ORIGINAL RESEARCH PAPER

Gynaecology

SUBLINGUAL MISOPROSTOL VS INTRA MUSCULAR OXYTOCIN COMPARATIVE STUDY – TO MINIMIZE BLOOD LOSS IN 3RD STAGE OF LABOUR

KEY WORDS: Misoprostol, Oxytocin, Post partum haemorrhage, labour.

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ABSTRACT

OBJECTIVE: To compare the efficacy of sublingual use of misoprastol 400µg with intra muscular use of 10units of oxytocin to minimize the blood loss in 3rd stage of labour.

MATERIALS AND METHODS: This prospective randomized controlled trial was carried with 120 pregnant women admitted in our OG department and they was randomized into 2 groups. 60 women in each group. Group A received 10 units of oxytocin intramuscularly and in Group B received 400µg of Misoprostol sublingually, immediately after delivery of the baby. The primary outcomes were measured in the form of amount of blood loss and fall of haemoglobin levels. Secondary outcome were measured for need of uterotonics, duration of 3rd stage of labour, manual removal of placenta, blood transfusion, PPH and side effects of the drugs.

RESULTS: The mean fall in haemoglobin was 1.08 ± 0.5 gms in oxytocin and 1.16 ± 0.64 gms in misoprostol group. This was statistically not significant. The amount of blood loss in oxytocin group was 200 ± 202 ml and in misoprostol group was 194 ± 181ml, which was also statistically insignificant. 10% of women in oxytocin group and 8.4% of women in misoprostol group needed additional uterotonics. Shivering and fever (≥38°C) were more common side effects in misoprostol group (8.3% in misoprostol and none of the women in oxytocin group).

CONCLUSION: This study concluded that use of sublingual misoprostol to reduce the blood loss in 3rd stage of labour is equally effective as intra muscular use of oxytocin. It can be used as an alternative to oxytocin in developing countries, where most of the deliveries are conducted by birth attendants and where it is difficult to maintain cold chain. Although shivering and pyrexia are more common side effects, they were transient.

INTRODUCTION:

Even in this Era of modern obstetrics maternal mortality still remains a challenge. Worldwide, it is estimated that per day 800 women die due to preventable cause associated with pregnancy and child birth. (WHO 2011)[1]. Nearly 99% of maternal death takes place in developing countries, mostly in rural areas, that too among poorer communities. Out of this 10-60% maternal deaths are due to Post Partum Haemorrhage (PPH) which can be easily prevented by active management of 3rd stage of labour and identification of risk factors[2]. Atonicity of the uterus is most common cause of PPH. Active management of 3rd stage of labor includes administration of prophylactic uterotonics after delivery of the baby, controlled cord traction and counter traction and uterine massage. Various uterotonic drugs like oxytocin, ergometrine and syntometrine have been used for prevention of PPH. They are given as injections requiring clean needle and syringes, which may increase the risk of injection associated diseases like hepatitis and HIV and they have to be refrigerated to maintain the potency.

Misoprostol is a synthetic prostaglandin E1 analogue and is an alternative for the prevention and management of PPH. It can be stored at room temperature, no need for refrigeration, easily available and cost effective. Misoprostol, selectively binds EP2, EP3 prostanoid receptors and cause effective myometrial contraction[3]. Various routes of administration like oral, vaginal, rectal and sublingual have been tried. Sublingual route of misoprostol has rapid on set of action, longer duration and reaches peak concentration 2 times more compared to oral route by avoiding first pass metabolism[4].

In developing countries like India, where most of the deliveries are conducted by semiskilled person or trained Dais at home, use of injectable uterotonic like oxytocin may not be possible in prevention and management of bleeding during delivery in poor resources settings. Misoprostol is easy to take, does not require temperature maintainence and there is no risk of injection related diseases[5].

AIM OF THE STUDY

The following study is designed to evaluate and compare the efficiency of 400µg of sublingual misoprostol with 10 units of intramuscular oxytocin in the active management of 3rd stage of labour to minimize the blood loss.

MATERIALS AND METHODS

Study Design: Prospective randomized controlled trial. The study was conducted in 120 pregnant women admitted in labour ward for vaginal delivery.

Study period: 8 Months

Women with singleton pregnancy, more than 36 weeks of GA, (Gestational age) with cephalic presentation, Hb more than 10gm/dl were included in this study.

Women with Severe Preeclampsia, Multiple Pregnancy, IUFD, Polyhydramnios, Epilepsy, Haemoglobin less than 8gm/dl were excluded.

STUDY PROCEDURE:

Eligible 120 pregnant women were enrolled into the study, after getting informed consent. They were randomly allocated into two groups by 1:1 ratio, 60 women in each group. Odd numbers were allotted into Group A (Oxytocin) and even numbers were allotted into Group B (Misoprostol).

Detailed History including age, parity, present and past medical and surgical illnesses were taken. Labour was monitored. Immediately after delivery women in Group A were given injection Oxytocin 10units intra muscularly and women in group B were given misoprostol sublingully 400 µg and instructed to keep under the tongue, until they were fully resolved. Blood loss estimation was done from the onset of 3rd stage of labor to the end of active bleed and immediate post partum period. Plastic blood collection drape was used as visual assessment of blood loss was inaccurate and give under estimates. Blood loss was measured using a jar with 100ml calibration, when profuse bleeding from episiotomy such patient were excluded. Spillage was mopped with pads and blood soaked pads were weighted in grams and dry weight of the pads were substracted (assuming 1g=1ml). This volume was added to measured blood.

