The prophylactic use of tranexamic acid for the reduction of blood loss after cesarean section and vaginal delivery in primiparas at a tertiary hospital in Manila: A single-blinded randomized controlled trial*

Jo-An Marie G. Aguedan, MD and Carolina Paula C. Martin, MD, FPOGS

Department of Obstetrics and Gynecology, Ospital ng Maynila Medical Center

ABSTRACT

Objectives: To determine whether Tranexamic Acid is effective in reducing postpartum blood loss in vaginal and cesarean deliveries and if intravenous Tranexamic Acid can be used as a prophylaxis to reduce blood loss for vaginal and cesarean deliveries in primiparas.

Methods: This is a Single-Blinded Randomized Controlled Trial wherein two groups were assigned for the patients included, one for primiparas undergoing vaginal delivery and the other group for primiparas undergoing cesarean section. A dose of 2 grams of Tranexamic acid (given during the second stage of labor and over 30 minutes before abdominal delivery) were compared to primiparas to whom Tranexamic acid was not given. Blood loss was estimated from the main difference between the pre- and post-test hemoglobin and hematocrit obtained for each group and measured during two periods: first period was 30 minutes before delivery and the second from the end of the delivery of the baby to 2 hours postpartum. The difference was then compared and was used in the computation of the statistics, where t-test on two independent samples was utilized.

Results: One hundred twenty women were recruited to this study. The study was able to determine that those assigned to the Tranexamic acid or treatment group had significant reduction of postpartum blood loss as compared to the control group.

Conclusion: This study demonstrates that use of Tranexamic Acid prior to vaginal or abdominal delivery can reduce blood loss and maternal morbidity in women.

Keywords: Tranexamic acid, postpartum hemorrhage, hemoglobin, hematrocrit

INTRODUCTION

Childbirth in much of the world is a study in contrast. Over half a million women die attempting to give birth, with 99% of all maternal death occurring in the third world; yet most of these tragedies could be prevented. Obstetrical hemorrhage continues along with hypertension and infections as one of the infamous "triad" of causes of maternal deaths in both developed and underdeveloped countries[1]. Postpartum hemorrhage is the leading cause of maternal mortality in low-income countries and the primary cause of nearly one quarter of all maternal deaths globally[2].

Postpartum Hemorrhage is commonly defined as a blood loss of 500 ml or more for vaginal deliveries and 1000 ml for cesarean deliveries within 24 hours after birth. The diagnosis of postpartum hemorrhage is mostly reserved for pregnancies beyond 20 weeks gestation, as deliveries at less than 20 weeks gestational age are termed spontaneous abortions. However, the definition of postpartum hemorrhage should take into account the predisposing health factors, since the quantity of blood loss oftentimes is less important than the actual effect of it has on the parturients. Therefore it has been suggested that postpartum hemorrhage should be diagnosed with any amount of blood loss that threatens the hemodynamic stability of the woman[3]. Most deaths resulting from postpartum hemorrhage occur during the first 24 hours after birth: the majority of these could be avoided through the use of prophylactic uterotonics during the third stage of labor and by timely and appropriate management. Improving health care for women during childbirth in order to prevent and treat postpartum hemorrhage is an essential step towards the achievement of the Millennium Development Goals [2].

Postpartum Hemorrhage is predisposed by several factors such as injuries to the birth canal, uterine atony, abnormal placentation, obstetric factors, vulnerable patients and coagulation defects that may intensify other causes [4].

Philippine national statistics show that, on average, one mother dies of pregnancy and childbirth associated causes every 6 hours, and a newborn baby dies every 5 minutes. Cases of postpartum hemorrhage were identified

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from the census of the Obstetrics and Gynecology department and the Records Section of the institution. About 23% (16 out of 67) of maternal deaths from 2010 to 2013 were due to postpartum hemorrhage wherein majority of these were considered to be preventable.

The proportions of maternal deaths attributable to postpartum hemorrhage vary considerably between developed and developing countries, suggesting that deaths from postpartum hemorrhage are preventable. Interventions to prevent postpartum hemorrhage in developing countries are therefore pivotal in the global effort to achieve by 2015 the Millennium Development Goal of reducing maternal mortality ratio. According to the Millennium Development Goals Report 2014 of the Philippines almost 300,000 women died globally in 2013 from causes related to pregnancy and childbirth. Based on the country progress on all indicators, the Philippines is in critical danger of not achieving the target on improving maternal health by 2015. While the maternal mortality rate (MMR) had been declining over the past two decades, from 209 per 100,000 live births in 1993 to 172 in 1998 to 162 in 2006, the rate of change has been relatively low. In addition, the decline appears to have stalled making the target reduction in maternal mortality rate of 52 deaths per 100,000 live births by 2015 highly improbable [5].

