A RANDOMIZED CONTROLLED TRIAL OF MISOPROSTOL AND OXYTOCIN IN THE MANAGEMENT OF THIRD STAGE OF LABOR

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ABSTRACT

The study was conducted to compare the effectiveness and safety of oral misoprostol with intramuscular oxytocin in the management of third stage of labor. One hundred patients were selected randomly who are expected to have vaginal delivery. Fifty patients received oral misoprostol 600 microgram and other fifty patients received oxytocin 10 IU intramuscularly after the birth of the baby. There were no significant differences between the prevalence of postpartum hemorrhage, duration of third stage of labor, additional oxytocin requirement, manual removal of placenta and blood transfusion. About the side-effects, shivering and fever were significantly higher in misoprostol group ($p<0.001$) and ($p<0.003$) respectively. But there were no significant differences in other side-effects. Oral misoprostol can be used instead of intramuscular oxytocin in the management of third stage of labor, to prevent postpartum hemorrhage, in developing countries, especially as it is administered orally and thermo stable in tropical climate.

Key words: *Misoprostol, Oxytocin, Postpartum haemorrhage*

(Bangladesh J Physiol Pharmacol 2008; 24(1&2) : 14-16)

INTRODUCTION

Postpartum hemorrhage (PPH) is an important cause of maternal mortality and morbidity. In the developing world, it is estimated to account for 28% of maternal death[1]. Failure of the uterus to contract adequately after childbirth is the most common cause of PPH[2]. Active management of third stage of labor (AMTSL) reduces the risk of PPH by 60%[3]. Active management involves giving an uterotonic drug within one minute of the birth of the baby, applying controlled cord traction when uterus is contracted and uterine massage through abdomen after placental delivery. These three interventions hasten placental delivery by increasing uterine contractions, decreasing blood loss and preventing PPH[4].

Standard agents used as a component of AMTSL include oxytocin, ergometrine and a combination of oxytocin and ergometrine. However the occurrence of side-effects especially of nausea, vomiting and hypertension are a major drawback of these conventional oxytocics [5]. These agents are less stable in tropical storage conditions, with a loss of 21-27% potency after only one month and over 90% after one year, particularly with ergometrine. These drugs are heat and light sensitive. They require parenteral administration with a sterile needle and syringe. Skilled manpower is needed for administration[6].

Misoprostol is a synthetic analog of PGE_1. When given orally, it is rapidly absorbed by the gastrointestinal tract and undergoes de-estirification to its free acid, which is responsible for its clinical activity. The peak concentration and half-life of misoprostol acid, the active metabolite are 12 and 21 minutes respectively[7]. Misoprostol is a proven uterotonic agent[8] and research using misoprostol suggests that it may be effective in the prevention of PPH[1]. It is inexpensive, has few side-effects, does not require special storage condition and has a self-life of several years[9].

MATERIALS AND METHODS

It was a prospective, randomized controlled trial study conducted between May, 2008 to October, 2008 in Maternal and Child Health Training Institute (MCHTI), Azimpur, Dhaka. The inclusion criteria were singleton live pregnancy at term and who are expected to have a

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vaginal delivery. Informed verbal consent was taken in early labor. When delivery was imminent i.e., at head crowning, alternate patients were selected for Misoprostol group and Oxytocin group. In Misoprostol group, 600 microgram of misoprostol was given orally after the birth of the baby and in Oxytocin group, 10 IU of oxytocin was given intramuscularly after the birth of the baby. The exclusion criteria were multiple pregnancies, history of PPH, APH, caesarean section or myomectomy, polyhydramnios, coagulation disorder, uterine leiomyoma, precipitate labor, malpresentation, severe anaemia and known allergy to oxytocin or prostaglandin.

After delivery, a data form for each woman containing the information regarding the woman's demographic, intrapartum and postpartum characteristics was completed. The main outcome measure was the prevalence of PPH. The results were analyzed statistically by Statistical package for the Social Sciences (SPSS) version 12.

