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ORAL VERSUS ORAL AND RECTAL USE OF MISOPROSTOL IN MANAGEMENT OF POST-PARTUM HEMORRHAGE

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Abstract:

Objective: *To determine the role of oral versus oral and rectal use of Misoprostol in the management of postpartum haemorrhage.*

Study Design and Setting: *This randomized controlled trial was conducted at gynae department of Peoples University of medical and health science.*

DURATION*: This study was conducted within 12 months February 2015 January 2016*

Material And Methods: *A data of total 100 patients was collected. All the grand Multi women (Parity ≥ 5), placenta previa, ante Partum Hemorrhage and with history of previous Partum Hemorrhage women were selected. All the patients were sub-divided into two groups. One receiving the drug 400µg oral and 400µg rectal misoprostol (experimental group or group A) and the other were underwent only oral 800µg misoprostol (control group or group B). All the data was collected on predesigned proforma.*

Results: *Only 2 patients who need for removal of placenta were from group A and no one from group B. Out of 99 patients who were underwent therapeutic oxytocin drug, 49 were from group A and 50 were from group B. Rate of the post-partum hemorrhage was found significantly decreased in patients of experimental group as 03(06.0%) out 50 cases as compare to control group (group B) as 11(22.0%) p-value 0.04. Nausea and vomiting condition were occurred only in 3(6.0%) patients of experiments group, shivering was noted among 7(14.0%) patients of experimental group and among 4(8.0%) of control group, while fever was found among 5(10.0%) patients of experiment group and 11(22.0%) of control group, this clinical presentation was statistically insignificant among both groups i.e. p-value= 0.17.*

Conclusion: *Oral and rectal administration of misoprostol showed significantly lower rate of postpartum haemorrhage as compare to oral administration of misoprostol only. Therefore misoprostol administered of oral+rectal route is the better management criteria for patients presented with grandmultiparity, placenta previa and APH.*

Key words: *PPH, misoprostol, oral + rectal route, oral rout.*

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INTRODUCTION:

Excessive bleeding i.e. the loss of blood greater than 500 ml following vaginal delivery, or 1000 ml of blood following cesarean section is termed as Post-Partum Hemorrhage (PPH); the leading cause of maternal deaths worldwide, has received international attention among medical and research communities. It accounts for at least 150 thousand deaths per year [1,2], World Health Organization (WHO) estimates that 20 million morbidities per year results from PPH [3]. The risk of dying from PPH depends upon the amount and rate of blood loss and also on the health status of mother [2]. In developing countries PPH is estimated to be responsible for 28% of maternal deaths [1,2] and in Pakistan it accounts for nearly 25%of maternal deaths [4]. However statistics are largely unavailable [5]. The common predisposing factors for PPH are multiparty, prolonged labor, fibroids, anemia, poor diet, and parasite infection. Pregnancy with above predisposing factors aggravated by maternal blood loss of as less of 250ml may prove fatal for patient. Four common causes of PPH include- Failure of uterus to contract {uterine atony}; Tear of genital tract {Traumatic PPH}; Retained products of conception; and Coagulopathy. Among all these Atony is the common cause of PPH and female without risk factors are faced with it. Therefore intervention should be targeted to all females during child birth to prevent PPH. The most important intervention that has been promoted so far by many obstetricians is Active Management of Third Stage of labor including administration of uterotonics after delivery of baby; early cord clamping and cutting; controlled cord traction; uterine massage after delivery of placenta [7,8]. A crucial component in the treatment of PPH resulting from atonic uterus is the administration of injectable uterotonics. The most commonly used agent in hospital based setting is oxytocin and/or ergometrin. Additional medical and surgical interventions, beyond the administration of conventional uterotonics, have also been investigated as alternative and adjuvant therapy options for postpartum bleeding. The use of misoprostol, a prostaglandin E1 analogue, has entered into clinical practice for this indication because of its strong uterotonic properties, and its ease in oral administration, stability at ambient temperatures, wide availability, and low cost. A 600mcg dose of oral misoprostol has been shown safe and effective in preventing PPH. Misoprostol was traditionally used for prevention and treatment of peptic ulcer disease. Oral absorption is rapid with mild and very few side effects [4,5]. It has been investigated in the induction of labor [9], cervical ripening, and termination of pregnancy. Misoprostol has also been investigated in prevention of postpartum hemorrhage when used orally, sublingual and rectal in different types of research studies.[2,10] Most of the studies so far have shown that it reduces the incidence of PPH without causing serious side effects. But these studies have failed to reveal a significant statistical difference regarding blood loss. When studied in comparison to other oxytocic drugs in the recent past, it is found that misoprostol is a promising and comparable drug to standard oxytocic. In the light of the above discussion misoprostol which is an inexpensive and easily available drug and having a self-life of several years makes it a useful drug in decreasing the incidence of PPH in developing countries. The current study is designed to evaluate and assess the oral route for its administration and comparison of different dose of misoprostol's which will enable us to prove and ascertain the efficacy of oral route of administration and stabilizing the minimal dose of misoprostol with no or at least minimal side effect.

