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Effect of Tranexamic Acid in Prevention of Post-Partum Haemorrhage: A Prospective Observational Study

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ABSTRACT

Background: Treatment of Post-Partum Haemorrhage (PPH) relies primarily on uterotonics, but early use of Tranexamic Acid (TXA) has become part of several recommended algorithms. Recent data has demonstrated that Tranexamic Acid (TXA), an antifibrinolytic agent, reduces death due to bleeding when used as a treatment for PPH. This study was conducted with an objective to see the role of tranexamic acid along with uterotonic agent (oxytocin) in prevention of postpartum hemorrhage.

Materials and Methods: The present prospective observational study carried out at the Maternal and Child Health (MCH) wing Department of a rural tertiary care hospital and medical college situated in the central India during January 2021 to December 2022. A total sample size of 1640 patients attending labour room for vaginal birth or caesarean section in 3rd stage of labour were included in the study. Total 1640 women were further divided into two groups, Group A (receiving both tranexamic acid along with oxytocin) and Group B (receiving only oxytocin). Blood loss in each group was measured by visual method and Gravimetric (measurement by weight) method. They were followed till delivery; maternal and neonatal outcome was studied. Statistical analysis was done by using SPSS 27.0 version and GraphPad Prism 7.0 version and $p<0.05$ considered as level of significance.

Results: The majority of patients in Group A and Group B were between 26-30 years of age group. There was no significant difference between the groups in terms of maternal age, gestational age, gravida and booking status. The mean foetal birth weight among Group A was 2421.28 ± 626.91 and Group B was 2381.38 ± 721.20 with no significant difference between the groups. There was significant reduction in blood loss in study group A as compared to control group in both vaginal and LSCS birth with statistically significant difference.

Conclusion: Tranexamic acid injection, an antifibrinolytic agent when given prophylactically after delivery of placenta along with oxytocin appears to reduce the blood loss during normal labour as well as caesarean sections effectively.

Keywords:

Tranexamic Acid (TXA), Prevention, Post-Partum Haemorrhage (PPH)

Introduction

Obstetric fistula is a major public health problem in the developing countries [1,2]. It an abnormal communication between the genital tract and either the urinary or the intestinal tract, or both, leading to leakage of urine and/or faeces following childbirth [3]. It continues to be a source of misery, inflicting serious morbidities among affected women [4].

The World Health Organization estimates that more than 2 million girls and women worldwide live with obstetric fistula, with an additional 50,000-100,000 new cases occurring every year, the vast majority of whom are in Africa and Asia [5]. Nigeria alone constitutes 7.5% of the global burden with an estimated 150,000 women awaiting repair and 12,000 new cases yearly [6]. The predisposing factors are poverty, illiteracy, early marriage/childbearing, patronage of unskilled birth attendants, late presentation to health facilities, ignorance, aversion to safe Caesarean section, harmful traditional practices, cultural restriction of women and transportation barriers [7,8]. Majority of obstetric fistulas are known to result from prolonged obstructed labour [8]. However, poorly-performed Caesarean section is increasingly becoming an important aetiology of fistula in parts of Nigeria [9]. The mainstay of treatment of obstetric fistula is surgery [8].

Obstetric fistula has been shown to occur in association with other medical morbidities [4]. These include depression, urinary tract infection, urine dermatitis, obstetric palsy, amenorrhea, infertility, anal sphincter rupture, perineal tear, bladder stone, vaginal stenosis, cervical retraction and cervical stenosis, among others [4,10]. Attention is usually not paid to these conditions as the immediate concern is to restore continence. Consequently, the treatment of these conditions is often excluded in the care of the fistula patient. It is thus imperative to identify these morbidities so that the patients can benefit from holistic care and not just fistula repair. The study was therefore carried out to determine the morbidities that occur in association with obstetric fistula among patients seeking care in Cross River State. This will form a basis for proper counseling, thorough preoperative preparation and multidisciplinary approach to fistula care.

Material and Methods

Post-Partum Haemorrhage (PPH) is a complication of delivery and the most common cause of maternal death, accounting for about 35% of all maternal deaths worldwide [1]. PPH is commonly defined as a blood loss of 500 ml or more within 24 hours after birth, while severe PPH is defined as a blood loss of 1000 ml or more within the same timeframe according to World Health Organisation (WHO) [2].

In practice, blood loss after delivery is seldom measured and it is not clear whether measuring blood loss improves the care and outcome for the women. In addition, some women may require interventions to manage PPH with less blood loss than others if they are anaemic [3,4].

