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Original Research Article

A Hospital Based Prospective Comparative Assessment of Anti-Hemorrhagic Effect of Uterotonics and Tranexamic Acid (TXA) for Postpartum Hemorrhage

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Abstract

Aim: The aim of the present study was to compare anti-hemorrhagic effect of uterotonics and Tranexamic acid (TXA) for postpartum hemorrhage.

Methods: The prospective observational study was conducted at Department of Obstetrics and Gynecology, Patna medical College and Hospital, Patna, Bihar, India for nine months. 200 pregnant women who were booked in this hospital and delivered vaginally and clinically diagnosed with postpartum hemorrhage were taken for the study. 100 patients received standard protocol with placebo and 100 received standard protocol with Tranexamic acid 1 gm IV.

Results: Majority of the patients belonged to age group 19-24 years 60% in group A and 56% in group B respectively followed by 26-30 years, i.e., 25% in group A and 24% in group B. According to parity, 60% belonged to multipara in group A and 65% in group B. 91% and 90% patients delivered full term normal delivery in group A and group B respectively. Two groups are comparable with respect to delivery. P value is significant ($p< 0.0001$). There was significant difference in FTND and VBAC. Mean blood loss in the control group was 750 ml +/- 100ml while that in study group was 650ml +/- 100ml. the difference between the two groups was significantly high and hence it was statistically significant ($p< 0.0001$).

Conclusion: Tranexamic acid significantly reduces bleeding in post-partum haemorrhage. TXA is not a new drug and is generally well tolerated without any thrombogenic side effects. This data strongly supports the need for double blind study to investigate the potential effects of Tranexamic acid to reduce incidence of PPH and related maternal morbidity and mortality.

Keywords: Postpartum Hemorrhage, Tranexamic Acid, Uterotonics, Blood Loss Vaginal Delivery.

Introduction

Obstetrical hemorrhages are the most common cause of morbidity and mortality of women. Annually, about 530000 women die in world as a consequence of pregnancy or childbirth. [1-4] Annually 14 million women suffer postpartum hemorrhage (PPH); 2% of deaths occur 2-4 hours after hemorrhage starts. In other words, of 14 million PPH cases each year, 2% leads to death. Although most of mortalities occur out of health care centers but a considerable amount of deaths occur in hospitals, where effective facilities are used to prevent this event. [5-7] Early PPH

has most recently been defined as "cumulative blood loss of 1000 ml or more of blood loss accompanied by sign and symptoms of hypovolemia within 24 hours following the birth process." [8]

Worldwide, approaches to PPH are dictated by resource availability and include mechanical means (e.g., bimanual compression, tamponade, antishock garments), replacement of fluid and blood products, embolization, and pharmacologic agents. [9,10] In the hemostatic process, coagulation occurs rapidly at the site of a damaged vessel building a tight net of fibrin while, the fibrinolytic system removes the fibrin deposits that could cause permanent vascular occlusion once vascular repair has taken place. [11] The coagulation and fibrinolytic system are believed to be in a state of dynamic balance which maintains an intact vascular system. Tranexamic acid is a potent antifibrinolytic agent that exerts its effect by blocking lysine binding sites on plasminogen molecules and has the potential to enhance the effectiveness of the patient's own hemostatic mechanism. Consequently, clot break down (fibrinolysis) is inhibited and excessive or recurrent bleeding is reduced. As TXA inhibits the breakdown of fibrin deposits already formed, it might theoretically increase the risk of thromboembolism. During delivery, when the placenta separates from the uterine wall, a sequence of physiologic and hemostatic changes occur that reduce bleeding, increase myometrial contraction, increase platelet activity, release of massive coagulant factors and a parallel increase in the fibrinolytic activity. [12]

The aim of the present study was to compare anti-hemorrhagic effect of uterotonics and Tranexamic acid (TXA) for postpartum hemorrhage.

Materials and Methods

The prospective observational study was conducted at Department of Obstetrics and Gynecology ,Patna medical College and Hospital, Patna, Bihar, India for nine months. 200 pregnant women who were booked in this hospital and delivered vaginally and clinically diagnosed with postpartum hemorrhage were taken for the study. 100 patients received standard protocol with placebo and 100 received standard protocol with Tranexamic acid 1 gm IV.

Diagnosis of PPH was made by the following clinical observation

1. Estimated blood loss after delivery >500 ml.
2. Estimated blood loss which compromise the haemodynamic status of the mother.

Inclusion criteria

1. Singleton pregnancy.
2. Term gestation.

Exclusion criteria

1. Multiple pregnancy.
2. History of previous thrombo-embolic events.
3. Intrauterine fetal demise.
4. Medical and surgical complications involving systems like cardiac, liver/kidney/blood disorders.
5. Anaemic patients (<7g/dl), severe anaemia.
6. Previous PPH

The blood loss following delivery was calculated using BRASS V DRAPE.

