Journal of Research in Medical and Dental Science
2018, Volume 6, Issue 3, Page No: 452-458

Available Online at: www.jrmds.in
eISSN No. 2347-2367: pISSN No. 2347-2545

Effect of tranexamic acid on postpartum vaginal hemorrhage in Sharieti Hospital of Bandar Abbas in 2014- 2015

Azin Alavi[1], Farzaneh Atiqpour[2], Shahram Zare[3], Zinat Nasiri[2]*

[1]Fertility and Infertility Research Center, Hormozgan University of Medical Sciences, Bandar Abbas, Iran.
[2]Student Research Committee, Hormozgan University of Medical Sciences, Bandar Abbas, Iran.
[3]Department of Social Medicine, Medical School, Hormozgan University of Medical Sciences, Bandar Abbas, Iran

DOI: 10.24896/jrmds.20186369

ABSTRACT

As a midwifery emergency, post-partum hemorrhage (PPH) might occur once a vaginal delivery or C-section is done. The prevalence of the hemorrhage has been estimated to range between 1 and 5 percent of deliveries. The present clinical trial was conducted as a randomized and controlled double-blind study in 2014-15 on 240 pregnant visitors of the natural delivery ward of Shariati university hospital in Bandar Abbas. The intervention group received 1 gram of venal tranexamic acid in 200 ml of normal saline while the control group received a placebo (distilled water) in 200 ml of normal saline injected within the second phase of the childbirth in 10 minutes. Patients' information was recorded including the severity of hemorrhage, pre- and post-partum hemoglobin level as well as the clinical symptoms. The data were later analyzed via SPSS. The severity of hemorrhage was 313.9±46.8 in the intervention group and 729.3±199.6 in the control group which showed to be statistically significant (p<.001). Moreover, hemoglobin showed to be reduced in the intervention group for .1±.16 and 1.72±.11 in the control group which was statistically significant (p<.001). The present findings revealed that prescribed tranexamic acid can significantly cut down on blood loss and reduced hemoglobin in pregnant women.

Key words: Tranexamic Acid, Delivery, Obstetric, Hemorrhage

HOW TO CITE THIS ARTICLE: Azin Alavi, Farzaneh Atiqpour, Shahram Zare, Zinat Nasiri. Effect of tranexamic acid on postpartum vaginal hemorrhage in Sharieti Hospital of Bandar Abbas in 2014- 2015. J Res Med Dent Sci, 2018, 6(3): 452-458, DOI: 10.24896/jrmds.20186369

***Corresponding author**: Zinat Nasiri
e-mail: yas4562000@yahoo.com
Received: 15/01/2018
Accepted: 10/04/2018

INTRODUCTION

As a midwifery-related emergency cases, post-partum hemorrhage (PPH) can occur after a vaginal delivery or C-section and stands among the three causes of mortality among mothers worldwide both in developed and developing countries though the former is far less threatened [1]. Blood loss, hypertension [2] and embolism are the three main factors involved in the mortality of pregnant women. The prevalence of post-partum hemorrhage depends on the criteria of disorder definition but has been generally estimated to range between 1 and 5 percent [3].

PPH is defined either as a primary or secondary type. The former occurs in 24 hours of the childbirth while the latter occurs between 24 hours and 12 weeks of the childbirth [4-5].

Annually, about 600,000 women die on account of PPH. Blood loss can be significantly reduced today with the help of a facile access to blood and blood products as well as modern medical and surgical technologies. Yet, in Iran the major cause of mortality among pregnant women is PPH [6-7]. Postpartum anemia can lead to fatigue, asthma, heart rate, loss of cognitive/emotional abilities, high risk of postpartum depression and infections especially urinary tract infection and is, therefore, considered as a serious healthcare problem worldwide among women in the age of fertility [8]. Due to the fact that PPH and its side effects

especially iron deficiency is a great global issue particularly in developing countries, it is recommended to use safe and affordable methods such as the use of tranexamic acid [9-10].

Fibrinolyses have rarely been considered as the preferred therapy. In recent years, however, they have shown to be considerably effective.

As a fabricated anti-fibrinolysis medication, tranexamic acid competes to bind to the lysine joints on plasminogen [11]. In case the hemorrhage is a function of the primary fibrinolysis, tranexamic acid enters into action as an effective inhibitor of fibrinolysis and further intensifies the hemostasis. It can be accompanied by side effects such as thromboembolism.