PPH may result from failure of the uterus to contract adequately (atony), genital tract trauma (vaginal or cervical lacerations), uterine rupture, retained placental tissue, or maternal bleeding disorders. Uterine atony is the most common cause and consequently the leading cause of maternal mortality worldwide [5].

Treatment of PPH relies primarily on uterotonics, but early use of Tranexamic Acid (TXA) has become part of several recommended algorithms. Tranexamic acid is an antifibrinolytic agent that reduces fibrinolysis by inhibition of plasminogen and plasmin by acting as a lysine analogue and binding to the lysine receptors on these proteins [6].

Recent data has demonstrated that Tranexamic Acid (TXA), an antifibrinolytic agent, reduces death due to bleeding when used as a treatment for PPH because its hypothesized mechanism of action in PPH supplements that of uterotonics and because it has been proved to reduce blood loss in elective surgery, bleeding in trauma patients, and menstrual blood loss. 7 Tranexamic acid has been proven to be a safe and effective option in the treatment of obstetric hemorrhage. However, use of tranexamic acid in routine practice in order to prevent and reduce the risk of postpartum study is still under study.

Therefore, this study was planned to see the role of tranexamic acid along with uterotonic agent (oxytocin) in prevention of postpartum hemorrhage.

Objectives

To study role of tranexamic acid in prevention of postpartum, haemorrhage in primigravida as well as multigravidas when used along with oxytocin.

Methodology

The present study was prospective observational study. The study was carried out at the Maternal and Child Health (MCH) wing Department of a rural tertiary care hospital and medical college situated in the central India during January 2021 to December 2022. The study was conducted after obtaining clearance from the Ethical Committee of the institute.

A total sample size of 1640 patients calculated using openepi SOFTWARE to detect the effect median score with 95% confidence level, 90% power and 10% non-response attrition were enrolled in the study. All patients attending labour room for vaginal birth or caesarean section in 3rd stage of labour were included in the study. Women with primary or secondary PPH not in active 3rd stage of labour, not giving consent, previous history of allergy to tranexamic acid, history of thrombosis (deep venous or pulmonary) or arterial thrombosis (infarct/ stroke) and any known cardiovascular, renal, or liver disorder were excluded from the study.

Total 1640 women were further divided into two groups, Group A (receiving both tranexamic acid along with oxytocin) and Group B (receiving only oxytocin) by computer assisted randomization fulfilling inclusion and exclusion criteria. Blood loss in each group was measured by visual method and Gravimetric (measurement by weight) method. Post partum haemorrhage defined by the World Health Organization (WHO) as postpartum blood loss in excess of 500 ml, it is a clinical diagnosis that encompasses excessive blood loss after delivery from a variety of sites: uterus, cervix, vagina and perineum.8 Standard treatment protocol was followed for all. They were followed till delivery; maternal and neonatal outcome was studied. Follow-up was done in these cases till discharge.

Statistical analysis was done by using descriptive and inferential statistics using chi square test, student's paired t test and student's unpaired t test and software used in the analysis were SPSS 27.0 version and GraphPad Prism 7.0 version and $p<0.05$ considered as level of significance.

Results

Table 1: Distribution of patients studied according to demographic variables.

Variables		Group A (T+O) (n=816) (%)	Group B (O) (n=824)	P value
Age group (years)	18-20	4 (0.49%)	2 (0.24%)	0.766 P=0.86 (NS)
	21-25	94 (11.52%)	98 (11.89%)	
	26-30	455 (55.76%)	462 (56.07%)	
	31-35	263 (32.23%)	262 (31.80%)	
Gestational age (weeks)	<34-36	489 (59.93%)	493 (59.83%)	0.01 P=0.96 (NS)
	≥37	327 (40.07%)	331 (40.17%)	
Gravidity	Primigravida	572 (70.10%)	535 (64.93%)	2.97 P=0.06 (NS)
	Multigravida	244 (29.90%)	289 (35.07%)	
Booking status	Booked	215 (26.35%)	178 (21.60%)	5.27 P=0.07 (NS)
	Registered	467 (57.23%)	495 (60.07%)	
	Unbooked	134 (16.42%)	151 (18.33%)	

The above table shows majority of the patients in Group A and Group B were between 26-30 years of age group (55.76% and 56.07%) with no significant difference between the groups in terms of mean age (p-value=0.84). The majority of patients in both groups were having gestational age <37 weeks (59.93% and 59.83%), primigravida (70.10% and 64.93%) and registered (57.23% and 60.07%) with no significant difference between the groups in terms of gestational age, gravida and booking status.

