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PREVENTION OF P.P.H: OXYTOCIN VERSUS MISOPROSTOL

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ABSTRACT

Objective: *The aim of this study was to compare the rectally administrated misoprostol 400 microgram with oxytocin 10 units I/V for the active management of the 3rd stage of labour for the prevention of primary postpartum haemorrhage and to assess the incidence and severity of the side effects of the both drug regimens.*
STUDY DESIGN: *Quasi-experimental study.*
STUDY PERIOD: *October 2006 – September 2007.*
SETTING: *Department of Gynaecology & Obstetrics Peoples Medical College & Hospital Nawabshah.*
MATERIAL & METHODS: *This study was carried out on 200 patients, misoprostol and oxytocin was given to 100 patients each. Women of any age and parity with singleton pregnancy delivered vaginally were included while those who refuses to give consent, with established PPH and have cesarean delivery were excluded .*
Data was collected on maternal and labour charactertstics. Active management of the 3rd stage of labour was done by giving misoprostol or oxytocin at delivery of the anterior shoulder of the baby and placenta was delivered by controlled cord traction and gentle uterine massage done after delivery of the placenta.
Women were observed up to one hour after the delivery and blood loss was collected in measured container. Treatment outcomes were recorded, like duration of 3rd stage, total blood loss and postpartum side effects of the drugs. Statistical analysis was performed by using chi square and student's t-test. A p-value of < .05 was considered statistically significant.
RESULTS: *No women in both groups had prolonged 3rd stage of labour. Mean 3rd stage duration of misoprostol group was 5.70 (SD = 4.25) and oxytocin group was 6.04 (SD = 4.25). Mean blood loss was greater in misoprostol group (p < 0.3). PPH developed in 36 % misoprostol group and 30 % in oxytocin group (p < 0.250). Uterine atony remained the commonest cause of PPH in both group. No patient in both groups had retained placenta. Postpartum side effects were more in the misoprostol group, 6 % had fever, 4 % had shivering, 1 % had nausea, 1 % had headache and 1 % had abdominal pain. While in oxytocin group, 7 % had fever and 2 % had shivering (p < 0.010).*
In both groups, primary PPH was well managed, without surgical intervention and none of the maternal death recorded.
CONCLUSION: *PPH occurred more frequently in the 400 mg rectally administrated misoprostol when compared to 10 units intravenous oxytocin although statistically not significant. Considering the safety of rectal route of misoprotal as compared to oral route administration, it just needs a dose adjustment for improving its safety.*

KEYWORD: Misoprostol, Oxytocin, Active management, 3rd stage, Prevention, Postpartum Haemorrhage

INTRODUCTION

Maternal mortality globally is estimated at 529,000 death/ year, a ratio of 400 maternal deaths / 100,000 live births. Postpartum hemorrhage remains the commonest cause of maternal death and accounts for one quarter of all maternal deaths world wide[1,2]. Considering the significance of problem WHO and FIGO recommended active management of the third stage of labor which include administration of uterotonics, controlled cord traction and uterine massage after delivery of placnta[3].This approach reduces the risk of PPH (40%), post partum anaemia, blood transfusion requirements; prolong 3rd stage

of labour and use of therapeutic drugs for PPH [4].

Multiple uterotonics like syntocinon, syntometrine, methergin and prostaglandins are in clinical use[5]. A world wide problem with oxytocin and ergot is their instability to heat, limiting their usage to cold climates or in developed countries with refrigeration and climate control. Apart from this they also require trained personnel and the use of syringes[6]. The same problem arises with the use of costly prostaglandins. Misoprostal a stable and low cost prostaglandin E1 analogue have potent uterotonic effect and its use does not need personal experty[7,8]. The present study designed to compare the effect of oxytocin and misoprotal, as the appropriate selection of drug can help to reduce the maternal mortality and morbidity associated with PPH in our set up.

PURPOSE OF STUDY

The purpose of this study was to ascertain the relative effectiveness of the misoprostol and oxytocin for the active management of the 3rd stage of labour, for the prevention of primary PPH and to assess the incidence and severity of the side effects of the both drug regimen.

MATERIAL AND METHODS

This was a quasi-experimental study carried out at Department of Gynaecology and Obstetrics Peoples Medical College and Hospital Nawabshah from October 2006 to September 2007.

Women of any age and parity with singleton pregnancy delivered vaginally were included in the study while those who had primary PPH, underwent cesarean section and refusal of consent were excluded.

The study was carried out on 200 women. The drugs used were prostaglandin E1 analogue misoprotsol (Cytotec) 400 mg per-rectally and oxytocin 10 units I/V that was given to 100 women each. The sampling procedure was a convenient sampling.

On admission into the labour room, labouring women were given detail information on the study protocol and consent taken. Complete history, general physical and systemic examination was done. Data was collected regarding maternal characteristics. Haemoglobin was measured pre delivery to assess the anaemic status.