Due to the anti-fibrinolytic effect of tranexamic acid, it can probably be used as an effective supplementary in the third phase of delivery so as to prevent PPH and cut down on its adverse effects.

Considering the high prevalence of PPH and the intensive care required for the target population, any attempt to prevent PPH and its side effects is quite expected. Therefore, it was intended to delve into this issue and reduce its side effects through an investigation of how tranexamic acid affects PPH in Shariati Hospital of Bandar Abbas in 2014-15.

MATERIALS AND METHODS

The present clinical trial was conducted as a randomized and controlled double-blind study in 2014-15 on 240 pregnant visitors of the natural delivery ward of Shariati university hospital in Bandar Abbas. The inclusion criteria were: pregnancy with a singleton, pregnancy age of 38-42 weeks, 18-35 years of age, 5 or fewer prior pregnancies and a normal blood pressure (<140/90 mmHg). The exclusion criteria were: long-lasting induction in the first phase of delivery (more than 13 hours), prior experience of uterine surgery or C-section, uterine fibroma, experience of internal diseases e.g. renal, cardiovascular diseases, liver or brain disorders, thromboembolism problems, anemia, preeclampsia, diabetes, asthma, epilepsy, prior experience of PPH or hemorrhage during the current pregnancy, placental abruption, placenta previa, placental anomalies and corioamnionitis, macrodome and poly hydramnios in the present pregnancy, vacuum extraction, need for a C-section or consistent compression of uterine fundus before the emergence of the fetus and placenta.

In the present research, tranexamic acid was injected in a 500-g syringe (manufactured by Caspian Co., Iran) while the placebo was injected in a 10-ml syringe (manufactured by Shahid Qazi Co., Iran). The sample was selected from those meeting the inclusion criteria and willing to participate. The purpose of the research was explained to the participants and they gave a written consent to take part. The randomized BBR method was followed to assign the participants to an intervention (tranexamic acid) and a control group (placebo). To blind the study, both the placebo and the acid were wrapped in paper and were numbered in a sequence. The preparations were done by a third party not involved in the study (as the researcher or patient). In the second phase of delivery (one the anterior shoulder is out, the intervention group received 1 g of tranexamic acid in 200 ml of normal saline whereas the control group received a placebo (distilled water) in 200 ml of normal saline as an injection in 10 minutes. General care was the same for both groups. Upon placental extraction, both groups received 20 units of oxytocin in 500 ml of normal saline within 20 minutes. Sterile gauze was used to measure the blood lost within the 2 hours of placental extraction. The blood was then extracted from the gauze and measured in a suction device. During the first 2 hours of the completion of childbirth, mothers were followed up for any probable side effect. All information including the time it took from hospitalization to delivery was recorded in a checklist. Vital signs along with the acclaimed side effects of tranexamic acid (nausea, vomiting, headache and dizziness) were monitored and recorded every 15 minutes in the first hour and every 30 minutes in the second hour of delivery. Blood samples were taken from the participants 1-12 hours before the delivery (upon admission to the ward) and also 12-24 hours (mean: 18) afterwards to test both hemoglobin and hematocrit. With a half hour, the samples were transferred to the lab. The acquired data were then statistically analyzed via SPSS ver21 with the help of descriptive statistics (frequency, percentage, standard deviation) along with chi-squared test, Fisher's test, independent-sample and paired t-test. The significance level was set at $p<.05$.

RESULTS

A total number of 240 patients entered the present study, 120 of whom received tranexamic acid as the treatment and the other 120 received a placebo as the control group. The mean age of the participants was 26.4±3.4 years. In the intervention group, the mean age was 26.4±3.5 years and in the control group it was 23.8±10.9. Moreover, the mean BMI score in the intervention group was estimated as 23.4±2.2 and in the control group was 24.2±15.4 (Table 1).

Table 1: Participants' demographic information

variable / Group	Age	BMI
G1(Tranexamic acid)	26.4±3.5	23.4±2.2
G2(Control)	26.7±3.4	24.2±15.4

The total number of gravid 1, 2, 3 and 4 in the intervention group was respectively 1, 48, 40 and 31. In the control group these were respectively 2, 44, 44 and 30. Those with no childbirth were 2 in the intervention group and 4 in the control. Those with 1 delivery in the intervention group were 49 and in the control group were 56. Those with 2-5 prior deliveries were 69 and 60 respectively in the intervention and control groups (Table 2).