Active management of the third stage of labor, which is an evidence-based intervention for the prevention of uterine atony, has been promoted in developing countries. However, both accurate knowledge about active management of the third stage of labor and its correct use remain low in developing countries. In 2007, the World Health Organization developed a set of guidelines for the prevention of postpartum hemorrhage. The recommendations in this guide are based on the available evidence for various interventions for the different components of active management of the third stage of labor. All women giving birth should be offered uterotonics during the third stage of labor for the prevention of postpartum hemorrhage; oxytocin (intramuscular/intravenous, 10 IU) is recommended as the uterotonic drug of choice. Other injectable uterotonics andmisoprostol are recommended as alternatives for the prevention of postpartum hemorrhage in settings where oxytocin is unavailable. In summary, the Guideline Development Group (GDG) of the WHO recommendations for the prevention of postpartum hemorrhage considered the use of uterotonics as the main intervention within the active management of third stage of labor package[6]. The use of tranexamic acid is advised in cases of refractory atonic bleeding or persistent trauma-related bleeding. The use of intrauterine balloon tamponade is recommended for refractory bleeding or if uterotonics are unavailable. Bimanual uterine compression, external aortic compression, and the use of non-pneumatic anti-shock garments are recommended as temporizing measures until substantive care is available. If there is persistent bleeding and the relevant resources are available, uterine artery embolization should be considered. If bleeding persists, despite treatment with uterotonic drugs and other conservative interventions, surgical intervention should be used without further delay[7]. According to WHO recommendations, the use of tranexamic acid is recommended for the treatment of postpartum hemorrhage if oxytocin and other uterotonics fail to stop bleeding or if it is thought that the bleeding may be partly due to trauma [7].

Tranexamic acid could be used in addition to current prophylactic uterotonic drugs in the third stage of labor, given intravenously to reduce the blood loss. It is used in the dose of 10 mg/kg given intravenously immediately after delivery of the baby or in a woman undergoing caesarean section, prior to the skin incision. Tranexamic acid acts within two to three hours after oral administration and immediately after intravenous administration, and its half-life is two to 10 hours. The oral route of administration is possible, but it is not ideal in the third stage of labor, when an immediate effect of the drug is required. (Novikova et, al. 2011)[8].

Tranexamic acid is 6 to 10 times more potent in terms of binding to plasminogen/plasmin than the other synthetic antifibrinolytic agent ε-aminocaproic acid (EACA). Suppression of fibrinolysis by tranexamic acid is manifested in surgical patients by reductions in blood levels of D-dimer, but the drug has no effect on blood coagulation parameters. Concurrent administration of heparin does not influence the activity of tranexamic acid[9]. Antifibrinolytic agents, mainly tranexamic acid and aprotinin, have been demonstrated to reduce blood loss and transfusion requirements in various elective surgeries [10]. Moreover, the Clinical Randomization of an Antifibrinolytic in Significant Hemorrhage (CRASH-2) study demonstrated that tranexamic acid safely reduces the risk of death in bleeding trauma patients[11]. In the field of obstetrics, three randomized, controlled trials[12,13,14] have suggested that tranexamic acid administration in women after vaginal or elective cesarean delivery reduces blood loss and the incidence of postpartum hemorrhage. Tranexamic acid potentiates the blood clotting system and is used to treat and prevent bleeding. The mechanism of action of tranexamic acid is related to its antifibrinolytic effect, which makes this drug potentially very effective in the third stage of labor. During placental delivery, there is rapid degradation of fibrinogen and fibrin occurs, as well as an increase in the activation of plasminogen activators and fibrin degradation products due to activation of the fibrinolytic system. This activation can last up to six to ten

hours postpartum, which may cause more hemorrhage. The antifibrinolytic effect of tranexamic acid in the third stage of labor could make it a safe and effective alternative or adjunct to other regimens currently used in the third stage of labor for prevention of postpartum hemorrhage[15].

Reductions of 34 to 57.9% versus placebo or control in mean menstrual blood loss were reported in women with menorrhagia receiving 2 to 3 cycles of treatment with tranexamic acid. The drug was at least as effective as nonsteroidal anti-inflammatory therapy and more effective than etamsylate (ethamsylate) or norethisterone. Efficacy of tranexamic acid in the control of bleeding has also been reported in individual patients with placental abruption or postpartum hemorrhage. A mean 71% reduction in postoperative blood loss was noted in a double-blind study in patients who received tranexamic acid 1.5 grams daily orally for 12 days after conization of the cervix. In another double-blind study, 1 of 38 patients who received tranexamic acid and 4 of 37 who received placebo experienced late bleeding after cervical conization with suturing; the difference between groups was not statistically significant[16].

However, according to the Clinical Practice Guidelines on Third Trimester Bleeding and Postpartum Haemorrhage (2012) an antifibrinolytic agent such as the Tranexamic acid may be useful as an adjunct in emergencies. A dose of 1 gram is given intravenously and can be repeated every 4-6 hours. Hemostatics are adjunctive forms of management for uterine atony and can be used in conjunction with or after primary measures[17].

OBJECTIVES

General Objectives:

1. To determine whether tranexamic acid is effective in reducing postpartum blood loss in terms of hemoglobin and hematocrit levels in vaginal and caesarean deliveries.
2. To determine if the use of intravenous 2 grams tranexamic acid can be used as a prophylaxis to decrease blood loss for vaginal or caesarean deliveries in primiparas.