Change in the Haemoglobin level and haemotocrit concentration was calculated by measuring the Hb level before and after delivery. As soon as the patient was admitted in the labor ward blood

sample was taken to estimate Hb level and Hct concentration and same repeated 24 hours after the delivery.

Primary outcome were measured as amount of blood loss and level of Haemoglobin fall. Secondary outcome were measured as duration of 3rd stage of labor, 3rd stage complications like post partumhaemorrhage, retained placenta, blood transfusion and use of additional uterotonics. Women were asked about side effects like nausea, vomiting, fever and shivering. Details of baby regarding birth weight, APGAR score, NICU admission were noted. The data analysis was done by the use of epidemiological information package (EPI 2010) developed by CDC Atlanta, with this, percentage, range, means, frequencies, standard deviations, 'P' and chi square test values were analyzed. To test the significant difference between quantitative variables Kruskul Wallis chi square test was used. The test of significance for qualitative variables, Yate's chi square test was used. To donate significant relationship 'P' value was taken as less than 0.05.

RESULTS:

In this present study demographic profile was comparable between 2 groups.

The commonest age group was 21-30 years. Mean age of Oxytocin and Misoprostol group was 25.8 ± 3.7 and26.4 ± 4.4. Nullipara was in majority in both groups with 43.30% in oxytocin and 48.30% in misoprostol group. BMI of the patient in oxytocin group 22.65 ± 3.55 and in misoprostol group was 22.95 ± 3.36 (Table -1). Most of the women in this study had spontaneous onset of labour and further accelerated with or without oxytocin. (70% in group A and 74% in group B had spontaneous onset of labour without any induction).

The birth weight of the babies were comparable in both groups (2.9 ± 0.39 kg in oxytocin, 2.82 ± 0.35 kg in misoprostol. The 5 minutes APGAR score in oxytocin group range from 7-9 minutes in oxytocin and in misoprostol group 6-9 minutes. The NICU admission in oxytocin group was 1.7%, 8.3% in misoprostol group. This was statistically not significant.

Table-1: Demographic Variables

Parameter	Oxytocin Group	Misoprostol Group	P – Value
Age distribution	25.8 + 3.7	26.4 + 4.4	0.5203
BMI	22.65 + 3.55	22.95 + 3.36	0.4249
Obstetric score – Primi	43.30%	48.30%	
Gravida 2 & 3	50.00%	45.00%	

Table-2: Primary and Secondary outcome

Parameter	Oxytocin Group	Misoprostol Group	P – Value
Blood loss (ml) (mean + SD)	200 + 202	194 + 181	0.8095
Hb Change (gm %) (mean + SD)	1.08 + 0.54	1.16 + 0.64	0.7791
Hb decline > 10 %	1.70%		0.5
Duration of 3rd stage in mts (mean	5.5 + 3.29	5 + 0.74	0.4075
Additional oxytocic (%)	10.00%	8.40%	

Table-3: Side effects

Parameter	Oxytocin Group	Misoprostol Group
Fever	1.70%	6.70%
Nausea	5.00%	5.00%
Retained placenta	1.70%	
Vomiting	3.30%	3.30%
Shivering	-	8.30%

DISCUSSION:

In this study the mean duration of 3rd stage of labor in oxytocin group was 5.5 ± 3.29 mints and in misoprostol group 5 ± 0.74. This was statistically insignificant (P-0.4075). The mean fall of haemoglobin concentration was 1.08gms ± 0.54 in oxytocin group and 1.16gms ± 0.64 in misoprostol group, which was statistically not significant. One case in oxytocin group had fall of Hb>10% due to retained placenta. Vimala et al showed[6] that alteration in the haemoglobin level within 24 hours of post partum was 0.78gm with misoprostol and 0.8gms in methyl ergometrine group (P>0.05) (Table-2).

In this study mean blood loss was 194 ± 181 in misoprostol group and 200ml ± 202 in oxytocin group and was statistically not significant. Cochrane systemic review described that there was no significant difference in mean blood loss and no post partumhaemorrhage in comparison between sublingual misoprostol with injectable oxytocics[5]. Our study compares with that of randomized controlled trial conducted by chaudhary et al[7], which showed blood loss was similar in oxytocin as well as in misoprostol group (146 ml & 153 ml). The incidence of post partumhaemorrhage (Blood loss > 500ml) was similar in both groups. (11% in oxytocin and misoprostol group.Bellad et al concluded that the incidence of PPH was 2.1% in oxytocin and 3.1% in misoprostol group (P=0.02)[9]

In our study 10% of women in oxytocin group and 8.4% of women in SL misoprostol group needed additional uterotonics either in the form of 20 units of oxytocin infusion, Methergin 0.25mg or PGF2 250µg. One women in oxytocin group needed blood transfusion because of retained placenta, no one in misoprostol group. In this study sheivering and fever were most common side effects (8.3% in misoprostol group and no one in oxytocin group. Vimala et al[6] found that 6.6% in SL misoprostol group had fever and 21.6% had shivering, but none in control group (Table-3). Baskest et al[8] found higher proportion of women with sheivering 65% and Pyrexia (12.5%) in oral misoprostol compared with oxytocin (1.03% fever). Nausea vomiting like other side effects were there in both groups though higher in misoprostol group failed to reach statistical significance.

CONCLUSION:

It is concluded that the sublingual misoprostol is as effective as oxytocin to minimize the blood loss in the 3rd stage of labour. Though fever and shivering are the most common side effects, they are transient. Misoprostol appears to be safe, cost effective and alternative option to prevent post partumhaemorrhage in resource poor setting.

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