, the data was analyzed using student 't' test and Chi-square test.

Results: The mean age was 23.44 ± 3.11 years and 23.78 ± 2.47 years in group 1 and 2 respectively. There was no statistically significant difference in the duration of third stage of the labor and mean fall in hemoglobin level in the two groups ($p > 0.05$). The mean blood loss was 260.35 ± 97.45 ml in the misoprostol group and 264.20 ± 103.68 ml in oxytocin group and the difference was not statistically significant.

Conclusion: It is concluded from the present study that sublingual misoprostol is as effective as intramuscular oxytocin in active management of third stage of labor and a good option especially for developing tropical countries like India where most of the deliveries are conducted at periphery by a nurse, midwife or a trained dai, and it is difficult to maintain the temperature chain.

Keywords: Misoprostol, Oxytocin, Third stage of labor.

INTRODUCTION

In this era of scientific advancement and best available obstetrical knowledge, maternal mortality still remains a challenge. Postpartum hemorrhage (PPH) is one of the most prevalent causes of maternal deaths.[1] Common causes of PPH are atonic PPH, traumatic PPH and retention of placental tissue, atonic PPH being the commonest.[2] It is crucial to prevent PPH at all the levels of obstetric care, which means active management of the third stage of labor.

As per Cochrane review, active management of the third stage of labor includes administration of prophylactic uterotonics after delivery of the baby, early cord clamping, and controlled cord traction.[3] WHO's integrated management of pregnancy and childbirth includes giving oxytocin immediately after the delivery of baby, removal of placenta by controlled cord traction, and the uterine massage.[1]

Various drugs like oxytocin, ergometrine, syntometrine, and prostaglandins have been used for long. The oxytocin, ergometrine and syntometrine are to be given in injectable form requiring clean syringe and needle, as there is a risk of injection related diseases like hepatitis and HIV. Moreover, these have to be refrigerated to maintain the potency. Misoprostol is a synthetic prostaglandin analogue and after sublingual administration, the serum levels are significantly higher than those achieved after oral and vaginal treatment.[4] It can be stored at room temperature. In a country like India, where most of the deliveries are conducted by a nurse or a trained dai in homes, active management with injectables like oxytocin becomes really difficult, and sublingual administration of misoprostol is an easy option as temperature maintenance is not required with no risk of injection related diseases.

AIMS AND OBJECTIVES

To compare the efficacy and safety of 400 µgm of sublingual misoprostol with 10 units of intramuscular oxytocin in active management of the third stage labor.

MATERIALS AND METHODS

The study was carried out in labor ward of the Department of Obstetrics and Gynecology on 200 women undergoing vaginal delivery. The women were randomized alternatively into two groups of 100 women each.

Group 1 (misoprostol group): included 100 women, who received 400 µgm misoprostol sublingually immediately after the delivery of baby.

Group 2 (*oxytocin group*): included 100 women, who received injection oxytocin 10 units intramuscularly immediately after the delivery of baby.

Women between 19 and 35 years with singleton term pregnancy, presented as cephalic, were included in the study. Women with history of uterine surgery, heart disease, pulmonary disease, glaucoma, liver, renal disease, known coagulation disorder, operative delivery (vacuum or forceps), and induced labor were excluded from the study. Women with Hb less than 8 gm% and hypersensitivity to oxytocin or prostaglandins were also excluded.

Primary outcomes measures were the amount of blood loss and drop in hemoglobin level. Secondary outcomes were need for additional oxytocics, manual removal of placenta, operative intervention for PPH and side effects of the drugs. After admission and informed consent, history regarding demographic profile and obstetric care was taken. Maternal blood sample for determination of hemoglobin level was taken and women were monitored for delivery as per existing protocol.

Immediately after the delivery of baby, the women were, given either 400 µgm of misoprostol sublingually or 10 units of oxytocin intramuscularly. Cord clamping was done and once the uterus was contracted, the placenta was removed by controlled cord traction, and maternal blood loss was measured. Duration of the third stage of labor, incidence of prolong labor (duration longer than 30 minutes), need for manual removal of placenta, use of additional uterotonics and any operative interventions, if required, were noted. Details of baby regarding weight, sex, and APGAR score were recorded. One hour after the delivery, the women were asked about the side effects of the drugs like nausea, vomiting, headache, chest pain, fever, shivering, etc. After 24 hours of delivery, a blood sample was taken for hemoglobin estimation.

The amount of blood loss in one hour of the delivery was noted by clinical estimation. Preweighted sterile linen, sponges and pads were kept ready. After the delivery of baby, amniotic fluid was allowed to drain away and a kidney tray was kept beneath the women's buttocks for blood collection. The amount of blood was determined by weighing the used linen and sanitary pads and subtracting their known dry weight. This was added to the measured blood amount from the kidney tray. At the end of the study, the data was analyzed using student 't' test and Chi-square test.

RESULTS

Results are shown in Tables 1 to 3. In groups I and II, there was PPH (blood loss > 500 ml) in 4 and 5% women respectively. One patient needed blood transfusion in misoprostol group and there was no case of retained placenta in any of the groups. The baby weight in group I and II was also comparable, mean weight was 2.77 ± 0.41 kg and 2.89 ± 0.44 kg respectively (p-value > 0.05).

DISCUSSION

PPH is the most important cause of maternal morbidity and mortality and still remains a challenge to the treating obstetrician. Active management of third stage of labor, using oxytocics, have significantly reduced the incidence of PPH. Misoprostol has been found to be effective in prevention and treatment of PPH. Various routes of administration like oral, vaginal, rectal, and sublingual have been tried. Sublingual route avoids the first pass effect through the liver and can also be given in patients where oral administration is not possible.

