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Research Article

**COMPARISON OF THE MEAN BLOOD LOSS WITH SUBLINGUAL
MISOPROSTOL VERSUS INTRAVENOUS OXYTOCIN IN LOW-RISK
FEMALES UNDERGOING NORMAL VAGINAL DELIVERY****Zahra Azeem¹, Iffat Naheed², Sara Ejaz³, Khadija waheed^{4*}, Amna khanum⁵,
Asim Khan⁶**^{1,4,5}MBBS, FCPS, Assistant Professor of Obstetrics & Gynaecology, KEMU/ Lady Aitchison Hospital, Lahore²MBBS, FCPS, Associate Professor of Obstetrics & Gynaecology, KEMU/ Lady Aitchison Hospital, Lahore³MBBS, FCPS, Professor of Obstetrics & Gynaecology, KEMU/ Lady Willingdon Hospital, Lahore⁶MBBS IH 299 Falcon complexes Lahore, Pakistan**Abstract:**

Background: Oxytocin and Misoprostol are considered to be the two most effective drugs in preventing PPH. But contradiction in literature was observed. So to confirm whether misoprostol is more effective than oxytocin for prevention of PPH, we conducted this study.

Objective: To compare the mean blood loss with sublingual misoprostol versus intravenous oxytocin in low-risk females undergoing normal vaginal delivery

Material & Methods: This randomized control trial was conducted at Unit IV, Department of Obstetrics and Gynecology, Lady Aitchison Hospital, Lahore. The duration of the study was six months from July 2016 to December 2016. The non-probability purposive sampling technique was used. The patients were randomly divided into two groups by using lottery method. The patients in group M received misoprostol 400µg sublingually and patients in group O, 20 units of oxytocin immediately after delivery of the baby. No Additional Oxytocin injection was given. Uterine massage was done if obstetrician noticed poor uterine contractions. Blood loss was estimated separately by measuring the blood in the kidney tray.

Results: In this study the mean age of the patients was 29.33±7.06 years with mean gestational age of 38.74±1.22 weeks. The mean value of total blood loss of the patients was 429.97±135.06ml. In this study the value of total mean blood loss in misoprostol group was 356.29±84.89 ml and the mean value of total blood loss in oxytocin group was 503.66±135.98 ml. Statistically there is highly significant difference was found between the study groups and total blood loss of the patients i.e. p-value=0.000

Conclusion: Our study results concluded that misoprostol showed more effective and satisfactory results as compared to intravenous oxytocin in low-risk females undergoing normal vaginal delivery.

Keywords: Blood Loss, Sublingual Misoprostol, Intravenous Oxytocin, Vaginal Delivery

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INTRODUCTION:

Postpartum haemorrhage (PPH) contributes enormously to maternal mortality. Its incidence varies from 5-10% in general population. According to WHO, PPH is responsible for one third of maternal mortality [1]. Oxytocic agents used to prevent PPH are oxytocin Ergot alkaloids, ergonovine (ergometrine), methylergonovine, syntometrine (5IU oxytocin + 0.5mg ergometrine) & prostaglandins [2, 3]. Surgical interventions includes surgical compression sutures, external aortic compression, stepwise devascularization (uterine artery followed by internal iliac artery) selective arterial embolization, intrauterine packs and non-pneumatic anti shock garment, and recombinant activated factor VI [4-6]. Oxytocins is an injectable uterotonic, unstable at high temperature, requires proper storage facilities and have side effects like tachycardia, hypotension, nausea, vomiting, negative inotropic, antiplatelet, antidiuretic effects, and require trained birth attendants for its administration. Misoprostol is PGE1 analogue, selectively binds with prostanoic receptors. It can be given in oral, sublingual, rectal routes.² It has longer half-life, noninvasive administration and stable at room temperature. But have dose related shivering and pyrexia [3,7-9]. A study from Iran (2009) demonstrate that sublingual misoprostol at low dose (400ug) is as effective as 20 IU of oxytocin infusion. The blood loss was significantly high in oxytocin group that misoprostol (673.9 ml Vs 608.9ml) respectively [10]. Another study from Nigeria (2011) showed that reduction in blood loss in group receiving misoprostol was significantly less than oxytocin group (58.2 ± 20.7 vs 80.5 ± 26.8 ; P-value = 0.02). Thus it was concluded that Sublingual misoprostol was more effective than IV oxytocin infusion in reducing blood loss at cesarean section [11]. But a recent trial has shown that mean blood loss was significantly lower in oxytocin group as compared to misoprostol (114.28 ± 26.75 versus 149.50 ± 30.78 ml; $p = 0.000$) [12]. Rationale of this study is to compare the mean blood loss with sublingual misoprostol versus intravenous oxytocin in females undergoing normal vaginal delivery. In routine oxytocin is most common drug in use. But it was found that misoprostol is more effective in preventing excessive blood loss and development of PPH and prevent patients undergoing complications due to PPH. But contradiction in literature is also observed. This study was planned to compare the mean blood loss with sublingual misoprostol versus intravenous oxytocin in low-risk females undergoing normal vaginal delivery.