SIGNIFICANCE OF THE STUDY

The importance of this study is to help us realize how to achieve the fifth target of the Millennium Development Goal which is to reduce by three quarters the maternal mortality ratio wherein most maternal deaths could be avoided by incorporating tranexamic acid as prophylaxis, reducing blood loss for those primiparas undergoing vaginal and cesarean deliveries. The high rate of maternal deaths especially in the Philippines attributes to inadequate access to integrated reproductive health services by women, including poor adolescents and men. According to Novikova et, al. (2011) Tranexamic acid decreases postpartum blood loss after vaginal birth and after cesarean section based on two RCTs of unclear quality which reported on only a few outcomes. Further investigations are needed to confirm efficacy and safety of this regimen for preventing postpartum hemorrhage. These results also provide the researcher a basis for the investigation of tranexamic acid for the treatment of postpartum hemorrhage.

METHODS

A. Time Frame

The trial was conducted between January 2014 - March 2014 at a tertiary hospital in Manila. The protocol was approved by the Institutional Ethics Review Board.

B. Study Design

There were 120 patients included in the study and an informed consent was secured from them. This is a single-blinded Randomized Control Trial wherein two groups were assigned for the patients included, one for primiparas undergoing vaginal delivery and the other group for primiparas undergoing cesarean section. Sociodemographic, past and family medical, obstetric and gynecologic histories were obtained and recorded. Basal vital signs were taken. The two groups were given appropriate patient numbers then randomized to receive either tranexamic acid (treatment group) or no antifibrinolytic treatment (control group) using the fish bowl technique. Those patients who picked the odd numbers were assigned to the treatment group and those who picked the even numbers were assigned to the control group. Blood sample were collected from the 2 groups from time of delivery up to 2 hours postpartum. Vital signs were monitored and recorded. Finally, result of baseline and postpartum complete blood count were analyzed and compared. (Figures 1 and 2).

C. Study Population

Inclusion Criteria:

1. Primigravidas admitted at the emergency room of a tertiary hospital in Manila.
2. Age 19-34 years old
3. Hemoglobin level of >/- 9.0 grams/dl

Exclusion Criteria:

1. Age </- 18 and >/- 35 years old
2. Hemoglobin of </- 9.0 grams/dl
3. Intrapartum complications
4. Hemorrhagic complications of pregnancy
5. Medical complications