RESULTS

Total 100 patients were enrolled in this study. Fifty patients were randomized for oral Misoprostol 600 microgram and fifty patients for Oxytocin 10 IU intramuscularly for the management of 3rd stage of labor. The two groups were comparable in terms of age, gravida and gestational age (Table-I). In both the groups there were no significant differences. Similarly the out come were compared (Table-II). There were no significant differences in the prevalence of PPH, duration of 3rd stage of labor, additional oxytocin, requirement, retained placenta and blood transfusion. Table III showed different side effects. Incidence of shivering was 42% in Misoprostol group and 8% in Oxytocin group. It was significantly higher (p< 0.001) in Misoprostol group. But it was self limiting, no treatment required, only counseling was sufficient. Nausea and vomiting were in few patients but statistically not significant. Fever was 12% in Misoprostol group but in Oxytocin group no patients had fever. It was significantly higher (ñ< 0.003) in Misoprostol group. But it was self limiting and only one patient got paracatamol. Shivering and high temperature were transient.

Table-I

Demographic characteristics of the patients.

Characteristics	Misoprostol n= 50	Oxytocin n= 50	P value
Maternal age in years	23.87± 4.02	24.81±5.11	0.321
Gravida Primigravida	11 (22%)	20(40%)	0.546
Multigravida	39 (78%)	30(60%)	0.478
Gestational age in weeks	38.35±1.13	38.08±3.31	0.596

Table-II

Comparison of outcome between Misoprostol and Oxytocin treated groups

Out come	Misoprostol n= 50	Oxytocin n= 50	P value
PPH	02(4%)	01(2%)	0.554
Duration of 3rd stage in minutes	7.51±4.51	6.21±2.21	0.088
Additional oxytocin	04(8%)	01(2%)	0.155
Retained placenta	01(2%)	00	0.237

Table-III

Comparison of side effects between Misoprostol and Oxytocin treated groups

Side-effects	Misoprostol n=50	Oxytocin n=50	P value
Shivering	21(42%)	04(8%)	0.001
Nausea	04(8%)	04(8%)	1.000
Vomiting	02(4%)	00	0.093
Fever	06(12%)	00	0.003

DISCUSSION

In this study, 600 microgram misoprostol was given orally in misoprostol group and 10 IU oxytocin was given intramuscular in oxytocin group for the management of 3rd stage of labor. With Misoprostol the prevalence of PPH, need for further therapeutic oxytocin and the length of 3rd stage of labor were compared with results obtained with oxytocin. These findings suggest that misoprostol may be an alternate to conventional oxytocics in the tropics for AMTSL. Here intramuscular oxytocin is used as it is the current management recommended by WHO[10]. The prevalence of PPH in misoprostol group and in oxytocin group were 4% and 2% respectively which is comparable to another study e.g., 3.8% and 2.63% respectively[11]. In both the studies, there was no significant difference in the prevalence of PPH in the study groups. In the present study, the duration of 3rd stage of labor in misoprostol group was 7.51±4.51 and in oxytocin group 6.21±2.21 in minutes, which were similar in another study[12] showed 8 minutes versus 9 minutes but both studies showed no significant difference between two groups. The present study showed no statistical differences in terms of additional oxytocin requirement, retained placenta and blood transfusion in both groups, which is similar to other studies[11,12,13]. In this study, shivering was significantly higher (p<0.001) in Misoprostol group than Oxytocin group. Incidence of shivering was little higher in another study , but that was

self limiting, no treatment required, only counseling was sufficient[14]. Shivering is regarded as nuisance rather morbidity. Nausea and vomiting were in few patients but statistically not significant. Fever was 12% in Misoprostol group but in Oxytocin group with no patients. It was significant higher than oxytocin group, which was also observed in other studies[11,12,14]. The occurrence of shivering and elevated temperature with Misoprostol may be related to prostaglandin E1 effect on the thermoregulatory center[15].

The study demonstrated that oral misoprostol and intramuscular oxytocin appear to be equally effective in the prevention of PPH. Shivering and transient pyrexia occurred more frequently with misoprostol. Both were self-limiting and did not require any intervention, only one patient got paracatamol for fever. Misoprostol has been shown to have more advantages as an alternative therapy including its low cost, oral administration, easily stored at room temperature, long shelf-life of several years and minimal side-effects. Because of the great potential of misoprostol in its use in 3rd stage of labor, it can be used instead of oxytocin in developing countries especially as it is administered orally and thermo stable in tropical conditions. Further large scale randomized controlled trial is required to confirm these results.

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