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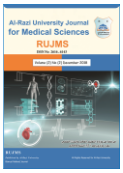

Misoprostol versus Oxytocin for the Prevention of Postpartum Haemorrhage among Women in Al-Thowrah Hospital, Sana'a City, Yemen

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Abstract

Background: *PPH is the leading cause of direct maternal death in developing countries. PPH is a real complication that should be studied and dealt with seriously.* ***Aim****: To compare the safety and efficacy of rectal misoprostol versus intravenous oxytocin in preventing PPH.* ***Methods****: A randomized control study was done for 6 months from 1st of May to 31 of October 2017. In the labor room of the obstetric unit at AMGH in Sana'a. The subjects were included 98 women divided into two groups: group I included 51 women were received 600 µg (3 tablets) misoprostol rectally and 2ml saline in Ringers lactate intravenously as placebo. Group II: included 47 women were received 30IU intravenous oxytocin in Ringers lactate and two lactose tablets rectally as placebo. The collected data for every woman, Patient kept under close observation for 4 hours, for any vaginal bleeding, nausea, vomiting, fever, shivering and etc. Then estimated of blood loss and side effects of uterotonic drugs by direct observation.* ***Results:*** *Incidence of PPH in the misoprostol group 23.5% was more than that found in the oxytocin group 6.4% (p-value<0.05). Risk factors were not significantly different in the two groups, except the prior history of PPH which is more in group I. Side effects: Shivering was more incidences in group I, 54.9% than group II, and 4.3%. While nausea was found in one case 2.1% in group II and no case found in group I. Pyrexia and vomiting were not found in the two groups. Additional uterotonic TTT was used to prevent PPH, within 4 hours of observation: 17.6% of group I needed 3 tablets misoprostol rectally and 6.4% of group II needed 30IU oxytocin infusion was added to prevent PPH.* ***Conclusion:*** *Misoprostol 600µg given rectally is less effective to control the PPH in the management of the third stage labour.*

Keywords: Safety; Efficacy; Postpartum haemorrhage; Misoprostol; Oxytocin

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Introduction

Postpartum hemorrhage (PPH) is one of the most important causes of maternal mortality[1]. PPH is a potential obstetric catastrophic contribute a major cause of maternal death. Every year, about 210 million women become pregnant. PPH is one of the major complications of pregnancy, accounting for 14 million cases annually. Of these, it is estimated that around 140,000 women die, resulting in a case fatality rate of 1%[1] adequate attention to this complication can mean the difference between life and death[2] Maternal mortality is high in

developing countries. In Yemen, it represents 385/100000 of live birth which is very high incidence.

The major cause of it is PPH is a significant cause of maternal morbidity and mortality. Most PPH are caused by uterine a tony and occur in the immediate postpartum period[3]. PPH is the leading cause of direct maternal death in developing countries. The incidence of postpartum hemorrhage may vary from less than 5% to more than 10%. The figures remain at least 100 times higher than those in developed countries[4] Although risk factors may increase a woman's chances of developing postpartum hemorrhage, two-thirds of cases of PPH occur without any predisposing factors. Several drugs reduce postpartum hemorrhage by causing the uterus to contract. Ergot derivatives have been used for decades, although oxytocin is the drug of choice in some centers[5]. Prophylactic use of an oxytocic agent after delivery of the infant has been shown to reduce the incidence of postpartum haemorrhage by 40%.

The most common practice in the United States for the prevention of PPH is intravenous oxytocin administration after placental delivery[6]. Now Im 10 IU oxytocin is used also several prostaglandins are used as second or third line agents. These drugs, however, must be refrigerated to remain effective. Moreover, most uterotonics must be administered by injection, which requires sterile equipment and training in safe administration, prerequisites unavailable for most women delivering in low-income countries [5].

Misoprostol was shown in several randomized controlled trials to be effective in preventing PPH because of its strong uterotonic effects. Moreover, misoprostol is inexpensive and easy to administer[6.] Misoprostol, a prostaglandin E1 analog, is heat stable and can be administered orally, rectally, or sublingually. Oral and rectal misoprostol has been used for routine management of the third stage of labour.

The main side-effects have been shivering and pyrexia, which is dose-dependent. Physiological studies have also shown a more rapid onset of uterine contractions following syntometrine than misoprostol after delivery. Misoprostol has been widely recommended for the prevention of PPH when other methods are not available[7,8]. Community-based distribution of misoprostol in Indonesia reduced the perceived frequency of excessive bleeding and the need for emergency referral for PPH compared with data from a control area where misoprostol was not available[8,9.]