The study was divided into 2 groups

Group 1: Control group 100 cases

Group 2: Study group 100 cases

Control Group

Standard protocol for the treatment of PPH (Oxytocin, Ergometrine, Prostaglandins) along with placebo (normal saline 10 ml) was given after the diagnosis of PPH

Study Group

Standard protocol for the study of PPH along with Tranexamic acid 1 gm IV

Results

Table 1: Age, parity and type of delivery distribution

Age in years	Group-A control	Group B –Tranexamic Acid
19-24	60	56
26-30	25	24
31-35	15	20
36-40	0	0
Parity		
PRIMI	40	35
Multi	60	65
Total	100	100
Type of delivery		
FTND	91	90
VBAC	09	10
TOTAL	100	100

Majority of the patients belonged to age group 19-24 years 60% in group A and 56% in group B respectively followed by 26-30 years, i.e., 25% in group A and 24% in group B. According to parity, 60% belonged to multipara in group A and 65% in group B. 91% and 90% patients delivered full term normal delivery in group A and group B respectively. Two groups are comparable with respect to delivery. P value is significant ($p< 0.0001$). There was significant difference in FTND and VBAC.

Table 2: Blood loss

Blood loss (ml)	Group A-control	Group B Tranexamic acid
500-600	05	12
600-700	20	70
700-800	60	10
800-900	10	06
900-1000	05	02
>1000	00	00
TOTAL	100	100

Mean blood loss in the control group was 750 ml +/- 100ml while that in study group was 650 ml +/- 100ml. the difference between the two groups was significantly high and hence it was statistically significant ($p< 0.0001$).

Table 3: Need for Surgical Intervention or Hysterectomy and side effects

Group	Surgical intervention or hysterectomy
A Control	02
B Tranexamic Acid	Nil
Thrombogenic S/E On Mother Or Baby	
A- Control	Nil
B- Tranexamic Acid	Nil

In the control group two patient required surgical interventions. Both the groups showed no side effects.

Discussion

Post-Partum Haemorrhage is commonly defined as blood loss more than or equal to

500 ml after vaginal delivery or more than or equal to 1000ml after caesarean section. [13] However these thresholds do not take into account pre-existing health status, and blood loss of as little as 200ml can be life threatening for a woman with severe anaemia or cardiac disease. Primary Postpartum Haemorrhage (PPH) is classically defined as blood loss of > or equal to 500ml in the first 24 hours after delivery. Prevalence estimates for PPH in the literature vary widely from 3-15% of deliveries. PPH remains a leading cause of maternal death accounting for about 3lakhs to 4lakhs death every year. [14]

Haemostatic drugs are categorised into local haemostats and advanced drugs including fibrin sealers and underlying haemostatic drugs. Information about all available haemostatic drugs, is limited and has been obtained based on studies with low sample size. [5] Tranexamic Acid (TXA) is a synthetic derivative of lysine amino acid which inhibits fibrinolysis via reversible blocking of lysine-binding sites on plasminogen.15 This drug has been used for menorrhagia treatment which results in considerable reduce (45-54%) in menstrual haemorrhage. [16] Homeostasis of placenta bed after child birth is a considerable physiological procedure, but this physiological procedure is not efficient enough. [17,18]

Tranexamic acid is a potent antifibrinolytic drug. The main action of Tranexamic acid is blocking of the lysine binding sites of the plasminogen molecule, which are of importance for the binding to fibrin. This prevents activation of plasminogen by plasminogen activator, also absorbed to fibrin. It can be given orally or intravenously, it enters tissues and fluids in various concentrations and crosses the placenta.

During placental delivery, fibrinogen and fibrin are rapidly degraded whereas plasminogen activators and FDP increase due to activation of fibrinolytic system. This activation will last upto 6-8 hour's post-partum, causing bleeding. It was because of this activation of fibrinolytic system we have used Tranexamic acid in our study. Our study compares standard protocol with placebo and standard protocol with Tranexamic acid in PPH. The mean age in the present study in both group was between 19-24 years. Similar study carried out by Ming ying Gai etal (2004) [19] had mean age group of 29 years. In our study, majority of the people were multigravidas in both the study groups. 40 in the control group and 35 in the study group were primiparous. Similar done by Yang H et al. [20] had 87 primiparous in the control and 94 primiparous in the Tranexamic acid group. study done by Ducloy-Bouthors AS [21] had 50 primiparous in the control group and 46 in Tranexamic acid group and 12 multiparas in control group 16 multiparas in Tranexamic acid in the present study, out of 100 patients in each group, 91 and 90 patients had FTND in control and Tranexamic acid group respectively.

In the present study the mean blood loss was 750 +/- 100 ml in control group and 650 +/- 100 ml in study group. The difference between two groups is statistically significant (P value <0.0001). Similar study carried out by Gai MY et al (2004)19 showed that Tranexamic acid significantly reduces bleeding. In the present study, 2 patients required surgical intervention in the control group. Study done by Ducloy-Bouthors AS [21] surgical intervention was done for 2 women in control group. [22]

Conclusion

Tranexamic acid significantly reduces bleeding in post-partum haemorrhage. TXA is not a new drug and is generally well tolerated without any thrombogenic side effects. This data strongly supports the need for double blind study to investigate the potential effects of Tranexamic acid to reduce incidence of PPH and related maternal morbidity and mortality.

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