Table 2: Distribution of patients studied according to type of delivery.

Type of delivery		Group A (T+O)	Group B (O)	P-value
Vaginal	Induced	163 (19.98%)	165 (20.02%)	87.20
	Spontaneous	163 (19.98%)	329 (39.93%)	
Vaginal Total		326 (39.95%)	494 (59.95%)	
LSCS		490 (60.05%)	330 (40.05%)	P=0.0001,S
Total		816 (100%)	824 (100%)	

The above table shows majority of women delivered by LSCS in Group A (60.05%) compared to Group B (40.05%). Out of 39.95% subjects who delivered vaginally were subjected to tranexamic acid along with oxytocin in immediate postpartum period. Of which almost 19% were induced and spontaneously delivered respectively. As of LSCS, 60.05% subjects were subjected to tranexamic acid along with oxytocin. There was a statistical significant difference between the groups (p-value=0.001)

Table 3: Distribution of patients studied according to foetal birth weight.

Birth weight (Kgs)	Group A (T+O)	Group B (O)	Group B (O)
<2.5	466 (57.11%)	452 (54.85%)	0.84
≥2.5	350 (42.89%)	372 (45.15%)	
Total	816 (100%)	824 (100%)	P=0.35,NS
Mean ± SD (Grams)	2421.28 ± 626.91	2381.38 ± 721.20	
Range	192-3868	192-3868	

The above table shows mean foetal birth weight among Group A was 2421.28 ± 626.91 and Group B was 2381.38 ± 721.20 with no significant difference between the groups.

Table 4: Distribution of patients studied according to blood loss.

Blood loss (ml)	Group A (T+O)		Group B (O)		P-value
	Vaginal	LSCS	Vaginal	LSCS	
<500	270 (33.08%)	228 (27.94%)	253 (30.70%)	152 (18.44%)	461.0 P=0.0001,S
500-1000	36 (44.11%)	98 (12%)	198 (24.02%)	0 (0%)	
>1000	20 (2.45%)	164 (20.10%)	43 (5.2%)	178 (21.60%)	
Total	326 (39.95%)	490 (60.05%)	494 (59.95%)	330 (40.05%)	
p-value	116.7, p=0.0001,S		266.4, p=0.0001,S		

The above table shows significant reduction in blood loss in study group A as compared to control group in both vaginal and LSCS birth with statistically significant difference (p-value=<0.001).

Table 5: Distribution of patients studied according to occurrence of PPH.

Blood loss (ml)	Group A (T+O)		Group B (O)		P-value
	Vaginal	LSCS	Vaginal	LSCS	
Present	56 (6.86%)	164 (20.10%)	208 (25.24%)	178 (21.60%)	103.80 P=0.0001,S
Absent	270 (33.09%)	326 (39.95%)	286 (34.71%)	152 (18.45%)	
Total	326 (39.95%)	490 (60.05%)	494 (59.95%)	330 (40.05%)	
p-value	26.38, p=0.0001,S		11.13, p=0.0009,S		

The comparison of the groups as per the incidence of PPH shows significant reduction in incidence of PPH in both vaginal and LSCS. However, there was more significant reduction in incidence of PPH in case of vaginal deliveries (6.86%) as compared to LSCS birth (20.10%).

The above table shows significant reduction in requirement of blood and blood products transfusion in study group A after both vaginal (2.45%) and LSCS (13.97%) compared to group B after both vaginal (5.21%) and LSCS (16.47%) with statistically significant difference between the groups (p-value=<0.001) Similarly, it was observed significant reduction in ICU admission in study group after both vaginal and LSCS as compared to control group (P<0.001).

Discussion

Post partum haemorrhage is the most common cause of maternal morbidity and mortality worldwide. The present study was planned to see the role of tranexamic acid along with uterotonic agent (oxytocin) in prevention of postpartum hemorrhage.

In the present study, patients in Group A and Group B were between 26-30 years of age group. There was no significant difference between the groups in terms of maternal age, gestational age, gravida and booking status.

Similar findings were seen in Urooj H, et al. [9] and Yang H, et al. [10] studies where they found that the mean maternal age was more than 25 years. There was significant no difference among gestational age and gravida. Thus, suggesting the increasing trend of delayed conception in older age.