Aim of the study

To compare the safety and efficacy of rectal misoprostol versus intravenous oxytocin in preventing PPH.

Subjects and Methods

This study was carried out in the obstetric unit at Al-Thawrah Modern General Hospital (AGMH), Sana'a. The hospital is the largest public and referral hospital in Yemen, it receives all obstetric emergency cases referred from different locations. The department of obstetrics and gynaecology has all facilities that serve the patients including blood bank, laboratory and a well expert staff. A randomized clinical trial study was undertaken among women admitted to labor room in AGMH from 1 May to 31 October 2017. After taken detail history 98 women were divided into two groups (Group I included 51 women were given 3 tablets

misoprostol (600Mg) rectally +5ml saline in 500cc Ringer lactate after clamping of the umbilical cord, and group II included 47 women were given 30 IV oxytocin in 500cc Ringer lactate +2 lactose tablets rectally after clomped of the umbilical cord).

Additional uterotonic treatment was used to prevent PPH within 4 hours was recorded. The exclusion criteria were all women in active labor with gestational age ≤34 weeks, all women in active labour who hypersensitive to prostaglandin, any patient indication for caesarean and any patient might be her delivery ended by caesarean.

The inclusion criteria were the women with maternal age <20-35 years, gravidity, parity, special habits, ANC, gestational age ≥ 34 weeks , PET, APH, anemia, past history of PPH, twin pregnancy, polyhydramnios , patient on Mg So4, women in active labour without any contraindication for vaginal delivery , past history of PPH and previous history to caesarean.

Detail history was taken from the patient regarding the inclusion criteria mentioned before. The patient keeps under close observation, fetal and maternal monitoring was done until the patient was delivered. Then patient who selected to given 3 tablets misoprostol (600Mg) rectally put in a group I, and 30 IV infusion oxytocin in group II. The placenta is delivered by Brandt –Androw method, a uterine massage done, placenta, perineum, and vagina were examined. Any tear or episiotomy was a stitch. Visual estimated of blood loss was made by the attending resident and the number of a sheet was changed, uterine massage was done every 10 minutes, vital signs checked every 30 minutes. The patient kept under close observation for 4 hours, for any vaginal bleeding, nausea, vomiting, fever, shivering and etc. Data were analysed using SPSS version 19 for frequency and cross tabulation. Chi-square test was applied to compare the categorical variable among groups. P-value <0.05 was considered significant.

Results

The majority of age among the two groups was between (20-25 years) 87.2% in group II, 83.3% in group I. and age >35 years old(11.8%) in group I and (10.6%) in group II. >20 years age represent 2.1% in group II and 2.0% in group I. The majority of cases were khat chewers in the two groups: 76.5% in group I and 68.1% in group II, while non-Khat chewers was 31.9% in group II and 23.5% in group I. As regards to smoking, the majority of cases were non- smokers in both groups 84.3 % in group I and 83% in group II, while smokers 17.0% in group II and 15.7 % in group I. The majority of cases were multipara in both groups (61.7%) in group II and 60.8% in group I), the next common was among primipara 29.8% in group II and 29.4% in group I. Most of the patients were gestational age between (37-40 weeks) 98% in group I and 97.9% in group II then>37 in 2.1% in group II and 2.0% in group I and most of the patients had regular ANC in both groups 60.8% in group I and 59.6% in group II, while 40.4% in group II and 39.2% in group I had irregular ANC.

Analysing risk factors of PPH in the two groups showed that 3 cases in each group had preeclampsia which represents 6%, while. MgSO4 and anemia were found in one case in each group. Others risk factors were one case twin and one case polyhydramnios in group II, and no any case found in group I. The most common factor affecting the study was a prior history of PPH which was more

in group I 13.7% than 2.1% in group II. Risk factors were not significantly different in the two groups, except the prior history of PPH which is more in group I. Table 1.

As regards to the side effects of both drugs, the findings of the study showed that in group I, the most common side effect was found within 4 hours was shivering in 28 cases 54.9%, and nausea, vomiting, and pyrexia were not found in any case while .in group II: nausea was found in one case 2.1%, shivering in 2 cases 4.3%, and vomiting and pyrexia were not found in any case. A significantly different in shaving was found, but not found in nausea among groups. Table 2.

