ORAL MISOPROSTOL VERSUS INTRAMUSCULAR OXYTOCIN IN ACTIVE MANAGEMENT OF THIRD STAGE OF LABOUR: A COMPARATIVE STUDY

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ABSTRACT

BACKGROUND

Postpartum haemorrhage continues to be leading cause of maternal death worldwide. In low resource set up, where there is non-availability of oxytocin, oral misoprostol effectively reduces the haemorrhage in third stage of labour.

The aim of this study was to compare the effectiveness of oral misoprostol 600 mcg with intramuscular oxytocin 10 IU in the active management of third stage of labour.

MATERIALS AND METHODS

This was a prospective study performed at R. G. Kar Medical College and Hospital to compare the efficacy of oral misoprostol with intramuscular oxytocin in the active management of third stage of labour. In group A, 27(50%) women without risk of PPH were randomly allocated to receive 600 mcg misoprostol orally and in group B also 27(50%) women included by random allocation among total 54 total samples to receive 10 units of oxytocin intramuscularly within 1 minute of delivery. The efficacy and the safety of these two drugs were assessed on the basis of, percentages reduced in haemoglobin (Hb) and haematocrit (Hct) level in pre-delivery and 24 hours post-delivery, requirement of extra uterotonic agents, need for exploration and evacuation of uterus, blood transfusion requirement and duration of third stage of labour.

RESULTS

It was observed that oral misoprostol was as effective as intramuscular oxytocin in prevention of post-partum haemorrhage (PPH). There was no statistically significant difference in the duration of third stage of labour, requirement of extra uterotonics (misoprostol group 11.1% vs. 7.4% oxytocin group), and blood transfusion requirements in the two study groups.

CONCLUSION

Oral misoprostol 600 mcg appears to be as effective as intramuscular oxytocin 10 IU in reducing blood loss during the third stage of labour.

KEYWORDS

Active Management of Third Stage of Labour; Misoprostol; Oxytocin, Blood Loss; Side Effects; Haemorrhage.

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BACKGROUND

Despite advances in global healthcare, Maternal Mortality Rate (MMR) is consistently high worldwide. Majority of maternal mortality takes place in Sub-Saharan Africa and South-East Asia.[1] About 60% of maternal mortality takes place in postpartum period, immediately following delivery. Of these Postpartum Haemorrhage (PPH) continues to be the leading cause of maternal mortality.[1]

PPH is also not only cause of maternal mortality but also causes morbidity shock, pituitary necrosis, failure of lactation, loss of fertility, Sheehan's Syndrome and severe anaemia which sometimes necessitate large amount of blood transfusion, major operative procedures including hysterectomy and increased hospital stay causing unnecessary loss of man hours, loss of productivity and burden to the exchequer. To prevent PPH the WHO recommends Active management of the third stage of labour (AMTSL) in all women by 10 units Oxytocin IM. Recently the WHO conducted a trial in south-east Asia to access the efficacy 600 mcg oral Misoprostol as an effective alternative to 10 units Oxytocin IM in AMTSL. This would be particularly effective in low resource settings where facilities for injection might not be available, or facilities for safe storage of Oxytocin not viable. Several studies showed that efficacy of oral misoprostol 600 as good as IM oxytocin in active management of third stage of labour to prevent PPH. As misoprostol is inexpensive, heat stable, and can be used in orally, vaginally or rectally they can be good alternative to IM misoprostol specially in low resource setting like rural India. In this background, the aim of our study is to compare the efficacy of oral misoprostol 600 vs. Oxytocin 10 units IM in active management of third stage of labour.

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In low-resource settings, PPH is a leading cause of maternal death which is undoubtedly the most preventable. Preventable attempts to reduce deaths from postpartum blood loss have been guarded by the fact that many deaths occur in out-of-hospital set up or poor transportation measures for the patient to be transferred to an advanced health facility. This is why, the use of misoprostol to prevent or treat postpartum haemorrhage has drawn remarkable attention.[2]

A recent placebo-controlled trial performed in rural areas of India has shown that vaginal deliveries conducted by auxiliary nurse midwives at home or in village sub-centres, a significant decrease in PPH and other hazards was observed with uterotonics without other components of the active management of the third stage of labour - umbilical cord clamping and controlled cord traction.[3]

Aims and Objective

- To compare the blood loss by visual estimation in the third stage of labour of the two intervention Groups and also by changes in level of haemoglobin and haematocrit after comparing these in both pre-delivery and post-delivery of the two intervention groups.
- To observe whether additional uterotonics were used in the two intervention groups.
- To compare the side effects of the two intervention groups.