Maximum number of the patients in the present study were in the early third decade of life and the mean age was 23.44 ± 3.11 years in misoprostol group and 23.78 ± 2.47 years in oxytocin group. Nullipara was in majority in both the groups, constituting 60% in misoprostol and 51% in oxytocin group. Almost a similar parity was reported by Ng et al where nullipara were 52.7 and 54.3% in oral misoprostol and syntometrine groups respectively.[5] There was no statistically significant difference in the duration of third stage of the labor in the two groups, i.e. 6.2 ± 3.61 minutes in group 1 and 5.6 ± 2.22 minutes in group 2 (p > 0.05). Bamigboye et al, who compared rectal misoprostol with syntometrine, observed no significant difference in the duration of third stage of the labor (7.7 ± 6.7 minutes and 7.9 ± 6.8 minutes respectively).[6] Vimla N et al compared sublingual misoprostol with methylergometrine and also found no difference in duration of third stage of labor.[7]

The mean fall in hemoglobin in the two groups was 0.52 ± 0.47 gm% in misoprostol group and 0.50 ± 0.35 gm% in oxytocin group and difference is not significant (p > 0.05). Ng PS et al, comparing oral misoprostol and syntometrine, also reported no significant difference in fall in hemoglobin, although it was slightly higher (1.2 and 1.8 gm% respectively).[5]

In the present study, the mean blood loss is 260.35 ± 97.45 ml in the misoprostol group and 264.20 ± 103.68 ml in oxytocin group and the difference is not statistically significant. There was no significant difference in amount of estimated blood loss in study done by Ng PS et al[5] (oral misoprostol and syntometrine), Vimla N et al[7] (sublingual misoprostol and methylergometrine), Kundodyiwa TW et al[8] (misoprostol group

Table 1: Distribution of patients according to various parameters

Parameter		Group 1	Group 2	P-value
Booking status	Booked	68%	71%	-
	Unbooked	32%	29%	-
Residence status	Urban	29%	27%	-
	Rural	71%	73%	-
Age (mean ± SD)		23.44 ± 3.11	23.78 ± 2.47	0.392 (p > 0.05)
Parity (mean ± SD)		0.5 ± 0.69	0.68 ± 0.76	0.084 (p > 0.05)

Table 2: Distribution of patients according to blood loss, fall in Hb, duration of 3rd stage of labor, need of additional oxytocics

Parameter	Group 1	Group 2	P-value
Blood loss (ml) (mean ± SD)	260.35 ± 97.45	264.20 ± 103.68	0.328 (p > 0.05)
Fall in Hb (gm %) (mean ± SD)	0.52 ± 0.47	0.5 ± 0.35	0.772 (p > 0.05)
Duration of 3rd stage in mts (mean ± SD)	6.20 ± 3.61	5.62 ± 2 .22	0.64 (p > 0.05)
Additional oxytocic (n)	6	5	0.191 (p > 0.05)

and intramuscular oxytocin) and Bamigboye et al[6] (rectal misoprostol and syntometrine).

In the present study, the incidence of PPH (blood loss > 500 ml) was 4% in group 1 and 5% in group 2. Kundodywia TW et al reported very high incidence of PPH, i.e. 15.2% in misoprostol group and 13.3% in oxytocin group and the reason was inclusion of high risk women in the study.[8] The study by Bamigboye et al reported an incidence of PPH, i.e., 0.9 and 0.4% in rectal misoprostol and syntometrine groups respectively and was comparable.[6]

In the present study, one patient needed blood transfusion in misoprostol group and there was no case of retained placenta in any group. Bamigboye et al reported one case of retained placenta requiring manual removal of placenta in syntometrine group.[6] Only one women in methylergometrine group needed manual removal of placenta in the study by Vimla et al.[7] Additional oxytocics were employed whenever the estimated blood loss was considered to be going towards higher side or whenever the uterine contractions considered to be inadequate. Six in misoprostol group and five in oxytocics group required additional oxytocics in the present study. Just like the present study, Vimla N et al[7] and Kundodywia TW et al[8] observed a similar need for additional oxytocics for misoprostol, i.e. 8.3% (sublingual) and 5% (oral). In the study of Bamigboye et al, additional oxytocics were needed in 1.66% (4/241) women in misoprostol group.[6]

In the present study, shivering was significantly higher with sublingual misoprostol, i.e., 13% ($p < 0.05$). A higher incidence of shivering was also observed with oral misoprostol by Kundudyiwa TW et al[8] (43.6%) and Ng et al[5] (30.2%).

Misoprostol has advantage of being cheaper, easy in administration, stored at room temperature, well-tolerated with insignificant side effects and long shelf life. Sublingual route has further advantage of better and quick absorption and can be given in nausea and vomiting and avoids the first pass effect through liver. Oxytocin has to be given by parenteral route requiring a clean needle and syringe—an important consideration in the era of HIV and hepatitis infections.

Table 3: Distribution of patients according to need of oxytocics and side effects

Parameter	Group 1	Group 2	P-value
Side effects			
Nausea	7%	3%	0.194 (p > 0.05)
Vomiting	3%	2%	0.69 (p > 0.05)
Diarrhea	1%	0%	1.00 (p > 0.05)
Shivering	13%	3%	0.009 (p < 0.05)
Pyrexia	7%	2%	0.169 (p > 0.05)

CONCLUSION

It is concluded from the present study that sublingual misoprostol is as effective as intramuscular oxytocin in active management of third stage of labor and a good option especially for developing tropical countries like India where most of the deliveries are conducted at periphery by a nurse, midwife or a trained dai, and it is difficult to maintain the temperature chain.

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