MATERIALS AND METHODS:

This Randomized Controlled Trial was conducted at department of Obstetrics and Gynecology, Lady Aitchison Hospital, Lahore, with duration of 6 months from July 2016 to December 2016. After taking approval from hospital ethical committee, 200 patients were included from labour room. Informed consent and

demographic details (name, age gestational age, and parity) was obtained. All the low risk multiparous patients (as per operational definition), parity <5, delivering alive full term babies (gestational age >36 weeks on LMP and ultrasound) were included in the study. All the females with gestational diabetes (GTT > 40IU), PIH (BP >140/90mmHg), preeclampsia (PIH with proteinuria +1 on dipstick method) or eclampsia (convulsions), oligohydramnios or polyhydramnios, normal fetus without congenital anomaly, normal BMI (19-25kg/m²), patients with placental abruption (accreta or previa) on USG, with previous cesarean sections and with twin pregnancy were excluded from the study. Then patients were randomly divided into two groups by using lottery method. The patients in group M received misoprostol 400µg sublingually and patients in group O, I/V stat 20 units of oxytocin immediately after delivery of the baby. No Additional I/V oxytocin injection were given. Uterine massage was done if obstetrician noticed poor uterine contractions. After the procedure all participants were cleaned vaginally by the obstetricians with sterile gauzes and blood clots retrieved were included in the blood loss estimation. Blood loss was estimated separately by measuring the blood in the kidney tray; drapes and gauze pieces used for procedure. It was assumed that 1 gram weight is equal to 1ml. Postnatal blood loss was measured by doctor during first 24 hours of delivery. Total blood loss was estimated. All this information was recorded on proforma (attached) for the analysis.

Data was entered and analyzed in SPSS version 20. The quantitative data (age, gestational age, blood loss) were presented in the form of mean \pm SD. The qualitative data (parity) was presented in the form of frequency and percentage. Independent sample t-test was used to compare the mean blood loss in both treatment groups. p-value ≤ 0.05 was taken as significant.

RESULTS:

Total 200 cases were enrolled in this study. The mean age of the patients was 29.33 ± 7.06 years with minimum and maximum ages of 18 & 40 years respectively. In this study the mean gestational age of the patients was 38.74 ± 1.22 weeks with minimum and maximum values of 37 & 41 weeks respectively. The study results showed that the mean value of total blood loss of the patients was 429.97 ± 135.06 ml with minimum and maximum values of 203 & 746 ml respectively. In this study the mean blood loss in misoprostol group was 356.29 ± 84.89 ml and the mean blood loss in oxytocin group was 503.66 ± 135.98 ml. statistically there is highly significant difference was found between the study groups and total blood loss of the patients i.e. p-value = 0.000. In patients of age <30 years, the mean blood loss in misoprostol group was 354.06 ± 81.56 ml and the mean blood loss in oxytocin group was 525.56 ± 128.65 ml.

