Original Article

Comparative study of efficacy of per rectal misoprostol, intravenous methylergometrine and intramuscular carboprost in active management of third stage of labour

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Abstract

Introduction: Postpartum haemorrhage (PPH) during the third stage of labour is the most common cause of maternal deaths in developing countries. Active pharmacological management of this stage to prevent haemorrhage with an uterotonic drugs leads to a decrease in postpartum vaginal haemorrhage. The aim of this study was to assess and compare the effectiveness of rectal misoprostol compared with an intravenous oxytocin and intramuscular carboprost in active management of third stage of labour. **Material and Methods:** A total of 400 women in labour were randomized into four groups (100 women in each). Within 1 minute of delivery of the anterior shoulder participants in group A received 800µg of rectal misoprostol; group B received 0.2mg of methylergometrine intravenously; group C received 125µg of carboprost intramuscularly and group D served as control and had not received any prophylactic uterotonics. **Results:** All groups were compared regarding the need for excessive uterotonics, amount of blood loss, and hematocrit drop. Per rectal misoprostol was found to be equal or better to rest of the drugs in the study with lowest duration of third stage of labor (mean =8.69 mins), lowest amount of blood loss (mean=149.90 ml), haematocrit drop (0.51±0.32) and lowest incidence of PPH. There was no significant difference in the duration of third stage of labor amongst the four groups. **Conclusions:** Per rectal Misoprostol is equal or better as compared to injection methyl ergometrine or carboprost and can prove to be better alternative because of several advantages.

Keywords: postpartum haemorrhage; misoprostol; methylergomtrine; carboprostol

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INTRODUCTION

Postpartum haemorrhage (PPH) is the most serious and preventable complication in obstetric practice. It is the leading cause of maternal morbidity and morbidity especially in developing countries. Reducing maternal mortality is an essential health objective in much of developing world. In the developing world, several countries have maternal mortality rates in excess of 1000 women per 100,000 live birth, and WHO statistics suggest that 25% of maternal deaths are due to PPH, accounting for more than 100,000 maternal death per year.[1] The third stage of labour is the most crucial stage of the labour and refers to the period following the completed delivery of foetus until the completed delivery of placenta and its attached membranes.[2, 3] The length of the third stage itself is 5-15 minutes.[4] The third stage of labour comprises the phase of placental separation, its descent to lower segment and finally its expulsion along with the membranes. In developing country like India where most of the women are anaemic, this PPH complication further aggravates the anaemia by increased blood loss during 3rd stage of labor.[5] There are various uterotonic agents available for prevention of PPH like oxytocin, methylergometrine, 15-methyl PGF-2α and

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misoprostol. The use of these uterotonic agents in the management of third stage of labour reduces the amount of bleeding and need for transfusion.[6] The present study is an attempt to evaluate the scope and feasibility of using rectal misoprostol in comparison with intravenous methyl ergometrine and intramuscular carboprost, which are being used by many clinicians in our country for the active management of third stage of labour.

MATERIAL AND METHODS

A prospective non-randomized uncontrolled clinical trial was carried out in the department of Obstetrics and Gynaecology, Government Medical College Kota and associated group of hospitals during the year 2012-13. A total 400 women were enrolled in the study. Women with singleton pregnancy, more than 37 weeks of gestation, anticipated vaginal delivery, vertex presentation, no high risk factors and ready to give written and informed consent were enrolled in the study. While women with multiple gestation, pregnancy induced hypertension, history of medical disorder, previous caesarean section, haemoglobin less than 10 mg% and not willing to participate were excluded from the study. Women were allotted to one of the 4 groups once they fulfilled all the selection and exclusion criteria such that every 5th woman was in the same group. Active management of 3rd stage of labor was done in Group A with tablet misoprostol 800 µg per rectal, Group B with injection methylergometrine 0.2 mg intravenously, Group C with 125 µg of carboprost intramuscularly and Group D served as control and had not received any prophylactic uterotonics. On admission, the age, parity, gestation age in weeks, antenatal risk factor if any were noted on preformed proforma. The hemoglobin level of every woman was noted on admission. All women were monitored in the first and second stage of labour and partogram was maintained. The first, second and third stage of labour was managed and delivery was conducted as per unit protocol. The drug was administered prophylactically at the time of delivery of anterior shoulder of baby as per the group in which they were enrolled. After delivery of baby, placenta was delivered by controlled cord traction following signs of placental separation. Placenta was examined for completeness and if there is any abnormality. The duration of third stage of labour was calculated from the time of birth of baby to the time of expulsion of placenta. The amount of blood loss during third stage was noted. A sterile kidney tray was placed at vulva after delivery of foetus and volume was measured in a measuring jar. The volume of blood loss was calculated from blood soiled linen and sponges by subtracting the weight of dry linen and sponges from blood soiled linen and sponges. A repeat hemoglobin estimation was done and 2nd post-partum day after 24 hrs. The women having significant bleeding after one dose were given an additional dose after 10-15 min depending upon the severity of blood loss. If the bleeding persists after two additional doses, the woman was given another oxytocic drug included in the study. Patient was kept in labour room under observation for a period of 2 hrs, any complaint such as nausea, vomiting, fever, headache, chills, diarrhoea and shivering was noted. The statistical analysis was performed using ANOVA, SPSS 15.0 and Open Epi 2.3 epidemiological calculator (CDC approved).