The proportion of PPH (blood loss >500 ml) within 4 hours was more in the misoprostol group (23.5%) than in the oxytocin group (6.4%) with p-value<0.05. Figure 1. The additional uterotonic drug was used to prevent PPH, within 4 hours of observation showed that 17.6% of group I needed 3 tablets misoprostol rectally and 6.4% of group II needed 30IU oxytocin infusion was added to prevent PPH with p-value<0.05. Figure 2.

Table1: Distribution of risk factors among both groups

Risk factors	Group I		Group II		Chi-square	P-value
	F	%	F	%		
PET	3	6	3	6	-	-
Tocolytic Mgso4	1	2.0	1	2.1	0.005	0.941
Anaemia	1	2.0	1	2.1	0.005	0.941
Twins	0	0.0	1	2.1	-	-
Poly -hydromnious	0	0.0	1	2.1	-	-
Prior Hx of P.PH	7	13.7	1	2.1	4.338	0.036

Table 2: Side effects within 4 hours of observation among groups

Side effects	Group I		Group II		P-value
	F.	%	F.	%	
Nausea	0	0.0	1	2.1	0.295
Shivering	28	54.9	2	4.3	0.000
Total	**28**	**54.9**	**3**	**6.4**	

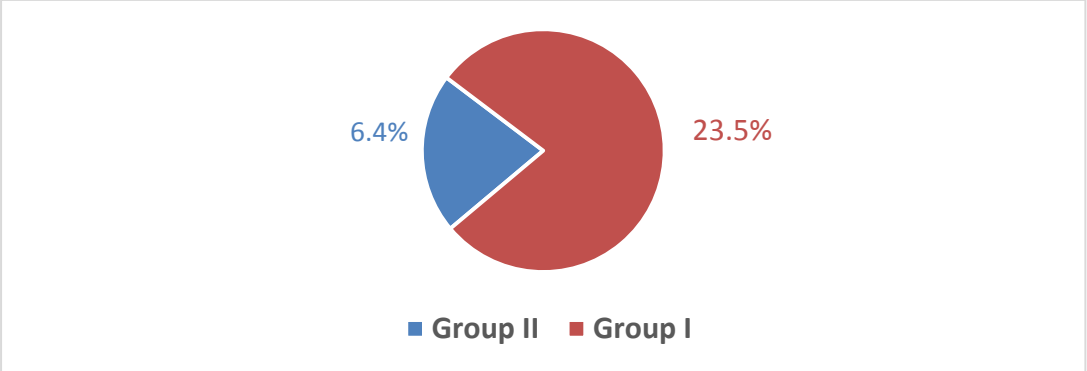

Figure 1: The incidence of PPH among both groups

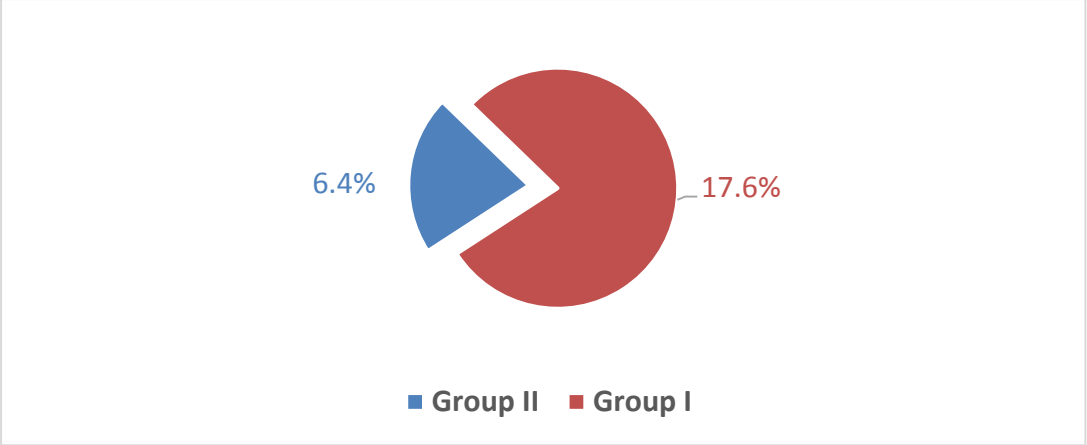

Figure 2: The additional uterotonic drugs to prevent PPH among groups

Discussion

In developing countries, PPH is regarded as one of the major causes of maternal mortality and morbidity[10, 11.] Consequently, the active management of the third stage of labour should be practiced along with the routine use of intravenous oxytocin. To add for oxytocin and to prevent postpartum hemorrhage misoprostol was chosen because it has similar advantages but with minimal side effects, low shelf life, inexpensive and easily available. It is easy to use and does not require special storage conditions (i.e., can be stored easily at room temperature; is thermostable and light stable; does not require specific conditions for transfer) and has a shelf life of several years. These advantages make it a useful drug in reducing the incidence of postpartum hemorrhage in developing countries.[12,13,14,15,16].