Table 2: Participants' experience of prior deliveries

Group / Variable		Intervention	Control	P-value
n. of pregnancies	1	1(.8%)	2(1.7%)	>.05
	2	48(40%)	44(36.7%)	
	3	40(33.3%)	44(36.7%)	
	4	31(25.8%)	30(25%)	
n. of deliveries	0	2(1.7%)	4(3.3%)	
	2	49(40.8%)	56(46.7%)	
	2-5	69(57.5%)	60(50%)	

In the present research, a significant correlation was found between the intensity of hemorrhage and the effect of tranexamic acid (p<.001). The mean score of hemorrhage in the treatment group was 9.313±8.461 and in the treatment group was 3.729±6.199 (Table 3).

Table 3: Mean hemorrhage score across research groups

	m.	P-value
G1 (treatment)	461.8±313.9	<.001
G2(control	199.6±729.6	

Similarly, no statistically significant correlation was observed in the present research between PPH and the frequency of deliveries. The frequency of deliveries, contrary to the research hypothesis, showed to have no effect on the severity of hemorrhage on either group (p> .4) (Table 4).

Table 4: Correlation of PPH and the frequency of deliveries

	f. of prior pregnancy	n. of patients	m. of hemorrhage	p-value
G1	0	2	79.1±256	>.5
	1	49	162.8±254.2	
	2-5	69	591.4±357.9	
G2	0	4	171.7±786	
	1	56	176±715.6	
	2-5	60	222.4±738.3	

As it can be observed in the following table, no statistically significant correlation was observed between PPH and pre-partum hemoglobin (p>.05) (Table 5).

Table 5: Correlation of PPH and pre-partum hemoglobin

	m. hemoglobin level	Normal hemoglobin	Abnormal hemoglobin	p-value
G1	18	102	1.3±12.2	.66
G2	12	108	1.2±12.7	

The two groups showed to diverge in terms of reduced hemoglobin (p<.05). All this shows that among those who received tranexamic acid, the reduced level of hemoglobin was significantly lower than the control group (Table 6).

Table 6: Reduced level of hemoglobin across research groups

	Mean hemoglobin before delivery	Mean hemoglobin after delivery	Mean reduced hemoglobin
G1	1.30±12.27	1.46±12.10	.16±.1
G2	1.25±12.78	1.36±11.06	.11±1.72
p-value	>.65	.04	.001

The present findings revealed no statistically significant difference between the two research groups in terms of the intensity of hemorrhage (Table 7).

Table 7: Correlation of hemorrhage and birth weight

	Birth weight (g)	n. of patients	Mean hemorrhage	p-value
G1	<1500	3	89.7±350	.9
	1500-2500	27	68±320	
	2500-4250	86	54.7±315	
	>4250	4	46.1±204	
G2	<1500	4	78.3±761.7	
	1500-2500	21	48.5±745.3	
	2500-4250	92	20.7±727.7	
	>4250	3	63.4±621.6	

The two research groups showed to diverge significantly in terms of the reduced level of placket. The treatment group showed to have more reduction in plackets than the control (p<.05) (Table 8).

Table 8: Reduced placket across the research groups

	Mean placket before delivery	Mean placket after delivery	Mean reduced placket
G1	225.3±253.5	157.8±232.3	.16±21.2
G2	130.1±215.3	57.6±201.4	72.5±13.9
p-value	>.051	.039	.001

Blood pressure and tranexamic acid did not show to be statistically significant in the present research (p>.05). Moreover, heart rate showed to make no statistically significant difference between the two research groups (p>.05). The rate of nausea and vomiting showed to be rather similar in the two groups and indicates no significant difference accordingly (p>.05) (Table 9).