RESULTS

The women in all the four groups were comparable as regards their age, weeks of gestation and mode of onset of labour. The mean age of patients was 24.6 years which ranged from 20 to 29 years. The sonographic gestational age in the group treated with rectal misoprostol was 38.4 ± 1.43 weeks and it was 38.4 ± 1.35 weeks for the group treated with intravenous ergometrine whereas, it was 38.4±1.35 for the group treated with intramuscular carboprost and 38.2±1.21 for the control group. The maximum no. of women were multigravida. In Misoprostol group 39% of women were primigravida and 61% were multigravida. In Methyl Ergometrine group 38% women were primigravida and 62% women were multigravida. In Carboprost 42% women were primigravida and 58% were multigravida. In Control group 37% women were primigravida and 63% women were multigravida. The average duration of the third stage of labour was shortest in Misoprostol group (8.69) and highest in control group (9.42 min). There was no statistically significant difference between groups as determined by one-way ANOVA (p=0.580). The reduction in the amount of blood loss was statistically significant with Misoprostol as compared to Ergometrine (p= 0.04), Carboprost (p=0.027), and control (p=0.001) as shown in Table 1.

Table 1: Average blood losses

Drug	Mean blood loss (ml)	SD	P value
Misoprostol (Group A)	149.90	98.34	
Methylergometrine (Group B)	180.40	113.89	0.0216
Carboprost (Group C)	185.90	128.42	(significant)
Control (Group D)	199.70	122.78	

The decrease in haemoglobin is the least in the misoprostol group as compared to the other groups. A statistically analysis revealed that difference in the pre and post delivery haemoglobin was statistically significant with misoprostol as compared to methylergometrine ($p<0.001$), carboprost ($p<0.001$) and control ($p<0.001$) (Table 2).

Table 2: Comparison of difference in haemoglobin pre and post delivery

Drug	Pre delivery Hemoglobin(gm/dl) (Mean)	Post delivery Hemoglobin (gm/dl) (Mean)	Difference in Hemoglobin (gm/dl) (Mean ± SD)	P value
Misoprostol (A)	10.57	10.05	0.51±0.32	
Ergometrine (B)	10.51	9.75	0.78±0.47	<0.001
Carboprost (C)	10.69	9.81	0.88±0.54	(significant)
Control (D)	10.58	9.77	0.81±0.26	

Ten patients required additional doses for control of bleeding. Two patients from carboprost group, six of methylergometrine group and two from misoprostol group required additional doses. Twenty patients from control group required an oxytocic to be given of which twelve were given oxytocin infusion and eight were given intramuscular methylergometrine. Six patients from control group and four patients from ergomterine group needed blood transfusion. Only one patient from each group of misoprostol and carboprost needed blood transfusion. As regards to other side effects, misoprostol was associated with shivering and pyrexia in few patients, while nausea, vomiting, pain in abdomen and diarrhoea were more associated with methylergometrine and carboprostol. However all the side effects were acceptable and preferable to the excessive blood loss.

DISCUSSION

The present study was aimed to find out whether intravenous methylergometrine and intramuscular carboprostol can be substituted with per rectal misoprostol so as to avoid use of intravenous canulas and needles which is most relevant in developing country like India with a high incidence of HIV and HBsAg infections. Rectal route of misoprostol administration has practical advantage of ease of administration in the patients who are vomiting or unable to take orally or are under anaesthesia. In the present study the mean duration of third stage of labour was 8.69 mins in the Misoprostol groups compared to 9.28 min, 8.86 min and 9.42 mins in ergometrine, carboprost and control groups respectively. In a study by Vrunda Joshi when misoprostol was compared to methylergometrine, there was reduction in mean length of third stage from 4.18 min in methylergometrine group to 3.98 min misoprostol group.[7] Diab KM *et al* who compared rectal misoprostol with combined intramuscular oxytocin and ergometrine also had similar results.[8] In the present study, the mean blood loss was 145.90 ml in misoprostol group as compared to 180.40 ml, 185.90 ml and 199.70 ml in methylergometrine, carboprost and control groups respectively. The results of our study were comparable to the study conducted by N Prata.[9] J Harriott compared syntometrine with rectal misoprostol. Mean blood loss in misoprostol group was 180.1±120 ml and in syntometrine group was 197±176.97 ml which was similar to our study.[10] Nagaria compared misoprostol with intravenous ergometrine in two hundred women and concluded that although associated with side effects, misoprostol is a safe alternative to ergometrine in reducing the duration of third stage of labour and blood loss associated with it.[11] In recent study of 1620 women by Derman RJ, giving birth in a rural setting in India, misoprostol given after delivery was more effective than placebo in reducing the rate of postpartum hemorrhage and mean postpartum blood loss, but side effects of shivering and fever were more frequent with misoprostol than with placebo.[12] Pharmacokinetics suggests that the median onset of action of oral misoprostol (6 min, range 4-10 min) resulting in earlier clinical efficacy but in practice rectal misoprostol offers a longer duration of sustained uterine contractility even though its onset of action is slower.[10] In the present study, rectal misoprostol was found to be superior to intravenous methylergometrine, intramuscular carboprost for limiting the side effects while maintaining the uterotonic effects and can be considered as a uterotonic for third stage of labour and appropriately for various reasons like drug shortage, staff not knowing intravenous/intramuscular administration, storage and refrigeration problem etc.

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