MATERIALS AND METHODS

Our study was conducted at labour room, in the department of obstetrics and gynaecology. R G Kar medical College hospital Kolkata for 1-year 2015 to 2016. All the patients admitted in maternity ward, department of obstetrics and gynaecology R. G. Kar Medical College, a tertiary care hospital in Kolkata.

This was across sectional study in which prospective observation was performed. Sample size had been calculated with help of Epi Info (TM) 3.5.3. EPI INFO which is a trademark of the Centers for Disease Control and Prevention (CDC).

The number of subjects required for this study was 53.783 ~ 54 with power 68%. Therefore, it is required to study 27 cases in one arm (50% misoprostol group A) and 27 cases in another arm (50% oxytocin group B) in the ratio 1:1.

The women who provided written and informed consent were enrolled for the study provided they met the inclusion and exclusion criteria. Inclusion criteria were singleton pregnancy, between 37 and 42 weeks of gestation, anticipated vaginal delivery, longitudinal lie, cephalic presentation, no high-risk factors, no significant medical illness.

Patients with history of medical disorders like asthma, epilepsy, heart or renal disease were excluded along with following conditions as well: haemoglobin <8 gm%, pregnancy induced hypertension, abruption placentae, marginal placenta previa/low lying placenta, multiple pregnancy, grand multipara, malpresentation, polyhydramnios, post caesarean pregnancy, prolonged labour, intrauterine fetal death, coagulation abnormalities were also excluded from the study. Institutional Ethical Committee's approval was taken before performing the study.

Active management of third stage of labour was done after allocating the patients in Group A (Misoprostol 600 orally) and Group B (Oxytocin 10 units IM) within 1 min of delivery of baby.

Out of the randomly selected 54 pregnant women active management of third stage of labour was done in Group A (50%) with misoprostol 600 mcg orally (n=27) and Group B (50%) with 10 units Oxytocin IM (n=27) after the delivery of the baby. Patients of the two groups of the study were also selected through Simple Random Sampling without replacement to avoid the selection bias. The parameters were observed during the study for both groups were Pulse rate and BP both before and after the third stage of labour, Duration of the third stage of labour (in min), The amount of blood loss (in ml), (using calibrated plastic blood collection container or drape) and blood were collected after drainage of liquor and delivery of baby and were continued till the completion of third stage of labour) Fall in Haemoglobin (Hb) level by comparing the Hb level during admission and after 24 hours of delivery, Whether blood transfusion was required. If yes, then how many cases in each group, whether any other Oxytocics were required or not. Laboratory investigations like Hb% and Haematocrit in both groups were performed as part of the study to reach a conclusion.

RESULTS

Statistical Analysis was performed with help of Epi Info (TM) 3.5.3. EPI INFO is a trademark of the Centers for Disease Control and Prevention (CDC). Using this software, basic cross-tabulation, inferences and associations were performed. Two tests were used to test the association of different study variables with the study groups. Z-test (Standard Normal Deviate) was used to test the significant difference between two proportions. t-test was used to compare the means. $p < 0.05$ was considered statistically significant.

The two groups of the patients in our study were matched for confounding variables like age, parity, socioeconomic status, religion, height, weight, BMI, booking status, gestational age, birth weight of baby, placental weight, and duration of third stage of labour.

Table 1 shows the distribution of demographic variables of two study groups where there were no statistical differences between two groups. Table 2 shows the comparison of study outcome between two groups (n=27 in each group i.e., misoprostol Group A and oxytocin Group B among 54 total patients). There were no significant differences in blood loss, Hb%, haematocrit, need of additional oxytocics between two groups of patients. In misoprostol group (n=27), there was statistically significant increased incidence of shivering.