Table 9: Correlation of blood pressure, nausea and vomiting as a function of tranexamic acid across research groups

	G1	G2	P-value
Normal blood pressure (100-120 mmHg)	110(91.7)	112(93.3%)	.624
Low blood pressure (<100 mmHg)	10(8.3%)	8(6.7%)	
Normal heart rate (60-100)	111(92.5%)	108(90%)	.493
Tachycardia (>100)	9(7.5%)	12(10%)	
Nausea/vomiting	109(90.8%)	108(90%)	.826

DISCUSSION

The present findings revealed that the pregnant women who received tranexamic acid, had a far less hemorrhage than the control. This all attests to the fact that tranexamic acid can be used as a medication to reduce blood loss during childbirth. Movafagh et al. (2011) conducted their research on 1—pregnant subjects in Iran who volunteered for a C-section [12]. They were divided into a case and a control group. The former received 10 mg/kg of tranexamic acid while the latter received only a placebo. Those who received tranexamic acid showed to have far less blood loss both during the surgery and two hours after that as compared to women who had not received any. This divergence between the two groups was statistically significant (p<.001). The level of reduced hemoglobin was also lower in the former which showed to be statistically significant too (p<.001). No significant difference was observed between the groups in terms of blood pressure, heart rate, nausea and vomiting (p>.05). The same research population and methodology followed in the two studies can partly account for the similar findings. Different sample sizes might be why the findings differed to a certain extent. In their investigation, Gobbur et al. (2014) worked on 100 pregnant women who opted for a C-section and observed that the amount of blood lost in the treatment group was 71.4±289.4 mmHg and in the control group 58.9±328 mmHg which was statistically significant (p<.05). This finding was consistent with the present research and tranexamic acid showed to succeed in reducing hemorrhage [13]. Gobbur et al. observed no statistically significant correlation between birth weight and blood loss in either group which was similar to the results of the present study. These divergences can be due to the differing methodologies followed. On the other hand, nausea and vomiting showed no significant correlation in either research group (p>.05) which was consistent with the present findings. The delivery type and differing sample sizes stand as the major differences between these two investigations. In some other research, Xu et al. (2013) compared 88 pregnant women (from among the total number of 174) who received tranexamic acid to 86 who received a placebo. As for the hemorrhage upon the extraction of placenta, the two groups showed no significant divergence. However, within 2 hours of the surgery, blood loss was significantly lower in the treatment group (p<.01). This result was also confirmed by the present findings and attests to the effectiveness of tranexamic acid in reducing PPH [14]. The reduced level of hemoglobin showed to diverge significantly between the two groups and was in favor of the treatment group (p<.01), which was also similar to the findings of the present research. However, the reduced level of placket was not significantly different between the two groups (p>.2) which was unlike the present findings which showed more reduction in the treatment group. Blood pressure and heart rate did not show to be correlated in both groups (p>.05) which was similar to the present research. No significant correlation was observed between nausea and vomiting which was again consistent with present findings (p>.05).

Evidently, the abovementioned research showed to be similar to the present research in many

ways. This similarity can be to a great extent explained by the similar sample size and target research population. Among the differences, mention can be made of ethnic/racial differences and the type of delivery. In another investigation by Mehmet et al. (2012), 223 pregnant women with a C-section were included. 101 belonged to the treatment group while 122 formed the control group for the sake of comparison. The intensity of hemorrhage showed to be significantly more in the control group (p<.001) [15]. The two groups showed to be significantly different in terms of the reduced level of hemoglobin (p<.05). It revealed a significantly lower level of hemoglobin in the control group. In the present research, a similar finding was reported. These similarities can be justified by the similar sample size as well as racial/ethnic convergences. The slight differences could be due to the differing type of delivery. In their research on 1144 women who had natural delivery, Bouthors et al. used tranexamic acid in the treatment 6 hours prior to their delivery [16]. This group showed to have much less hemorrhage than the control group that only received a placebo (p<.05). This finding is also similar to that of the present research. Howeevr, the level of reduced hemoglobin in this research was reported to be less in the treatment group than the control. This divergence was statistically significant (p<.05). A similar finding was obtained in the present study. The duration of hemorrhage was shorter in the treatment group than the control group (p<.05) which was also statistically significant. This variable was not, however, measured in the present research. The similarities between these two investigations can be their similar design while the slight differences might be due to the racial/ethnic variances.

In Turkey, Gungorduk et al. (2010) conducted their research on 660 pregnant women who had a C-section. The treatment group with 330 participants received tranexamic acid while the control group received a placebo. The amount of blood lost showed to be significantly lower in the former (p=.03). This has been in line with the observations of the present research. Hemoglobin showed to be lower in the control group than the treatment group after the surgery which was statistically significant (p<.001). This finding was also consistent with that of the present research. In this investigation, such factors as the heart rate, blood pressure, nausea and vomiting showed no statistically significant divergence between the two research groups (p>.05). These factors did not reveal any significant divergence between the groups in the present study either. These common findings can be due to the similar designs as well as racial/ethnic similarities. The type of delivery can account for the differences.