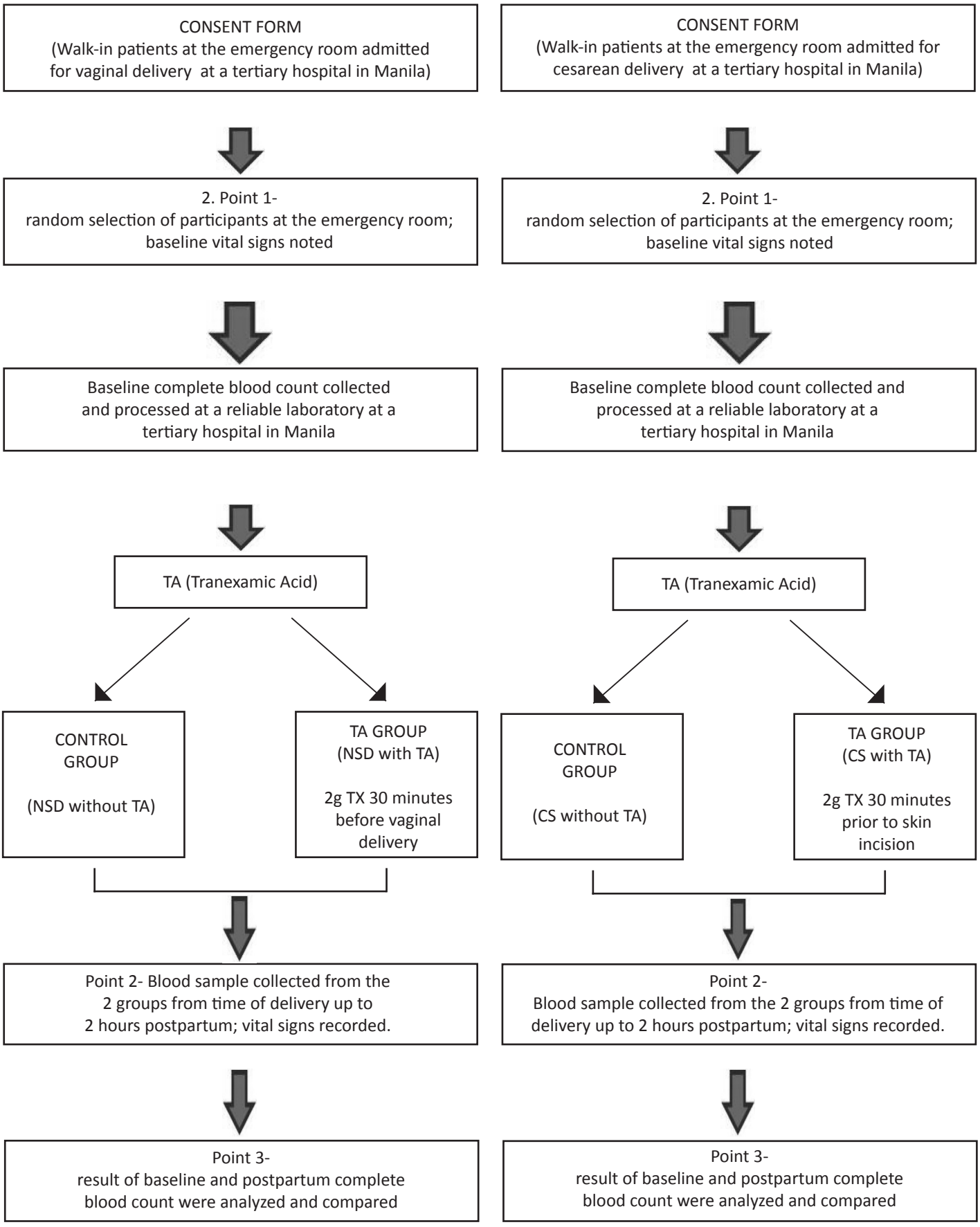

Figure 1. Study Design for Normal Spontaneous Delivery

Figure 2. Study Design for Cesarean delivery

6. Hematologic disorders
7. History of thrombosis or epilepsy

D. Sample Size

All the primigravidas admitted at the emergency room were all included in the study. Among 124 women who were eligible for inclusion, 4 did not agree to be included, so 120 were included. Therefore, 120 women fully completed the protocol (60 in the control group and 60 in the Tranexamic acid group). Estimate of the proportions of patients admitted would be 30% in the control and treatment group. This study would have about 80% power at the 0.05 level of significance (two sided test) to detect a treatment effect of this magnitude. All included women, apart from the one who did not meet the inclusion criteria, were included in the analysis.

E. Data Collection

After inclusion, patients were randomized to receive either treatment (tranexamic acid group) or no antifibrinolytic treatment (control group). The randomization sequence was generated by a single blinded selection of those primigravidas in labor for admission, and randomization was balanced by the researcher. The tranexamic acids administered to patients in this study were all provided by the researcher. Data collection was done by collecting the patient's case number, age, parity, diagnosis, course of labor and delivery and procedure done. Vital signs such as blood pressure, heart rate, respiratory rate were obtained in each patient included in the study. Assessment of hemodynamic stability was also assessed during the monitoring. Baseline hemoglobin was obtained prior to admission at the delivery suites and the second from the end of the delivery to 2 hours postpartum. The operators or surgeons were unaware of the group allocation participated in the collection of blood samples. All the data obtained from the study were encoded in Excel. Selected characteristics of patients were described using frequencies and percentages for categorical data and means and range for continuous data. A t-test was used to determine whether significant differences exist in the hemoglobin and hematocrit levels pre and post-delivery of the two groups being studied among primiparas who delivered vaginally or abdominally. Statistical significance was determined by a *p* value of less than 0.05.

F. Methodology

After the patients were included in the study and grouped either vaginal or cesarean delivery, the subjects were randomized to either tranexamic acid (treatment group) or no antifibrinolytic treatment (control group). In the tranexamic acid group, a dose of 2 grams of tranexamic acid was administered intravenously 30 minutes prior to delivery. In the tranexamic acid group, a dose of 2 grams of tranexamic acid, mixed with 50 ml of normal saline was administered intravenously 30 minutes prior to delivery over a period of 30 minutes. For the vaginal delivery group, it was given when the internal examination is 9-10 centimeters. For the cesarean section group, it was given 30 minutes prior to skin incision. The obstetric procedures were performed by the OB/GYN senior resident staff at a tertiary hospital in Manila. All patients were managed to the same timing according to the clinical practice guidelines: oxytocin, 10 units intramuscularly within a minute of baby's birth and oxytocin IV incorporation if needed, uterine massage after placental delivery, bladder catheterization, manual removal of retained placenta, genital tract examination.

Among those patients that belong to the control group who presented with signs of postpartum hemorrhage or blood loss of more than 500 ml for vaginal deliveries and 1000 ml for cesarean deliveries either from any cause of postpartum hemorrhage (genital tract lacerations, uterine atony, uterine rupture, uterine inversion) were eventually subjected to receive maximum doses of oxytocin and second line uterotonics, intravenous tranexamic acid, blood transfusion and invasive procedures (uterine packing or balloon tamponade, compression sutures and hysterectomy) for further management to address increasing blood loss. These patients were automatically excluded from the study.

G. Ethical Considerations

This study was brought to the Institutional Ethical Review Board of a tertiary hospital in Manila for approval. All investigations conformed to the guidelines of the use of human subjects in clinical research as embodied by the declaration of Helsinki where the confidentiality and anonymity of the subjects will be preserved.

H. Statistical Analysis

For test of the Mean Difference – The difference between pre and post-test hemoglobin and hematocrit was obtained for each group. The difference was then compared and was used in the computation of the statistics, where t test on two independent samples was utilized.

RESULTS

NORMAL SPONTANEOUS DELIVERY

A total of 60 primiparas who delivered vaginally were included in the study. The mean age of patients who delivered vaginally was 20 years old (Table 1). Majority of the patients who underwent vaginal delivery had hemoglobin ranging from 11-12 g/dL (51.67%) with mean hemoglobin of 12.216 g/dL (Table 2).

Table 1. Distribution of patients by age who delivered vaginally (n=60)

Age (years)	Number	Percentage
19-24	46	76.67
25-29	11	18.33
30-34	3	5.0
Mean Age	20 years old	

Table 2. Distribution of patients by hemoglobin who delivered vaginally (n=60)

Hemoglobin (g/dL)	Number	Percentage
9-10	10	16.67
11-12	31	51.67
13-14	19	31.67
Mean Hemoglobin	12.216 g/dL	

Majority of the patients who underwent vaginal delivery had episiotomy (median episiotomy and right mediolateral episiotomy) Out of the 60 patients under the tranexamic acid and control group, 47 of which (97%) underwent median episiotomy, 1 (1%) patient had right mediolateral episiotomy and 2 (2%) with restrictive episiotomy (Figures 3 and 4).