Active management of the 3rd stage of the labour was done by giving either 400 mg misoprostol per-rectally or 10 units oxytocin intravenously at delivery of the anterior shoulder of the baby. The placenta was delivered by controlled cord traction (Brand Andrew's method) and gentle uterine massage done after delivery of the placenta.

After delivery of the baby, blood loss was collected by putting the clean fractured bed pan beneath the patient's buttocks to facilitate subsequent blood collection. Further, blood collection was done by placing swabs and pads beneath the patient's buttocks. Blood collection continued until one hour after delivery of the baby. Perineal trauma (episiotomy, perineal tears), vaginal and cervical trauma were noted and sutured; swabs were particularly saved and weighted. The women were carefully observed for the features of excessive blood loss.

In cases of the primary PPH due to uterine atony, patient managed immediately with administration of the Syntometrine (oxytocin 5 units plus ergometerine 0.5 mg) intravenously, if the patient was hypertensive then oxytocin 10 units intravenously given. If the bleeding remains persisted then bimanual uterine massage was done and 40 units oxytocin infused in 500 ml normal saline solution plus misoprostol 400 mg (two tablets) administered per-rectally.

One hour after delivery, collected blood loss from bed pan decanted into jug and measured, all pads and swabs used was weighted (1ml is equal to 1gm). The known dry weights of the materials used were subsequently subtracted form the measured weight and added to that blood measuring jug. Duration of 3rd stage, possible causes of primary PPH, total blood loss and any apparent side effects of the drugs were recorded.

Statistical analysis was performed, categorical variables were presented in the form of frequency and percentage, and analysis of association was made using chi-square test of significance. Quantitative data was presented in the form of mean and standard deviation. Comparison of means made by using student's t-test. A p-value less < 0.05 was considered statistically significant.

RESULTS

Table-I: BASELINE CHARACTERISTICS OF THE WOMEN

Characteristic	Misoprostol n = 100	Oxytocin n = 100	p-Value
AGE (Years) Mean ± SD	26.49 ± 5.50	25.60 ± 5.60	0.2
PARITY (n)			
Primigravida	31	42	0.010
1 – 4	50	40	
5 & Above	19	18	
BOOKING STATUS			
Booked	37	39	0.250
Un-Booked	63	61	
GESTATION AGE (In weeks) Mean ± SD	37.57 ± 2.826	37.79 ± 2.538	0.9
PRE-DELIVERY HAEMOGLOBIN (g/dl) Mean ± SD	9.53 ± 1.72	9.89 ± 1.77	0.9

Note: A p-value < 0.05 was considered statistically significant.

Table-II: LABOUR CHARACTERISTICS

Type of Vaginal Delivery (n)	SVD	Vertex Delivery with Episiotomy	Breech	Instrumental Delivery	p-Value
Misoprostol= 100 0.500	45	37	08	10	
Oxytocin = 100	43	37	05	15	

Note: SVD= Spontaneous vaginal delivery

RESULTS

Our study comprises 200 women, 100 from each group. Both groups did not differ significantly, in variables like age ($p < 0.2$), booking status ($p < 0.250$),duration of gestation ($p < 0.9$)and pre delivery haemoglobin ($p < 0.9$),while parity ($p < 0.010$) was significantly comparable (table-I). Table-II describes labour characteristics which were not found to be statistically significant ($p < 0.500$).Outcome after treatment (table-III) like duration of third stage ($p < 0.09$), cause of PPH ($p < 0.25$) and total blood loss ($p < 0.3$) did not differ significantly between the groups.

Both groups were significantly comparable with regarding to the side effects of the drugs ($p < 0.010$) (table-VI).

Table-III: OUTCOME AFTER TREAMENT

Characteristic	Misoprostol	Oxytocin	p-Value
THIRD STAGE DURATION (in minutes)	**n = 100**	**n = 100**	
Mean ± SD	5.70 ± 3.20	6.04 ± 4.25	0.9
BLOOD LOSS (ml)	**n = 100**	**n = 100**	
Mean ± SD	381.60 ± 356.05	334.39 ± 356.05	0.3
CAUSE OF PPH	**n = 36**	**n = 30**	
Uterine Atony	20	15	0.25
Retained Placenta	00	00	
RPOCs	02	03	
Genital Tract Trauma	14	12	

Table-1V: SIDE EFFECTS OF DRUGS

Side Effects	Misoprostol n = 13	Oxytocin n = 09	p-Value
Shivering	04	02	1.010
Fever	06	07	
Headache	01	00	
Nausea	01	00	
Vomiting	00	00	
Abdominal Pain	01	00	
Diarrhoea	00	00	