In 2013, Halder et al. performed their research on 100 pregnant women with a C-section [17]. The treatment group in this study received tranexamic acid prior to the surgery while the control received none. The intensity of hemorrhage since the placental extraction till the following 2 days showed to be significantly lower in the treatment group (p<.05). This observation was similar to that of the present study. Similar findings were also reported for the reduced level of hemoglobin in the two works of research (p<.05). No significant divergences were observed between the two groups in terms of the heart rate and blood pressure (p>.05). This was also consistent with the observation in the present research. Similar findings were reported concerning nausea and vomiting (p>.05).

The similar research design as well as variables under investigation in both investigations can at least partly justify the similar findings. A number of variables did not match between the two and were not investigated in both. The differences can be partly due to the small sample size and demographic divergences. In their research in India, Goswam et al. (2013) divided their 90 subjects (with elective C-section) into three groups. The first group received 10 mg of tranexamic acid in dextrose while the second group 15 mg of tranexamic acid in dextrose and the third group received a placebo [18]. The amount of blood lost in the second group showed to be significantly less than the first and the third groups. The amount of blood lost in the first group was similarly much lower than the third one (p<.05). This observation was similar to that of the present research. The three research groups showed no statistically significant divergences in terms of tachycardia, blood pressure and vomiting (p>.05). This was similar to the present findings. The point of departure has been the division of three research groups and the sample size while the similarities between the two studies could be explained by racial/ethnic similarities.

In some other research, Gungorduk et al. (2013) investigated 454 pregnant women with vaginal delivery in Turkey. Two research groups were involved, one with tranexamic acid and the other

with a placebo (dextrose 5%). The intensity of hemorrhage showed to be significantly lower in the treatment group than the control (p<.05). This finding accounted for a similarity to the present research [19]. Tranexamic acid showed to be effective in reducing the level of hemoglobin to a significant degree (p<.05). The two groups did not diverge significantly in terms of the heart rate, tachycardia or blood pressure which was similar to what the present research observed (p>.05). The type of delivery and research design can be considered the commonalities of the two investigations whereas the sample size accounted for the differences.

In some other investigation, Simonazzi et al. (2015) conducted a meta-analysis of more than 9 clinical trials with a sample size of over 2,365 that looked into the effect of tranexamic acid on PPH in C-section [20]. In all treatment groups, tranexamic acid managed to reduce PPH to a significant extent (p<.05). The present research was not an exception with this regard. All the studies included in the meta-analysis showed a significant reduction of hemoglobin in the group receiving tranexamic acid (p<.05). The same observation was made in the present study. Such side effects as tachycardia, lowered blood pressure, nausea and vomiting accounted for no significant differences between the research groups (p>.05). This finding was also similar to the present research. These commonalities can be explained by the similar research designs followed while the differences can be partly due to the ethnic/racial divergences or the delivery type.

CONCLUSION

As the review of the related literature revealed, the majority of findings attest to the effectiveness of tranexamic acid in reducing PPH either surgical or vaginal. Prescription of tranexamic acid, similarly, showed a highly significant effect on reducing PPH and confirmed the previous findings.