Table 3 shows the mean difference of pre and post-delivery for primiparas who underwent normal spontaneous delivery. It shows that the p value suggest that the mean reduction of hemoglobin between the tranexamic acid and control group of normal spontaneous delivery patients is significantly different with each other. Moreover, the mean reduction (Pre – Post) of each suggests that the control group (2.38) has a significantly higher mean hemoglobin changes than the tranexamic acid group of only 1.05. It also clearly shows that the baseline hemoglobin in the tranexamic acid group has a baseline change of 8.70% as compared to the control group which has a baseline change of hemoglobin of 19.45%. Also, the mean reduction in terms of hemoglobin of control group (2.38) is higher than the tranexamic acid (1.05) group in normal deliveries among primiparas (Figure 5).

The mean difference of hematocrit among primiparas who delivered vaginally as shown in Table 4 demonstrates that the *p* value suggest that the mean reduction of Hematocrit between tranexamic acid group and control group of normal spontaneous delivery patients is significantly lower (1.75) in the tranexamic acid group. The mean reduction (Pre – Post) of each suggests that the control group (4.94) has a significantly higher mean hematocrit changes than the tranexamic acid group. A

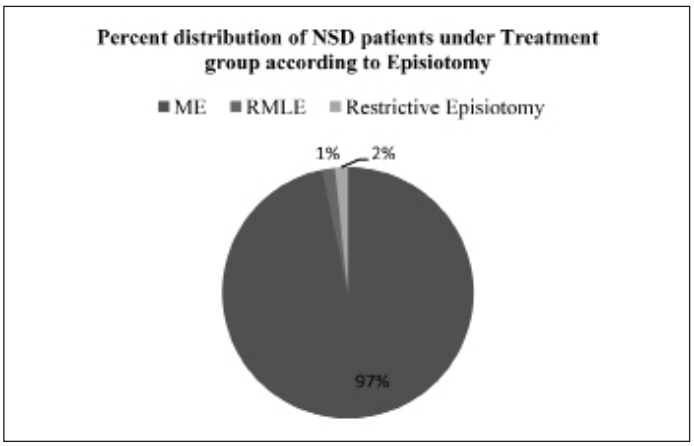

Figure 3. Distribution of vaginal delivery with or without episiotomy under the treatment group

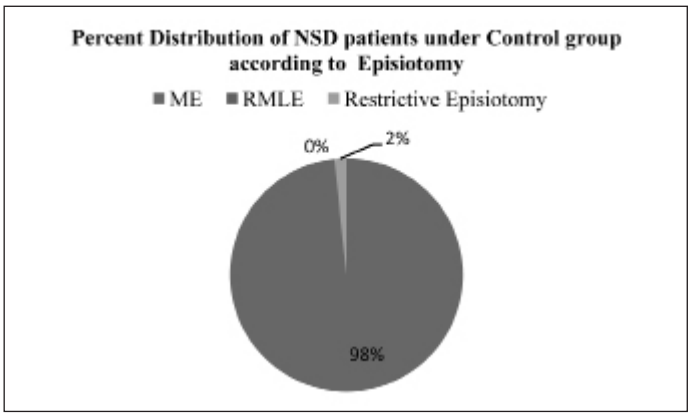

Figure 4. Distribution of vaginal delivery with or without episiotomy under the control group

significant change from the baseline hematocrit in the control group (13.87%) was also noted as compared to the tranexamic acid group (4.98%). Moreover, the mean reduction of hematocrit in the treatment group was lower as compared to the control group (Figure 6).

CESAREAN DELIVERY

A total of 60 primiparas were included in the study that underwent abdominal delivery. As shown in Table 5 the mean age of primiparas who delivered via cesarean section was 20 years old. The mean hemoglobin of patients under this group was 12.33 g/dL (Table 6). The mean difference of hemoglobin for pre and post cesarean deliveries demonstrates that the p value suggest that the mean reduction of hemoglobin between the tranexamic acid and control group of cesarean section patients is significantly different with each other. Moreover, the mean reduction (Pre – Post) of each suggests that the control group (2.21) has a significantly higher mean hemoglobin changes than the tranexamic acid group of only 0.98. The percent change from the baseline hemoglobin among those patients under the tranexamic acid was observed

Table 3. Normal Spontaneous Delivery: Mean Difference of Hemoglobin Pre and post delivery

	Group N= 60	Mean Difference (Pre – Post delivery)	Percent change from the baseline	t computed	p-value
Hemoglobin	Tranexamic Group N= 30	1.05	8.70 %	5.557	0.00000072
	Control Group N=30	2.38	19.45 %		

