e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2022; 14(5); 609-614

Original Research Article

Assessment of Uterotonics and Tranexamic Acid for the Treatment of Postpartum Hemorrhage: A Comparative Study

Sangita Kumari[1], Pratima Kumari[2]

[1]Assistant Professor, Department of obstetrics & Gynecology, Nalanda Medical College and Hospital, Patna, Bihar, India.

[2]Assistant Professor, Department of Obstetrics&Gynecology, Nalanda Medical College and Hospital, Patna, Bihar, India.

Received: 17-02-2022 / Revised: 23-03-2022 / Accepted: 19-04-2022
Corresponding author: Dr. Pratima Kumari
Conflict of interest: Nil

Abstract

Aim: To compare anti-hemorrhagic effect of uterotonics and Tranexamic acid (TXA) for postpartum hemorrhage.

Material & Method: This is a prospective observational study done over a period of two years. 260 pregnant women who were booked in this hospital and delivered vaginally and clinically diagnosed with postpartum hemorrhage were taken for the study. 130 patients received standard protocol with placebo and 130 received standard protocol with Tranexamic acid 1 gm IV.

Results: Two groups are comparable with respect to delivery. P value is significant ($p< 0.0001$). As there is 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 hemorrhage. TXA is not a new drug and is generally well tolerated without any thrombogenic side effects.

Keywords: Postpartum Hemorrhage [PPH] 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]

Thus, we aim to compare anti-hemorrhagic effect of uterotonics and Tranexamic acid (TXA) for postpartum hemorrhage.

Material & Method:

This is a prospective observational study done over a period of two years. 260

pregnant women who were booked in this hospital and delivered vaginally and clinically diagnosed with postpartum hemorrhage were taken for the study.

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 hemodynamic 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. Anemic patients (<7g/dl), severe anemia
6. Previous PPH

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

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 Distribution

Age in years	Group-A control	Group B –Tranexamic Acid
19-24	78	75
26-30	35	23
31-35	17	22
36-40	0	0
Total	130	130

The mean age of the patients in both group was between 19-25 years

Table 2: Parity Wise Distribution

Parity	Group A Control	Group B Tranexamic Acid
PRIMI	55	59
Multi	75	71
Total	130	130

Two groups are comparable with regards to parity distribution multigravidas were more in the study

Table 3: Type of Delivery

Type of delivery	Group A-control	Group B –Tranexamic acid
FTND	121	117
VBAC	09	13
TOTAL	130	130

Two groups are comparable with respect to delivery. P value is significant ($p< 0.0001$). As there is significant difference in FTND and VBAC.

Table 4: Blood Loss

Blood loss (ml)	Group A-control	Group B Tranexamic acid
500-600	07	22
600-700	29	80
700-800	74	21
800-900	16	06
900-1000	04	01
>1000	00	00
TOTAL	130	130

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 ($p< 0.0001$)

Table 5: Need for Surgical Intervention or Hysterectomy

Group	Surgical intervention or hysterectomy
A Control	04
B Tranexamic Acid	Nil

In the control group four patients required surgical intervention.

Table 6: Side Effects

Group	Thrombogenic S/E On Mother Or Baby
A- Control	Nil
B- Tranexamic Acid	Nil

Both the groups showed no side effects.

Discussion:

Pregnancy is characterized by physiologic alterations incoagulation and fibrinolytic pathways. During pregnancy, there is (1) an increase in clotting factors (I, II, VII, VIII, IX, and XII), (2) a decrease in anticoagulation activity (protein S and activated protein C) and (3) a decrease in fibrinolysis resulting in a hypercoagulable state. [13] This hypercoagulable state

increases throughout pregnancy, peaking at term, and continues in the immediate postpartum period. [14,15] During the stress of labor, clotting factors further increase, and fibrinolytic activity decreases. After the separation of the placenta from the decidua, myometrial contractions occur, platelet aggregation at the placental site increases, and there is a release of coagulation factors that results in reduction of bleeding. [14] The balance between coagulation and fibrinolysis maintains an intact vascular system, which diminishes the risk of PPH.

A study of Beigi et al., [16] in our study hemorrhage level was lower in group receiving Misoprostol. Despite the study of Beigi et al., also the difference between two groups in terms of hemorrhage and hemoglobin level was not statistically significant.

Nasr et al., concluded that two groups had no difference in terms of PPH and the need for blood transfusion and loss of more than 10% in blood hemoglobin makes that study different from present study. [17]

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.

Research on the use of TXA to prevent PPH in women anticipating vaginal birth has been conducted, but results to date are less robust than the positive effects noted for women who have a cesarean birth.33 [18] In a Cochrane review of the use of prophylactic TXA for women with vaginal and cesarean birth, 3 trials from Turkey, Iran, and China studied the effectiveness and safety of TXA in 832 women who had a vaginal birth.31,34-36 [19-21] One study was a prospective, double-blinded, RCT in which women received a 1-g infusion of TXA (n =228) or 5% glucose (n = 226) at birth of the new-born anterior shoulder. [22]

Samimi et al., studied the effect of rectal misoprostol and muscular syntometrine in preventing PPH and it was concluded that rectal suppository misoprostol is more effective and less harmful than syntometrine injection for reducing PPH. So it could be used as a selective drug for preventing PPH; [23] it was in contrast with results of present study which had PPH diagnosis. In study of Samimi et al., the mentioned drugs have been used as primary prophylaxis; which is in contrast with our study. Zafarghandi et al., studied hemorrhage duration and its relationship to different factors. [24]

Conclusion:

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. Tranexamic acid significantly reduces bleeding in post-partum hemorrhage. TXA is not a new drug and is generally well tolerated without any thrombogenic side effects.