MATERIAL AND METHODS:

This randomized controlled trial was conducted at gynae department of Peoples University of medical and health science. This study was conducted within 12 months from February 2015 January 2016. Total 100 patients were included. All the patients with grand multiparty (Parity $\geq$ 5), placenta previa, ante partum hemorrhage and previous PPH were selected. All the cases on anticoagulant therapy, polyhydramnios, intrauterine fetal deaths, uterine Scar, hypertension and with cardiac disease were excluded from the study. All the cases were divided into two groups 50 patients in experimental and 50 patients in control group. One receiving the drug 400micrograms oral and 400micrograms rectal (experimental group) and the other only oral 800micrograms (control group). The data was analyzed on the latest version of SPSS version 16.

RESULTS:

In this study the mean age of patients in group A and in group B was 29.84±6.59 years and 32.1±6.46 years respectively, which was statistically insignificant i.e. P-value 0.156. 59 patients were from urban areas and out of them 34 from group A and 25 from group B. Similarly 41 patients were from rural areas, particularly 16 from group A and 25 from group B. These residential findings were statistically insignificant i.e. p-value= (0.10) **(Table - 1)**

In this study from control group, there were 17 (34%) females were Gravida 1-3, 23(46%) were gravida 4-6, 9(18%) were gravida 7-9 and only 1(2%) were gravida 10-12. From experimental group, there were 14(28%) females were Gravida 1-3, 19(38%) were

gravida 4-6, 13(26%) were gravida 7-9 and only 4(8%) were gravida 10-12. **(Table # 1)**

There are only 2 patients who had active and these both patients were from group A. 18 patients were presented with APH and out of them 10 were from group A and 8 were from group B. There was only 1 patient was found with both diagnosis and this patients was from group A. 79 patients were in nil categories and out of them 37 were from group A and 42 were from group B. All these results were insignificant. i. e. P-value= (0.316). **(Fig # 1)**

In this study the mean duration of labor was noted as 4.19 ± 3.27 hours among patients of group A and 5.02 ± 3.62 hours in group B. This mean duration labor was statistically insignificant in both study groups, i.e. p-value= (0.274). There were only 1 patient who need for removal of placenta and this was from group B. There are 99 patients who use therapeutic oxytocin drug, out of them 50 were from group A and 49 were from group B. Similarly there is only one patient who do not use the therapeutic oxytocin drug and that is belong to group A. **(Table # 2)**

Patients of group A showed significant lower arte of postpartum haemorrhage as 3(6.0%) out of 50 cases as compare to group B as 11(22.0%) i. e. p-value= 0.04. **(Table # 3)**

In this study clinical presentation after management was statistically insignificant p-value 0.17 as out of 50 cases of group A, 03/(06%) were noted with nausea and vomiting, 07/(14%) presented with shivering and 05/(10%) were seen with fever. While out of 50 cases of group B 04/(08%) were found shivering and 11/(22%) noted with fever.**(Table # 3)**

Table 1: Basic Variables of the Patients= 100

Variables	Frequency/(%)	
	Experimental n=50	**Control n=50**
Age (Mean±SD)	32.1±6.46	29.84 ±6.59
Parity		
1-3	14/ (28%)	17 /(34%)
4-6	19 /(38%)	23/ (46%)
7-9	13/ (26%)	09/ (18%)
10-12	04/ (8%)	01 /(2%)
Residence		
Rural	25/(50%)	14/(28%)
Urban	25/(50%)	36/ (72%)