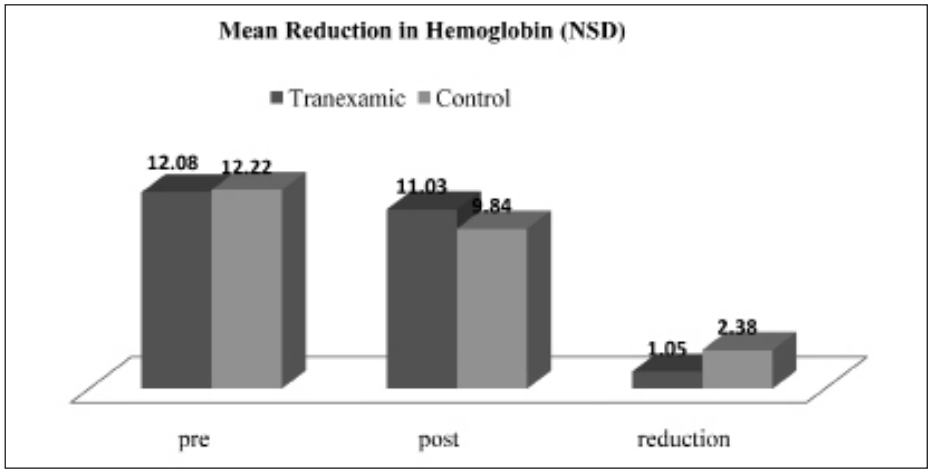

Figure 5. Mean reduction of hemoglobin in the tranexamic acid group and control group

Table 4. Normal Spontaneous Delivery: Mean Difference of Hematocrit Pre and post delivery

	Group N= 60	Mean Difference (Pre – Post delivery)	Percent change from the baseline	t computed	p-value
Hematocrit	Tranexamic Group N= 30	1.75	4.98 %	3.8105	3.8105
	Control Group N=30	4.94	13.87 %		

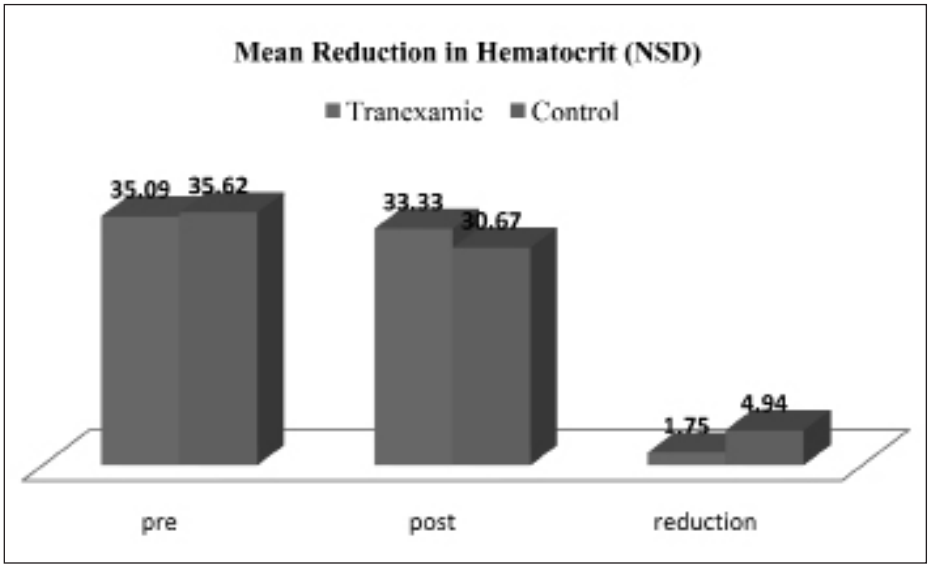

Figure 6. Mean reduction of hematocrit in the tranexamic acid group and the control group

Table 5. Distribution of patients by age who delivered abdominally (n=60)

Age (years)	Number	Percentage
19-24	47	78.33
25-29	11	18.33
30-34	2	3.33
Mean	20 years	

Table 6. Distribution of patients by hemoglobin who delivered abdominally (n=60)

Hemoglobin (g/dL)	Number	Percentage
9-10	5	8.33
11-12	34	56.67
13-14	21	35.00
Mean	12.33g/dL	

Table 7. Cesarean Delivery: Mean Difference of Hemoglobin Pre and post delivery

	Group N= 60	Mean Difference (Pre – Post delivery)	Percent change from the baseline	t computed	p-value
Hemoglobin	Tranexamic Group N= 30	0.98	7.66 %	4.2661	0.00007437
	Control Group N=30	2.21	17.93 %		

Table 8. Cesarean deliveries: Mean Difference of Hematocrit Pre and post delivery

	Group N= 60	Mean Difference (Pre – Post delivery)	Percent change from the baseline	t computed	p-value
Hemoglobin	Tranexamic Group N= 30	2.21	5.98 %	2.6239	0.0137
	Control Group N=30	4.50	12.63 %		

to be lower (7.66%) as compared to the control group (17.93%) (Table 7). Thus, as shown in Figure 7 there was a significant change in the mean reduction in terms of hemoglobin among primiparas in the tranexamic acid group (0.98) and control group (2.21).

Table 8 shows that the p value suggest that the mean difference of hematocrit between tranexamic acid and control group of patients delivered abdominally was significantly lower in the tranexamic acid group. The mean reduction (Pre – Post) of each group suggests that the control group (4.50) has a significantly higher mean hematocrit changes than the tranexamic acid group of only 2.21 which now gave us a percent change from the baseline hematocrit higher to be noted from the control group (12.63%) as compared to the tranexamic acid group (5.98%). Moreover, Figure 8 clearly shows that the mean reduction in terms of hematocrit of control group is higher than the tranexamic acid group in cesarean deliveries.