Sl. No.	Parameter	Measure	Misoprostol (n = 27)	Oxytocin (n = 27)	t-test	p-Value (p <0.05)
1.	Age (in years)	Mean	24.48±3.53	25.03±3.95	2.72	0.43
2.	Weight (in Kg)	Mean	61.03±3.50	63.62±3.51	1.78	0.08
3.	Height (in cm)	Mean	159.73±5.09	160.86±4.77	0.84	0.20
4.	BMI (in Kg/m2)	Mean	24.32±1.07	24.58±0.68	0.38	0.53
5.	Period of Gestation (in weeks)	Mean	38.84±1.31	38.89±1.38	0.13	0.89
6.	Duration of Third Stage Of Labour (in hours)	Mean	5.07±0.26	5.11±0.32	0.46	0.64
7.	Birth Weight of Babies (In kilograms)	Mean	2.75±0.21	2.75±0.19	0.27	0.60
8.	Placental Weight (in grams)	Mean	542.96±34.86	548.33±30.41	0.60	0.50

Table 1. Distribution of The Demographic Variables of The Two Groups

Sl. No.	Parameter	Measure	Misoprostol (n = 27)	Oxytocin (n = 27)	t-test	p-Value (P<0.05)
1.	Amount of Blood Loss (in millilitres)	Mean	262.59±36.28	259.62±34.61	0.22	0.63
2.	Change in Haemoglobin (in g/dL)	Mean	0.78±0.29	0.84±0.32	0.72	0.47
3.	Level of Haematocrit (in%)	Mean	0.76±0.21	0.66±0.22	0.02	0.98
4.	Side Effects	Fever	3.7%	0.0%	1.94	0.0524
		Shivering	14.8%	0.0%	3.99	<0.001*
		Both	3.7%	0.0%	1.94	0.0524
5.	Pulse Rate (per min) (pre-delivery)	Mean	80.59±2.62	81.29±2.64	0.97	0.33
	Pulse Rate (per min) (post-delivery)	Mean	91.77±2.67	91.40±2.59	0.51	0.61
6.	Systolic BP (in mmHg) (pre-delivery)	Mean	119.03±4.30	119.18±4.19	0.12	0.90
	Systolic BP (in mmHg) (post-delivery)	Mean	124.81±3.15	125.11±3.43	0.33	0.74
7.	Diastolic BP (in mmHg) (pre-delivery)	Mean	75.33±3.13	74.51±3.35	0.92	0.36
	Diastolic BP (in mmHg) (post-delivery)	Mean	78.59±1.44	78.44±1.39	0.38	0.70

Table 2. Comparison of The Study Outcome of The Two Groups

DISCUSSION

The number of patients in each group was 27 to make the groups comparable with the proportion of patients in the groups as 1: 1. (Table-1) In other studies conducted in other places also the proportion of patients was as 1:1.[4-10]

Thus, as per other studies, the two study groups were matched during randomization for potential confounding variables like age, BMI, parity, religion, socio-economic status, booking status and gestational age at delivery. In our study, the two groups were also matched with the baseline prognostic labour characteristics like duration of third stage labour, mode of delivery, mean birth weight of the baby and the mean placental weight. There was no statistically significant difference in duration of third stage of labour between misoprostol group as well as oxytocin group.[4-10] As per the Table -2, there was no significant difference in mean heart rate, systolic blood pressure and diastolic blood pressure of the patients of the two groups before delivery and after delivery (p>0.05).

As per Table-2 the mean amount of blood loss (mean± S.D.) of the patients treated with misoprostol was 262.59±36.28 ml with range 200 - 350 ml and the median

was 260 ml. The mean amount of blood loss (mean± S.D) of the patients treated with oxytocin was 259.62±34.61 ml with range 210 - 350 ml and the median was 260 ml.