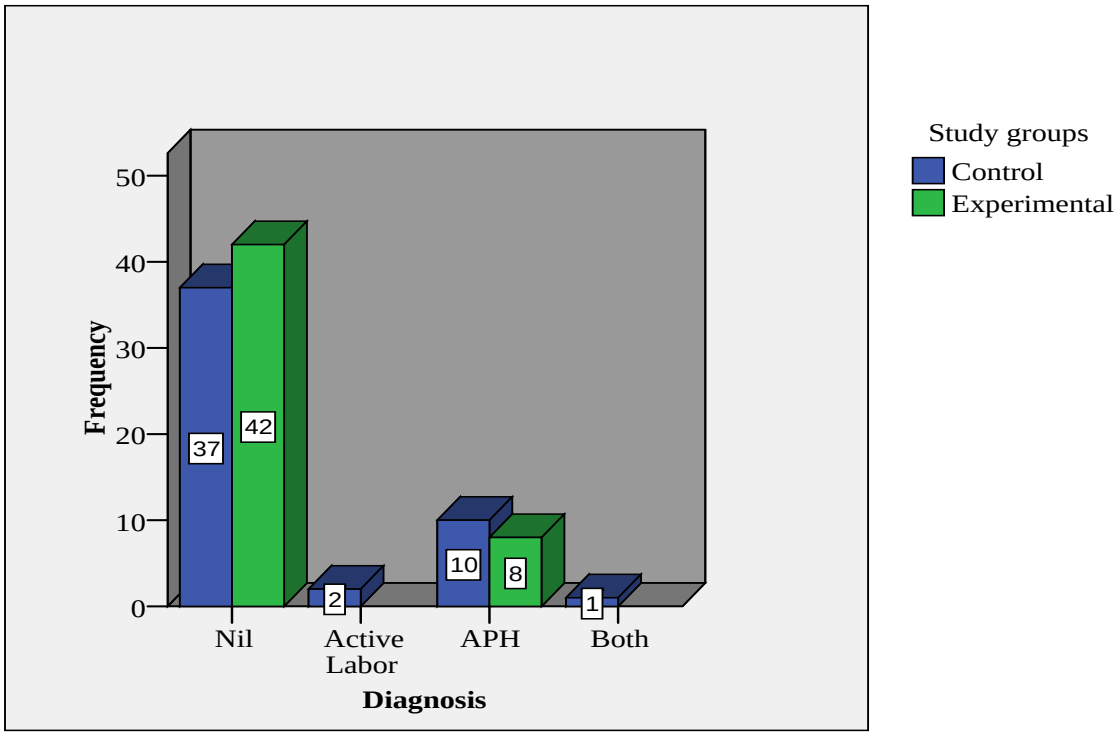

Fig 1: Description about the diagnosis of the patients in study groups n=100

Table 2: Duration of Labour and Therapeutic Oxyctocin Drug uses in both groups N= 100

Variables	BOTH STUDY GROUPS	
	Experimental n=50	Control n=50
Duration of Labor (Mean±SD)	4.19±3.27 hours	5.02±3.62 hours
Need Of Manual Removal		
Yes	00	1/(02%)
No	50/(100%)	49/(98%)
Oxytocin Drug Use		
Yes	00	1/(02%)
No	50/(100%)	49/(98%)

Table 3: Frequency of Postpartum Hemorrhage and Complications of Both Groups Post = 100

Variables	Study groups (Frequency/%)		
	Experimental n=50	**Control n=50**	***P*-value**
POST PARTUM EMORRHAGE			
Yes	03/(06%)	11/(22%)	0.04*
No	47/(94%)	39/(78%)	
COMPLICATIONS			
Nausea and vomiting	03/(06%)	00	
Shivering	07/(14%)	04/(08%)	0.17NS
Fever	05/(10%)	11/(22%)	

DISCUSSION:

Postpartum hemorrhage (PPH) is the leading cause of maternal mortality. All women who carry a pregnancy beyond 20 weeks' gestation are at risk for PPH and its sequelae. Although maternal mortality rates have declined greatly in the developed world, PPH remains a leading cause of maternal mortality elsewhere. The direct pregnancy-related maternal mortality rate in the United States is approximately 7-10 women per 100,000 live births. National statistics suggest that approximately 8% of these deaths are caused by PPH. World Health Organization statistics suggest that 25% of maternal deaths are due to PPH, accounting for more than 100,000 maternal deaths per year [11,12]. The definition of PPH is somewhat arbitrary and problematic. PPH is defined as blood loss of more than 500 mL following vaginal delivery or more than 1000 mL following cesarean delivery. A loss of these amounts within 24 hours of delivery is termed early or primary PPH, whereas such losses are termed late or secondary PPH if they occur 24 hours after delivery. Estimates of blood loss at delivery are subjective and generally inaccurate. Studies have suggested that caregivers consistently underestimate actual blood loss. Another proposal suggests using a 10% fall in hematocrit value to define PPH, but this change is dependent on the timing of the test and the amount of fluid resuscitation given [13,14]. High-quality evidence suggests that active management of the third stage of labor reduces the incidence and severity of PPH. Active management is the combination of (1) uterotonic administration (preferably oxytocin) immediately upon delivery of the baby, (2) early cord clamping and cutting, and (3) gentle cord traction with uterine counterattraction when the uterus is well contracted (ie, Brandt-Andrews maneuver) [15].