Our study showed that the proportion of PPH (blood loss >500 ml) was more in group I (23.5%) than group II (6.4%) which is going with the previous studies carried out in different countries under different studies. [10,17,18]

In Gerstein, Wing in California at 2001 the study SAS performed on 325 women. 154 women received 2 tablets (400µg) misoprostol rectally and 161 women received 20 IU oxytocin in Ringers' lactate intravenously, the incidence of PPH in misoprostol group 21% was more than oxytocin group 15%[17], which is similar to our study.

In Turkia, 1606 women were randomly grouped to receive10 IU oxytocin plus rectal misoprostol, Rectal Misoprostol, Oxytocin 10 IU, 10 IU oxytocin plus methylergometrine. Where the result of PPH was 9.8% in the group received only rectal misoprostol compared with less incidence of PPH 3.5% in the group received oxytocin and methylergometrine.[18]

In Blum et.al. (2010) 80% of women were 407 women received 800µg sublingual misoprostol and 402 women received 10 IU oxytocin intravenously. The two groups did not differ in baseline demographic characteristic (age, parity, Hb & education).[19] The incidence of PPH was similar in two groups (11% in misoprostol and 10% in oxytocin) this not going with our study, the possible explanation for that is the small sample size, and less dose of misoprostol was used in our study.[19]

A study done in South Africa compared a combination of intramuscular syntometrine injection and oxytocin infusion to rectal misoprostol and found that those who

received misoprostol had a statistically significant reduction in bleeding and further medical cointerventions to control the bleeding (6% versus 34%)[20].

In study performed by Karkanis et al. (2002)[20] among 240 women who randomly received 400 micrograms rectal misoprostol after delivery of the infant or parenteral oxytocin (5 units intravenously or 10 units intramuscularly) with the delivery of the anterior shoulder. No difference in Hb was observed between the groups and also the duration of the third stage of labor did not differ between the two groups. Those criteria are not considered in our study. In our study, No severe blood loss had occurred in both groups, these findings were similar to Winikoff study[21]. The change Hb concentration is not involved[21].

Winikoff et al (2009)[21], in his study: the total number of women was 978; 488 women received 800µg sublingual misoprostol and 490 women received 40 IU oxytocin IV. The incidence of severe blood loss was rare ≤ 1% of women in both groups, bleeding was controlled in 90% in misoprostol group and 96% in oxytocin group within 20 minutes additional blood loss was 30% in misoprostol and 17% in oxytocin groups.

Investigation for the WHO concluded that 600µg of oral misoprostol is less effective than parenteral oxytocin in minimizing blood loss as defined by the incidence of discrete outcome (Measured blood loss >1000 ml) or use of additional uterotonics[21]

Regarding the side effects, the shivering was more frequent in group I, 54.9% as compared with 4.3% in group II. This result was similar to other studies [9,19, 22, 23,24,]. No, any cases found with nausea, vomiting, and pyrexia with misoprostol group and only one case with nausea 2.1% in the oxytocin group. The result of pyrexia was different from other studies[9,19,22,23,24]. A study of 800µg oral misoprostol compared with IM Oxytocin was found a higher rate of shivering and fever with misoprostol than oxytocin[25]. In a group, I more uterotonic drug than group II was needed. misoprostol tablets rectally were given to group I in 17.6%, while IV infusion oxytocin was given to group II in 6.4%. This result similar to other studies [17, 18].

Conclusion

Misoprostol 600µg given rectally is less effective to control the PPH when utilized as a pharmacologic agent in active management of the third stage labor, as measured by visual estimation with 4 hours. The usual side effects of shivering were noted frequently. Oxytocin still the effective treatment of prevention of PPH.

Recommendations

A number of measurements can be done to determine the possible risk factors of PPH and this implies implementation of a number of measurements were including: 1) Antenatal care visits for follow up of pregnancy to predict cause at high risk for PPH and manage it accordingly, 2) Most PPH can be avoided by delivery of patients at hospital and every effort should be made to decrease blood loss, 3) The staff should be qualified & have good training for active management of the third stage of labor to decrease incidence of PPH, 4) Improvement in health care services and increase the number of blood banks by the Ministry of health allowed more supplies of blood to patients.

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