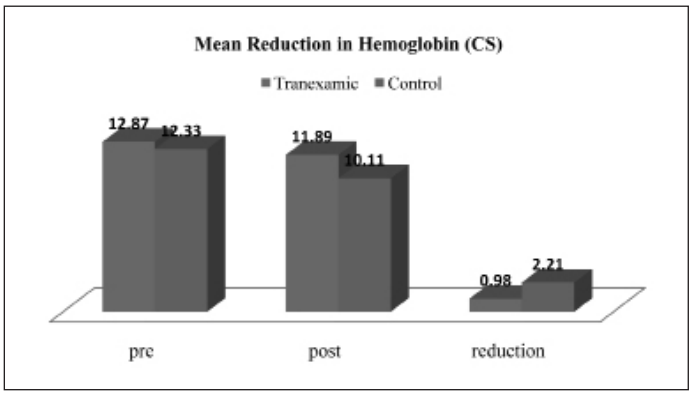

Figure 7. Cesarean Delivery: Mean reduction of Hemoglobin in the tranexamic acid group and control group

DISCUSSION

Interventions to prevent postpartum hemorrhage have always been the basic standard of care we provide to our women during delivery. This has been the foundation to every strategic policy and program that the WHO, different bodies and institutions adopt and recommend. These interventions have been effectively implemented to reduce the burden of postpartum hemorrhage.

Causes for postpartum hemorrhage may be considered to relate to one or more of 'the four Ts': Tone (abnormalities of uterine contraction), Tissue (retained

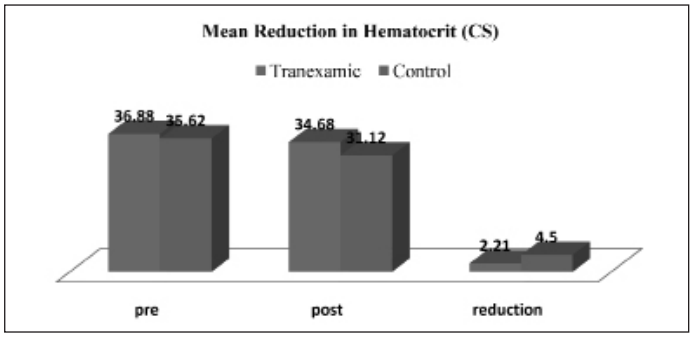

Figure 8. Cesarean Deliveries: Mean reduction of hematocrit in the tranexamic acid group and control group

Table 9. Causes of Postpartum hemorrhage

Delivery by emergency caesarean section	Trauma
Delivery by elective caesarean section	Trauma
Induction of labor	Tone
Retained placenta	Tissue
Perineal Trauma increase Episiotomy	Trauma
Operative vaginal delivery	Trauma
Prolonged labor (> 12 hours)	Tone
Big baby (> 4 kg)	Tone/Trauma
Coaguation problems in labor	Thrombin
Age (> 40 years, not multiparous)	Tone

products of conception), Trauma (of the genital tract) and Thrombin (abnormalities of coagulation). During labor and delivery; these factors should prompt extra vigilance among clinicians (Table 9). Uterotonics particularly oxytocin and ergometrine primarily acts on the first "T" of causes of postpartum hemorrhage while tranexamic acid, an antifibrinolytic agent acts on the last "T" which is to address thrombin as one cause of postpartum hemorrhage.

WHO recommends that the use of uterotonics particularly Oxytocin (10 IU, intravenous [IV]/intramuscular [IM]) for the prevention of PPH during the third stage of labor is strongly recommended for all births, with moderate quality evidence. In settings where oxytocin is unavailable, the use of other injectable uterotonics (e.g. ergometrine/methylergometrine or the fixed drug combination of oxytocin and ergometrine) or oral misoprostol (600 µg) is also strongly recommended, with moderate-quality evidence[7]. Novikova, et al, concluded in their study that Tranexamic acid decreases postpartum blood loss after vaginal birth and after caesarean section based on two RCTs of unclear quality which reported on only a few outcomes. Further investigations are needed on efficacy and safety of this regimen for preventing postpartum hemorrhage [8].

This study was able to investigate the potential for reducing bleeding by administering tranexamic acid in primigravidas delivering vaginally and abdominally. Only the primigravidas with term pregnancies were included in the study since a higher parity increases the risk of postpartum hemorrhage. Since the half-life of tranexamic acid is 2 to 10 hours, it still covers for the length of allowable time for the second stage of labor for primigravidas (usually 50 minutes) who will deliver vaginally. Factors that are associated with postpartum hemorrhage among those who are delivering vaginally that may cause a decrease in hemoglobin and hematocrit are as follows: prolonged third stage of labor, preeclampsia, mediolateral episiotomy, previous postpartum hemorrhage, twins, arrest of descent, soft-tissue lacerations, augmented labor, forceps or vacuum delivery, Asian or Hispanic ethnicity, midline episiotomy, and nulliparity [18]. In a similar study conducted by Coombs et, al., the authors also cited factors having a significant association with hemorrhage in cesarean deliveries that may also give a significant impact on the mean reduction of hemoglobin and hematocrit were as follows general anesthesia, amnionitis, preeclampsia, protracted active phase of labor, second-stage arrest, and Hispanic ethnicity [18].