REFERENCES

1. Mousa HA, Alfirevic Z. Treatment for primary postpartum haemorrhage. Cochrane Database Syst Rev. 2003;1.:CD003249.
2. Soghra F, Niloufar A, Simin N, Aida N, Amin Q, Exploring the Causes of Prevalent Preterm Delivery after Pre-Eclampsia in Pregnant Women Visiting Shariati Hospital of Bandar Abbas in 2011-2012, 2015; 32: 6(2).
3. Lu MC, Fridman M, Korst LM, Gregory KD, Reyes C, Hobel CJ, Chavez GF. Variations in the incidence of postpartum hemorrhage across hospitals in California. Maternal and Child Health Journal. 2005 Sep 1;9(3):297-306.
4. Lockwood CJ, Nemerson YA, Krikun GR, Hausknecht VI, Markiewicz LE, Alvarez MA, Guller SE, Schatz FR. Steroid-modulated stromal cell tissue factor expression: a model for the regulation of endometrial hemostasis and menstruation. The Journal of Clinical Endocrinology & Metabolism. 1993 Oct 1;77(4):1014-9.
5. Lockwood CJ. Regulation of plasminogen activator inhibitor 1 expression by interaction of epidermal growth factor with progestin during decidualization of human endometrial stromal cells. American journal of obstetrics and gynecology. 2001 Apr 30;184(5):798-805.
6. Tsu VD, Langer A, Aldrich T. Postpartum hemorrhage in developing countries: is the public health community using the right tools?. International journal of gynecology & obstetrics. 2004 Jun 1;85(S1).
7. Novikova N, Hofmeyr GJ. Tranexamic acid for preventing postpartum haemorrhage. Cochrane Database Syst Rev. 2010 Jan 1;7(7).
8. Ferrer P, Roberts I, Sydenham E, Blackhall K, Shakur H. Anti-fibrinolytic agents in post partum haemorrhage: a systematic review. BMC pregnancy and childbirth. 2009 Jul 15;9(1):29.
9. World Health Organization. WHO recommendations for the prevention and treatment of postpartum haemorrhage. World Health Organization; 2012. Available at: http://ww.who.int/iris/bitstream/10665/75411/9789241548502_eng.pdf. Accessed 2012.
10. Movafegh A, Eslamian L, Dorabadi A. Effect of intravenous tranexamic acid administration on blood loss during and after cesarean delivery. International Journal of Gynecology & Obstetrics. 2011 Dec 31;115(3):224-6. DOI:10.1016/j.ijgo.2011.07.015
11. Gobbur VR, Shiragur SS, Jhanwar UR, Tehalia MJ. Efficacy of tranexamic acid in reducing blood loss during lower segment caesarean section. International Journal of Reproduction, Contraception, Obstetrics and Gynecology. 2017 Jan 2;3(2):414-7.

12. Jianjun Xu, Wei Gao, Yingnan Ju. Tranexamic acid for the prevention of postpartum hemorrhage after cesarean section: a double-blind randomization trial. Arch Gynecol Obstet (2013) 287:463–468.
13. Mehmet B. Sentu¨rk,Yusuf Cakmak,Gazi Yildiz,Pınar Yildiz. Tranexamic acid for cesarean section: a double-blind, placebo-controlled, randomized clinical trial. Arch Gynecol Obstet (2013) 287:641–645. DOI 10.1007/s00404-012-2624-8
14. Ducloy-Bouthors AS, Jude B, Duhamel A, Broisin F, Huissoud C, Keita-Meyer H, Mandelbrot L, Tillouche N, Fontaine S, Le Goueff F, Depret-Mosser S. High-dose tranexamic acid reduces blood loss in postpartum haemorrhage. Critical care. 2011 Apr 15;15(2):R117. http://ccforum.com/content/15/2/R117
15. Gungorduk K, Asıcıoğlu O, Yıldırım G, Ark C, Tekirdağ Aİ, Besımoglu 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. American journal of perinatology. 2013 May;30(05):407-14. DOI http://dx.doi.org/10.1055/s-0032-1326986
16. Halder S, Samanta B, Sardar R, Chattopadhyay S. Tranexamic acid used before caesarean section reduces blood loss based on pre- and postoperative haemoglobin level: a case-control study. J Indian Med Assoc. 2013 Mar;111(3):184-6.
17. Goswami U, Sarangi S, Gupta S, Babbar S. Comparative evaluation of two doses of tranexamic acid used prophylactically in anemic parturients for lower segment cesarean section: A double-blind randomized case control prospective trial. Saudi journal of anaesthesia. 2013 Oct;7(4):427.doi: 10.4103/1658-354X.121077
18. Gungorduk K, Yıldırım G, Asıcıoğlu O, Gungorduk OC, Sudolmus S, Ark C. Efficacy of intravenous tranexamic acid in reducing blood loss after elective cesarean section: a prospective, randomized, double-blind, placebo-controlled study. American journal of perinatology. 2011 Mar;28(03):233-40.
19. Simonazzi G, Bisulli M, Saccone G, Moro E, Marshall A, Berghella V. Tranexamic acid for preventing postpartum blood loss after cesarean delivery: a systematic review and meta-analysis of randomized controlled trials. Acta obstetricia et gynecologica Scandinavica. 2016 Jan 1;95(1):28-37.