In this study the mean age of the patients was 30.97 ± 6.59 years in which the mean age of patients in group A and in group B was 29.84 ± 6.59 years and 32.1 ± 6.46 years respectively. It was revealed form the analysis of data that there were 31 (31%) females with Gravida 1-3, 42 (42%) females with gravid 4-6, 22 (22%) with gravid 7-9 and only 5 (5%) with gravida 10-12.. There were 47 (47%) females with parity 0-2, 36 (36%) females with parity 3-5, 14 (14%) with parity 6-8 and 3 (3%) females had parity 9-10. There were more patients with multigravidity and grand multiparity. In our study, there are only 2 patients who had active labor, 18 patients had APH category. There is only 1 patient which had both categories; active labor and APH. In this study the mean of the hemoglobin level before drug administration of the patients was noted as 9.12±1.50 mg/dl in which the mean hemoglobin level which was slightly raised to 9.37 ± 0.89 mg/dl after drug administration. The mean duration labor in group A was 5.02 ± 3.62 hours and group B was 4.19 ± 3.27 hours respectively. The difference for mean duration labor of the patients was statistically insignificant in both study groups. The study results shows there are only 2 patients who need for removal of placenta in which 2 belong to group A and no one belong to group B and there was insignificant difference between both groups for need of manual removal of placenta. All females showed some or severe postpartum blood loss. Mild blood loss was observed in 34 cases, 52 patients showed moderate level of blood loss while 14 patients had severe blood loss. There were less patients in control group which had mild to moderate blood loss as compared to

experimental group but severe blood was compared it was noticed that number of patients was significantly higher in control group as compared to experimental group. Almost all patients (99%) required therapeutic oxytocin drug. The result shows that there are 32 patients needed blood transfusion, out of which 20 were from group A and 12 were from group B. The trial showed trends toward a benefit for early administration of oxytocin, including a 25% reduction in PPH and a 50% reduction in the need for transfusion [16]. Postpartum hemorrhage was observed in 14 patients. More patients (22%) were from control group and only 3 (6%) are from experimental group. There was significant difference between both groups. (P-value= 0.04). Misoprostol has been used both as prevention and treatment of postpartum hemorrhage secondary to its uterotonic properties. Several randomized, controlled trials and a large, prospective, observational study have examined the use of misoprostol as an agent for the prevention of postpartum hemorrhage [17,20]. There are insufficient data to support the use of misoprostol as a primary preventive measure for postpartum hemorrhage when conventional injectable uterotonics are available as part of the management of the third stage of labor. Misoprostol has also not yet been found to be better than oxytocin or ergotamine in well-controlled, randomized trials for the treatment of postpartum hemorrhage. However, it remains an important option for treating postpartum hemorrhage when other agents are not available or fail. A descriptive study showed that 1000 µg of rectally administered misoprostol, when given to patients who failed to respond to oxytocin and ergotamine, controlled postpartum hemorrhage within 3 minutes. However, further studies, with randomized designs, are needed [2,21]. In experimental group, there were 3 patients who suffer from nausea and vomiting while none of the patient in control group showed nausea and vomiting. Nausea and vomiting may occur and will resolve 2-6 hours after taking misoprostol. An anti-emetic can be used if needed, but in general no action is required except to reassure the woman and her family [22]. Shivering was also observed in 11 patients are [Control: 4 vs. Experimental: 7]. 16 patients showed symptoms of fever. The difference was insignificant between both groups for fever and shivering. Pyrexia and shivering were common side-effects of misoprostol, as found in previous studies. In one study, 3 women, all in the misoprostol group, had severe pyrexia >40°C [23]. Fever is commonly associated with use of misoprostol. When used to treat PPH, hyperpyrexia (>40ºC) has been reported in several cases following 1000g (delivered orally, rectally and sublingually), and hyperpyrexia with delirium and/or ICU admission has been reported following 800g orally or sublingually. When used as prophylaxis for PPH prevention at a dose of 600g orally, 0.1% women experienced fever >40ºC. Chills are a common side effect of misoprostol but are transient. In studies of misoprostol for PPH prevention, chills were reported in 32%-57% of women receiving misoprostol. Fever should be carefully monitored. Women experiencing fever can be offered paracetamol and physical cooling [22-24].

CONCLUSION:

It was concluded that oral+rectal route administration of misoprostol may decrease the chances of postpartum hemorrhage as compared to misoprostol administration orally alone. Side effects of both trial groups were also statistically insignificant. This showed that experimental group is better management criteria in patients with grandmultiparity, placenta previa and APH.

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