Tranexamic acid in a concentration of 1mg/ml does not aggregate platelets in vitro. Tranexamic acid in concentrations up to 10mg/ml blood has no influence on the platelet count, the coagulation time or various coagulation factors in whole blood or citrated blood in normal subject[9]. This study aimed to evaluate on only one parameter for postpartum related outcome which was decrease in hemoglobin concentration that when administered earlier prior to delivery, evidence suggests that this drug reduces postpartum bleeding. Tranexamic acid safely reduces blood transfusions and duration of hospitalization. The CRASH 2 trial also concluded that the early administration of tranexamic acid to bleeding trauma patients is likely to be highly cost effective in low, middle and high income settings[20]. The researcher prefers a low dosage form of tranexamic acid since the higher dose of tranexamic acid tended to cause mild side effects such as nausea and vomiting for a very few of the women. Women who received a lower dose of tranexamic acid had no side effects but more research is needed [19].

It is shown in this study that the mean age of primiparas are those belonging to the age group of 19-34 years-old and majority received episiotomy (median episiotomy and right mediolateral episiotomy). Nulliparity and presence of episiotomy poses a higher risk for postpartum hemorrhage.

In this study among those primiparas who received 2 grams of intravenous tranexamic acid, 8 out of the 60 patients had a hemoglobin level of 9-10 g/dL. Minimal reduction in blood loss was noted as shown in their post-delivery hemoglobin and hemactocrit levels compared

to the pre delivery levels. This is supported by a study done by Upasana et, al. said concluded that tranexamic acid was found to be effective in reducing blood loss and transfusion in anemic parturients undergoing abdominal delivery [21].

According to the Clinical Practice Guidelines on third trimester bleeding and postpartum hemorrhage (2009), postpartum hemorrhage is a decrease in postpartum hematocrit levels of more than 10% from prenatal or baseline values. In this study it showed that the hematocrit levels of those primiparas under the tranexamic acid group had hematocrit levels not exceeding 10% reduction from their baseline hematocrit levels as compared to those patients under the control group [17].

The use of tranexamic acid cannot only be used as adjunct for the prevention of postpartum hemorrhage when all cases were initially managed using standard medical therapy which included included intramuscular/ intravenous oxytocin and or intravenous/intramuscular methylergometrine has been administered but rather it can be used as a prophylaxis to reduce or decrease postpartum blood loss to prevent postpartum hemorrhage. This suggestion was confirmed by the observation that the number of postpartum hemorrhage cases was lower in the tranexamic acid group than in the control group. The decrease in hemoglobin concentration was observed to be reduced in the tranexamic acid group.

There was no complication encountered with the use of 2 grams tranexamic acid when administered to the patients under the tranexamic acid group. The manner of administration prevented the adverse side effects of tranexamic acid to be experienced by our patients. Likewise, there was no reported significant complication in other studies mentioned. Therefore, the above dosage and mode of administration of tranexamic acid can be safely given. With this study, even primary level health workers can safely give this medication in rural areas especially in the Philippines without the need for skin testing prior to administration of the drug. It can be used in the initial management of midwives in lying centers before referring to hospitals.

Since tranexamic acid is readily available and is cost effective, it would be logical to use as a prophylaxis to reduce or decrease blood loss among primiparas without any concomitant medical problems who will deliver either vaginally or abdominally.

SUMMARY AND CONCLUSION

Postpartum hemorrhage is a potentially life-threatening event.

This study demonstrates that use of Tranexamic Acid 2 grams intravenously as a prophylaxis prior to vaginal or abdominal delivery can reduce blood loss and maternal morbidity in women. The observed reduction in blood loss, although significant and effective, was modest in terms of median values. Nonetheless, the time course (length of vaginal and cesarean delivery) of blood loss clearly suggests that tranexamic acid prevented further increase in blood loss in the women in this study. Therefore, the researcher concludes that the effect of tranexamic acid on post hemoglobin and post haematocrit values was clinically relevant and effective and that may have prevented the need for blood transfusion or other invasive procedures (compression sutures, uterine artery ligation, postpartum hysterectomy) to treat postpartum hemorrhage. An additional benefit in terms of the decrease in maternal morbidity associated with tranexamic acid when properly used outweighing its side effects/risk is a potential to spare medical cost especially in third world countries.

RECOMMENDATIONS

A major objective of the study was to determine if there was a significant reduction in blood loss among patients delivering vaginally or abdominally, and based on the results of this study the researcher concluded that tranexamic acid 2 grams administered intravenously prior to delivery has a significant impact in the postpartum hemoglobin and hematocrit values obtained. It can be recommended to use tranexamic acid as a prophylaxis before delivery in reducing postpartum blood loss. Further studies on a nationwide basis should be conducted to support this recommendation. With more cases of postpartum hemorrhage now being conservatively managed especially in primiparas, the researcher would like to recommend further studies on the role of tranexamic acid in the early detection of postpartum hemorrhage which will include pad count, changes in vital signs and clinical signs and symptoms as these changes has more correlation to increasing blood loss postpartum.

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