In present study, Tranexamic acid was more effective in primigravidas as compared to multigravidas, whereas oxytocin was a better single uterotonic agent in multigravida. Similar results were observed in study conducted by Yildrium MD, et al. [11] As the study was conducted in a rural tertiary care centre in central India majority of patients in either group were primigravidas, as a result efficacy of the drug was better assessed in primigravidas and further studies may be required to establish the efficacy of TXA in multigravidas.

The study shows, no significance of association was found between use of tranexamic acid and birth weights of the new-born. Though study observations highlight on prematurity and low birth weight, other causes of prematurity and low birth were not considered here. Other causes of prematurity such as maternal hypertensive disorders, infections, anaemia, intrauterine fetal growth restriction, age etc also are to be considered and require further studies [12,13].

The blood loss was less in study group A as compared to control group in both vaginal and LSCS birth with statistically significant difference. (p-value=< 0.001)

TRAAP 2 study suggested that in an addition to prophylactic uterotonic administration, a complementary component of the management of third stage of labor acting on the coagulation process may be useful in preventing PPH thus making TXA a promising candidate drug which is inexpensive, easy to administer, and simple to add to the routine management of deliveries in hospitals [14]. In another study it was found that among women with vaginal delivery who received prophylactic oxytocin, the use of tranexamic acid reduced the rate of postpartum hemorrhage of at least 500 ml that was significantly lower than the rate with placebo [15]. Similarly, Urooj H, et al. [9] found that mean blood loss in TXA group was less (30 ml ± 6.02) while it was 40 ml ± 7.88 in control group. In another study conducted at the Centre Hospitalier Regional Universitaire, France in 2010, the mean total blood loss in the study group which was given tranexamic acid along with uterotonics was 120ml compared to 232.45ml in the control group (only oxytocin) [16]. In a study by Abdel Aleem H, et al. [17] (2013), they noted that the mean total blood loss in the tranexamic acid group was 241.6 (SE 6.77) ml compared to 510 (SE 7.72) ml in the control group which was similar to findings of present study [18-20].

The comparison of the groups as per the incidence of PPH shows significant reduction in incidence of PPH in both vaginal and LSCS. There are fewer studies to prove role of tranexamic acid as preventive drug for prevention of PPH there have been multiple trials which have proved its efficacy for treatment of PPH. One such trial was World Maternal Antifibrinolytic Trial (WOMAN Trial) which successfully concluded that tranexamic acid was beneficial in reducing incidences of PPH and requirement of subsequent blood transfusions and ICU stay. 21

Another study conducted by Sentilhes L, et al. [22] (TRAAP trial) also concluded that rate of PPH in study group was less as compared to control group. In a similar way TRAAP trial phase 2 suggested that among women who underwent cesarean delivery and received prophylactic uterotonic agents, tranexamic acid treatment resulted in a significantly lower incidence of calculated estimated blood loss or red-cell transfusion by day 2 than control group, however it did not result in a lower incidence of hemorrhage-related secondary clinical outcomes [14,22].

In the present study, significant reduction in requirement of blood and blood products transfusion in study group compared to group B and significant reduction in ICU admission in study group after both vaginal and LSCS as compared to control group. (P<0.001)

In all patients, TXA reduces transfused volume by 1.1 units (95% CI 0.64 to 1.59). TXA may also reduce the need for re-operation due to bleeding (RR=0.67, 95% CI 0.41 to 1.09). Li, et al. [23] (2017) concluded in the meta-analysis of the review that TXA reduced blood loss, the need for transfusion in patients, the occurrence of severe PPH. As per TRAAP 2 trial also reported that TXA reduces the requirement of blood or blood products in the study group [14]. However, in TRAAP trial which was conducted in vaginal deliveries, no significant decrease in the need of blood transfusion was found. In a study conducted by the Division of Obstetrics and gynaecology, University of Oslo, Norway in 2009 similar results were found where significant reduction in blood transfusion was seen [22,24]. This showed that prophylactic use of tranexamic acid along with uterotonic agents not only reduced the blood loss but also reduced the requirement of ICU management by reducing maternal morbidity and mortality due to excessive bleeding.

On an overall view from the study, it was found that TXA has positive outcome in prevention of PPH when used along with uterotonic agent irrespective of mode of delivery. However, the study had fewer limitations also which would require further evaluation and analysis for better outcomes in the future [22,24].

Conclusion

The present study concludes that, Tranexamic acid injection, an antifibrinolytic agent when given prophylactically after delivery of placenta along with oxytocin appears to reduce the blood loss during normal labour as well as caesarean sections effectively.

Conflict of Interests

None declared.

Funding

None.

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