TABLE#1: DESCRIPTIVE STATISTICS OF AGE, GESTATIONAL AGE AND BLOOD LOSS COMPARISONS

		<i>Mean</i>	<i>S.D</i>	<i>Range</i>
<i>Age (years)</i>		29.23	7.06	18-40
<i>Gestational age (weeks)</i>		38.74	1.22	37-41
<i>Comparison of mean blood loss in both study groups</i>				
<i>Blood loss (ml)</i>	<i>Misoprostol</i>	356.29	84.89	p-value < 0.011
	<i>Oxytocin</i>	503.66	135.98	

DISCUSSION:

Post-partum haemorrhage (PPH) accounts for 25% of maternal deaths [13]. In Pakistan haemorrhage is the most common cause of maternal mortality [14,15]. Current approaches to address PPH at the community level focus on reducing the incidence of PPH, but often fail to address the issue of PPH prevention [16]. Administration of misoprostol, a synthetic prostaglandin that has effects similar to those of oxytocin, has been proposed as an alternative way to prevent postpartum hemorrhage in resource-limited settings [17,18]. Oxytocin, a hormone that stimulates uterine contractions and limits uterine bleeding after birth, is the standard of care for prevention of PPH during the third stage of labor [19]. The use of oxytocin in low-income countries, however, has historically been limited by a number of factors including a perceived requirement for administration by skilled personnel, cold chain storage, and a requirement for sterile syringes and needles [17,20]. In our study the mean blood loss in misoprostol group was 356.29 ± 84.89 ml and in oxytocin group was 503.66 ± 135.98 ml. statistically highly significant difference was observed between both the groups i.e. p-value=0.000 Our study results showed that misoprostol is an effective drug in comparison with oxytocin in patients with normal vaginal delivery. Zhao et al in their study comparing 600 µg oral misoprostol with oxytocin (20 U intrauterine plus 20 U IV) found misoprostol more effective in the reduction of postpartum bleeding [21]. Acharya et al comparing the effectiveness of 400 µg oral misoprostol with 10 U IV syntocinon found misoprostol to be as effective as intravenous syntocinon in the reduction of intraoperative blood loss [22]. Vimala et al. found sublingual misoprostol to be as effective as oxytocin [23]. In a placebo-controlled double blind study, comparing 800 µg oral misoprostol with 20 U oxytocin infusion after initial administration of 5 U of IV oxytocin, Lapaire et al found misoprostol to be as effective as oxytocin in reducing postoperative blood loss [24]. Meta-analyses of randomized trials shows that misoprostol administered by sublingual route as compared with IV oxytocics may be equally effective

in prevention of PPH, but has more side effects like shivering, pyrexia but it is dose related [25].

Esther C. Atukunda et al demonstrated that sublingual misoprostol is inferior to oxytocin for prevention of primary PPH in women undergoing uncomplicated vaginal deliveries at a publically funded regional referral hospital in southwestern Uganda [17].

A similar study comparing lower dose sublingual misoprostol with oxytocin 10 IU found a non-significant decrease in blood loss with oxytocin at 1 h postpartum [26]. A small study (n = 60) compared sublingual misoprostol 600 µg to syntometrine in place of oxytocin, and found no difference in PPH between the two groups [27]. In contrast, another study also comparing low-dose sublingual misoprostol 400 µg with oxytocin 10 IU found misoprostol more effective in prevention of PPH at 2 h postpartum. Importantly, that study used a powdered sublingual formulation of misoprostol and was unintentionally unblinded because of lack of proper placebos [28].

But a recent trial has shown that mean blood loss was significantly lower in oxytocin group as compared to misoprostol (114.28 ± 26.75 versus 149.50 ± 30.78 ml; p = 0.000) [12]. Jennifer Blum, et al concluded in their study that Misoprostol is clinically equivalent to oxytocin when used to stop excessive post-partum bleeding suspected to be due to uterine atony in women who have received oxytocin prophylactically during the third stage of labour [29]. Lokugamage compared rectally administered misoprostol (800 mcg) versus oxytocics (combined syntometrine and oxytocin infusion) for the treatment of primary PPH, defined as blood loss greater than 500ml [30]. An RCT of 120 women that compared 12.5 mcg oral misoprostol with 25 mcg vaginal found no difference in outcomes in terms of mode of delivery, induction to delivery time, need for oxytocin, or complications [31].

CONCLUSION:

We concluded that misoprostol showed more effective and satisfactory results as compared to intravenous oxytocin in low-risk females undergoing normal vaginal

delivery. Thus the controversy has been resolved. Now in future we will be able to implement the use of misoprostol to prevent PPH in low-risk females to reduce the mortality of females due to excessive blood loss.

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