DISCUSSION

Haemorrhage is still one of the major cause of maternal mortality in the developing countries like Pakistan and PPH is its largest component. In Pakistan 5 – 10 % deliveries takes place in the hospitals and 24 % of births are attended by trained persons[9].The prediction of PPH using antenatal risk assessment is poor, only 40 % 0f women who develop PPH have an identified risk factor[10]. The importance of prevention, particularly where there is limited access to emergency medical facilities, is therefore obvious. Prevention of PPH include antenatal risk assessment and management that assure that anaemia and other health problems are treated, women must be in good health with appropriate management of labour especially of 3rd stage[11]. The misoprotal provided a potential benefit which may be greater in an environment in which personal experty is not up to the mark and conventional oxytocics are not available[7,12]. Regarding present study, no patient in either group had prolonged 3rd stage of labour, which is consistent with the study by Bambigboye A et al[12]. In one randomized comparison, active management was associated with meaningful reduction in clinically important outcomes, including PPH and severe PPH, postpartum anaemia and need for transfusion during the puerperium, as well as with a reduced risk for prolonged 3rd stage of labour[13].

Visual estimation of blood loss after delivery has been shown to underestimate true blood loss[14,15]. This problem was tried to overcome by using objective measurement of blood loss as primary outcome. The use of bedpan proved to be a valuable tool for educating delivery ward staff over the course of the study on the diagnosis and management of postpartum haemorrhage, but the value of its continued use outside a clinical trial is not yet apparent. In the present study, 36 % patients in misoprostol group, while 30 % in oxytocin group developed PPH, this is consistent with the study done by S.Tammy and colleagues[16].

The present study shows that, three main classes of variables are associated with the risk for primary PPH in both groups. The commonest cause was found to be the uterine atony 55.55 & 50 %, traumatic lesions of the genital tract 39 & 40 % and retained products of conception 5.55 & 10 %. There was no patient in either group who had retained placenta. The study by Chohan M.Arshod and Ansari Asma, found uterine atony in 39.5 % cases, retained placenta in 37 % and traumatic lesions of genital tract in 23 % cases[17]. The study by Reed found common causes of PPH were uterine atony, disruption of genital tract and placental abnormalities[18].

The measured mean postpartum blood loss in the present study is greater in misoprostol group. If the definition of PPH is upto 800 ml then 20 % in misoprostol group while 17 % in oxytocin group had PPH, while if definition is upto 1000 cc then 11 % in misoprostol group, while 6 % in oxytocin group and if blood loss is above 1000 cc then 5 % in misoprostol group and 7 % in oxytocin group had primary PPH. In the study by S. Tammy and colleagues when the 800 ml was threshold 17 % in misoprostol group and 18 % in oxytocin group and if computed blood loss is more than 1000 cc then 11 % in misoprostol group and 9 % in oxytocin group had primary PPH[16].

As found in previous studies on misoprostol, use of the drug was significantly associated with fever and shivering. These effects, however, were described as transient and did not result in any additional complication to the women[19,20]. This study had 04 (6 %) cases with fever ranging from 99 – 101 °F among which 02 patients had PPH, 4 % had shivering which occurred within 10 – 15 minutes of drug administration, it was transient for about 20 – 30 minutes, 1 % had headache, 1 % had nausea, both patients had PPH and 1 % had abdominal pain. No patient developed vomiting or diarrhoea.

In oxytocin group, 7 % had developed fever ranging from 99 – 101 °F among which 03 patients had PPH, 2 % developed shivering that was transient for 20 – 30 minutes and both had PPH. No patient developed

headache, nausea, vomiting or diarrhoea.

In a trial between 400 mg per-rectal misoprostol with 20 units intravenous oxytocin, side effects were infrequently found, postpartum shivering was 4.4 % in misoprostol group, while 4.21 % in oxytocin group. No nausea, vomiting or diarrhoea was noted in either group[16].

In addition to standard oxytocics, misoprostal was given for PPH management shows great potential in improving women's health outcomes after experiencing this obstetrical complication[2]. Our study findings suggests women who bled less overall had a smaller drop in hemoglobin and did not require additional interventions, such as blood transfusion, additional oxytocics, uterine packing, to manage their postpartum bleeding. No patient in both groups required surgical intervention like systemic pelvic devascularization/ emergency postpartum hysterectomy and no death was reported in the present study.

The rectal route used in this study would have several advantages. Gastrointestinal side effects might be reduced, administration to patients who have vomiting, or under anaesthesia would be possible as well as if used by inexperienced or untrained personal in community based settings with limited access to conventional injectable uterotonics could be appropriate.

CONCLUSION

The study shows that primary PPH is still a serious problem encountered in our daily obstetric practice. Therefore, prevention of PPH is most important. Though PPH occurred more frequently in 400microgram rectally administrated misoprostol but statistically not significant. Higher doses of rectally administrated misoprostol may be needed in our patient population to prevent PPH. Further investigation should focus on optimal dose and route of administration as well as side effect profile and safety.

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