Though the mean amount of blood loss of the patients treated with misoprostol was higher than that of the patients treated with oxytocin, t-test showed that there was no significant difference between the two means (t52=0.30; p=0.76). There was no statistically significant difference in amount of blood loss observed in both groups. Similar observation was shown by Amant et al in a study where the mean blood loss in the misoprostol group was 115.5 ±39.5 ml and in oxytocin group, it was 118 ± 48.6 ml,[9] which was less than the blood loss in other studies i. e. Choudhury et al, Walley et al and Parson et al.[11-13] The reason behind might be the estimation of blood loss made visually in the index study whereas in other research works objective measurement of blood loss was taken into account by placing drape under the buttocks of mothers pre-delivery and removing it 1 hour post-delivery. Most of the studies i.e. (Gulmezoglu et al, Sultana et al, Singhal et al) were unable to find the statistical significance difference in the blood loss while comparing these drugs in AMTSL.[14,15,16]

3 (11.1%) patients in misoprostol group and 2 (7.4%) patients in oxytocin group had blood loss more than 300 ml which was the maximum blood loss estimated visually but visual estimation generally underestimates blood loss by 30%, which is clinically inadequate and has presented practical problem.

As in Table-2, t-test showed there was no significant difference in pre-delivery level of haemoglobin of the two groups (t_{52}=1.18; p=0.24). However, post-delivery level of haemoglobin of the patients treated with misoprostol was lower than that of the patients treated with oxytocin (t_{52}=0.80; p=0.42) but it was not significant. But there was no significant difference in change in haemoglobin of the two groups (t_{52}=0.72; p=0.47). Similar trend had been observed in other studies.[4-10]

Several other studies, Bugalho et al and Bajwah et al have also shwon that peripartum decrease in haematocrit level by at least 10% from pre- delivery to 24 hours post-delivery, is a better definition than the volume criteria of PPH.[17,18] In these studies, the effectiveness of the two regimes in the active management of the third stage of labour was primarily based on measurement of the degree of fall in haematocrit following delivery in the two study groups.

t-test showed there was no significant difference in pre-delivery mean level of haematocrit of the two groups (t_{52}=1.04; p=0.30). There was no significant difference between post-delivery mean level of haematocrit of the patients treated with misoprostol and that of the patients treated with oxytocin (t_{52}=0.12; p=0.90). Also, no significance difference was found for mean change in the level of haematocrit of the patients of the two groups (t_{52}=0.02; p=0.98). (Table-2)

These findings show that oral misoprostol and intramuscular oxytocin are more or less equally efficacious for AMTSL and these are consistent with data from another similar comparative study by Gulmezoglu et al.[14]

In our study test of proportion showed that proportion of patients with additional oxytocics or uterotonics who were treated with misoprostol (11.1%) was higher than that of the patients treated with oxytocin (7.4%) (Z=0.90; p=) but it was not significant.

In a similar comparative study performed by Parsons et al has observed less use of additional uterotonics inthe misoprostol group in comparison to the oxytocin group (7.1% vs 9.3%), probably due to use of increased dose of misoprostol (800 mcg) in their study as compared to the index study but the result was not significant.[16]

Fortunately, blood transfusion or uterine exploration/evacuation was not required by any women in two groups as they were well booked and had high haemoglobin and haematocrit in pre- delivery. Similarly, Choudhury et al showed in a comparative study that 1.9% of women in misoprostol and 1.1% of women in oxytocin needed blood transfusion.[14] Probably because of lesser number of women had participated in our study there was no requirement of blood transfusion in index study.

There were no significant side effects observed either in misoprostol group or oxytocin group in this study. All the adverse effects were mild, and they were self-limiting. In this study, among the two uterotonics it was revealed that the presence of side-effects only in misoprostol group. Test of proportion showed that proportion of patients with shivering within 1 hour postpartum who were treated with misoprostol (14.8%) was significantly higher than that of the patients treated with oxytocin (0.0%) (Z=3.99; p<0.001). But though the proportion of patients with fever and shivering with fever (max temp 100^{o}F) who were treated with misoprostol (3.7%) was higher than that of the patients treated with oxytocin (0.0%), no significant difference was found among them (Z=1.94; p=0.05). (Table-2) These findings are also consistent with that of Gulmezoglu et al.[14]

CONCLUSION

It is concluded that the misoprostol which is as effective as oxytocin can be used for the active management of third stage of labour, with minimal self-limiting side effects. Misoprostol is easily available, more stable, has self-limiting side effects and useful in low resource settings. A research work based on a considerably large number of patients may be conducted to get a better idea regarding the outcome.

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