References:

1. Ford J, Roberts C, Simpson J, Vaughan J, Cameron C. Increased postpartum hemorrhage rates in Australia. Int J Gynaecol Obstet 2007; 98:237-43.
2. Blum J, Alfirevic Z, Walraven G, Weeks A, Winikoff B. Treatment of postpartum hemorrhage with misoprostol. Int J Gynecol Obstet 2007;99: S202-5.
3. Bahadori F, Ayatollahi H, Naghavi-Behzad M, Khalkhali H, Naseri Z. Predicting factors on cervical ripening and response to induction in women pregnant over 37 weeks. Med Ultrason 2013; 15:191-8.

4. Quantin C, Benzenine E, Ferdynus C, Sediki M, Auverlot B, Abrahamowicz M, et al. Advantages and limitations of using national administrative data on obstetric blood transfusions to estimate the frequency of obstetric hemorrhages. J Public Health 2013; 35:147-56.
5. SHAH, M. and WRIGHT, J. D., editors. Surgical intervention in the management of postpartum hemorrhage. Seminars in perinatology, 2009. Elsevier, 109-115.
6. Sehhati-Shafaii F, Norouzi-Panahi L, Piri R, Naghavi-Behzad M, Naghi-Zadeh S. Comparative analysis of pregnancy outcome in pregnant women in active and latent phase of pregnancy; A study from a Referral Center in Northwestern Iran. Life Sci J 2013; 10:2095-101.
7. Berg CJ, Callaghan WM, Syverson C, Henderson Z. Pregnancy-related mortality in the United States, 1998 to 2005. Obstet Gynecol 2010; 116:1302-9.
8. Menard KM, Main KE, Currigan MS. Executive summary of the re-VITALize initiative: standardizing obstetric data definitions. Obstet Gynecol. 2014;124(1):150-153.
9. Committee on Practice Bulletins-Obstetrics. Practice bulletin no. 183: postpartum hemorrhage. Obstet Gynecol. 2017;130(4):e168- e86.
10. California Maternal Quality Care Collaborative. Tranexamic Acid (TXA) for Obstetric Hemorrhage. Stanford, CA: California Maternal Quality Care Collaborative; July 2017. https://www.cmqcc.org/resource/tranexamic-acid-txa-obstetric-hemorrhage. Accessed August 24, 2019
11. Prentice CR: Basis of antifibrinolytic therapy. J Clin Pathol Suppl (R Coll Pathol) 1980; 14:35-40.
12. Hellgren M. Hemostasis during normal pregnancy and puerperium. Semin Thromb Hemost 2003;29(2):125-30.
13. King TL. Anatomy and physiology of pregnancy. In: King TL, Brucker MC, Osborne K, Jevitt CM, eds. Varney's Midwifery. 6th ed. Burlington, MA: Jones & Bartlett Learning; 2019; 633-662.
14. Anderson CA, Avery MD. Anatomy and physiology during labor and birth. In: King TL, Brucker MC, Osborne K, Jevitt CM, eds. Varney's Midwifery. 6th ed. Burlington, MA: Jones & Bartlett Learning, LLC; 2019:861-880.
15. Physiology of parturition. In: Coad J, Dunstall M. Anatomy and Physiology for Midwives. 3rd ed: London: Churchill Livingstone; 2012:317- 362.
16. Beigi A, Tabarestani H, Moini A, Zarrinkoub F, Kazempour M. Sublingual misoprostol versus intravenous oxytocin in the management of postpartum hemorrhage. Tehran University Med J 2009;67.
17. Nasr A, Shahin AY, Elsamman AM, Zakherah MS, Shaaban OM. Rectal misoprostol versus intravenous oxytocin for prevention of postpartum hemorrhage. Int J Gynecol Obstet 2009; 105:244-7.
18. Sentilhes L, Lasocki S, Ducloy-Bouthors AS, et al. Tranexamic acid for the prevention and treatment of postpartum hemorrhage. Br J Anaesth. 2015;114(4):576-587.
19. Yang H, Zheng S, Shi C. Clinical study on the efficacy of tranexamic acid in reducing postpartum blood loss: a randomized, comparative, multicenter trial [in Chinese]. Chinese J Obstet Gynecol. 2001;36(10):590-592.
20. Gungorduk K, Asıcıo˘glu O, Yildirim G, Ark C, Ismet Tekirda˘g A, Besimoglu B. Can intravenous injection of tranexamic acid be used in routine practice with active management of the third stage of labor in vaginal delivery? A randomized controlled study. Am J Perinatol.2012;30(5):407-413.

21. Mirghafourvand M, Mohammad-Alizadeh S, Abbasalizadeh F, Shirdel M. The effect of prophylactic intravenous tranexamic acid on blood loss after vaginal delivery in women at low risk of postpartum hemorrhage: a double-blind randomised controlled trial. Aust NZ J Obstet. 2015;55(1):53-58.
22. Tomasi, D., & Webb, S. Human Gastrointestinal Microbiota and Neural Activity: Effects of Probiotics on Mental and GI Health. Journal of Medical Research and Health Sciences, 2020:3(9), 1070–1077.
23. Samimi M, Kalahroudi MA, Imani A. Comparison of the effect of rectal Misoprostol and IM Syntometrin in the prevention of post partum hemorrhage. Sci J Hamadan Univ Med Sci Health Services 2011.
24. Zafarghandi N, Torkestani F, Rabiyi M, Yaghoubian K, Faliah N. Study of postpartum bleeding duration and it's relationship with various factors in women referring to shahed university clinics. J Sabzevar Sch Med Sci 2004.