ORIGINAL ARTICLE

Efficacy of Preoperative Intravenous Tranexamic Acid Before Cesarean Section in Placenta Previa: A Randomized Double Blind Control Trial

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Background: Placenta previa is a common cause of postpartum hemorrhage (PPH) that contributes substantively to maternal morbidity and mortality rates. Tranexamic acid is an antifibrinolytic drug that is useful for the treatment of PPH. The recommendation from many guidelines is to start giving tranexamic acid as soon as PPH is diagnosed to reduce postpartum blood loss. Furthermore, some studies report the beneficial use of tranexamic acid given as a prophylactic before Cesarean section to decrease intraoperative blood loss and prevent PPH. To the authors' knowledge, in high-risk obstetrics case such as placenta previa, there was insufficient data to support recommendations of the use of tranexamic acid for prevent PPH.

Objective: To evaluate the efficacy of supplementary intravenous tranexamic acid before cesarean section versus prophylactic intravenous oxytocin after placenta delivery alone to decrease intraoperative blood loss and prevent PPH in placenta previa.

Material and Methods: The present study conducted a double blinded placebo control trial comparing adjunct 1 g tranexamic acid given intravenously before skin incision with prophylactic intravenous oxytocin after placenta delivery alone before cesarean section for placenta previa. The study recruited 60 women who were diagnosed with placenta previa at gestational age (GA) of more than 28 completed weeks undergoing emergency cesarean section due to active bleeding or scheduled for elective cesarean section at 37 completed weeks at Chonburi Hospital between July 2021 and July 2022. The primary outcome was intraoperative blood loss.

Results: Sixty diagnosed placenta previa women were recruited, with 30 patients per group. Group I patients were given 1 g tranexamic acid and Group II were given a placebo of 100 ml NSS before skin incision. Both groups received intravenous oxytocin 20 units after placenta delivery. The main outcome showed that preoperative tranexamic acid intravenous reduced intraoperative blood loss significantly compared with the placebo at 349.5 ml (range of 168 to 2,200) versus 619 ml (range of 288 to 3,243), p<0.001. The secondary outcome showed a significant decrease in the incidence of PPH at 4 (13.33%) versus 10 (33.33%), p=0.030 and decreased in the incidence of blood transfusion of more than one unit from 5 (16.67%) versus 13 (43.33%), p=0.047.

Conclusion: Prophylactic supplementary 1 g tranexamic acid intravenously before cesarean section to prophylactic intravenous oxytocin after placental delivery was found to effectively reduce intraoperative blood loss and PPH.

Keywords: Tranexamic acid; Preoperative; Placenta previa; Intraoperative blood loss; Cesarean section

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One of the leading causes of maternal death globally is obstetric hemorrhage. It accounts for 8% of maternal deaths in developed regions of the world and 20% of maternal death in developing regions[1]. Frequent causes of hemorrhage include uterine atony with placental site bleeding. Placenta previa or low-lying placenta both contribute substantively to maternal morbidity and mortality rates, classified as high risk of postpartum hemorrhage (PPH) and the potential need for blood transfusion[2]. The maternal mortality ratio is increased approximately threefold for women with a placenta previa. Incidences of placenta previa have increased during the past 30 years. Reported incidence range from 0.3% to 1% globally[3]. In Thailand, obstetric hemorrhage is the leading cause of maternal death. Data from the Department of Health in Thailand between 2021 and 2022 showed that the maternal mortality rate of 27.8 per 100,000 caused by obstetric hemorrhage had an average of 16% of cases where the main cause was placenta previa. The incidence of placenta previa at

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Chonburi Hospital between 2017 and 2020 was 60 to 80 per 1,000 live births at an average of 0.1% per year[4].

Tranexamic acid is an antifibrinolytic agent, Food and Drug Administration (FDA) category B, that is safe in pregnancy. Its mechanism of action is synthetic reversible competitive inhibition at the lysine binding sites on plasminogen molecules, enhancing the effectiveness of the hemostatic mechanism by preventing plasmin from binding to the fibrin matrix and inhibiting blood clot breakdown. The concentration reaches its peak in the plasma rapidly following administration with a half-life of 2 to 11 hours[5-8].

Side effects of tranexamic acid include nausea, vomiting, headache, and myalgia, and a serious side effect needed to concern was thromboembolism.

Studies evaluated the safety profile of tranexamic acid for cesarean section. Agrawal et al.[9] conducted a prospective study to evaluate the safety of tranexamic acid during and after cesarean section in 100 cases and found that tranexamic acid was not associated with thromboembolism. Li et al.[10] conducted a systematic review and meta-analysis recruiting 25 randomized control trials (RCTs) with 4,747 participants to evaluate the efficacy and safety of tranexamic acid administered before cesarean section. The results demonstrated that tranexamic acid was both efficient and safe for patients undergoing cesarean sections and was not associated with thromboembolism.

Tranexamic acid is useful for the treatment of PPH, and many large RCTs report a significant reduction in death from obstetric hemorrhage, and modest reductions in obstetrics blood loss such as WOMAN trial[2]. Now, the recommendation from many guidelines is to start giving tranexamic acid as soon as PPH is diagnosed, by giving 1 g over 10 minutes within three hours of cesarean or vaginal delivery. If bleeding persists after 30 minutes or stops and restarts within 24 hours of the first dose, a second dose may be administered[11-13].

However, there was insufficient data to support recommendations of the use of tranexamic acid for prophylaxis. Some studies reported the beneficial use of tranexamic acid given prophylactic before cesarean section to decrease intraoperative blood loss and prevent PPH. Sentilhes et al.[5] reviewed evidence from 10 RCTs evaluating the efficacy of tranexamic acid before cesarean section in low-risk elective cesarean section case for preventing PPH. Tranexamic acid showed a significant decrease in postpartum blood loss.

Placenta previa is classified as high risk of PPH[2] due to characteristic of poor smooth muscle contraction at lower uterine segment[3] that led to difficult controlled placental implantation site bleeding. Accordingly, the authors hypothesized that Tranexamic acid could be used to facilitate the hemostatic process, inhibit fibrin degradation, and promote hemostasis adjunct to prophylactic uterotonic drug administration in the third stage of labor that enhanced myometrial contraction. The authors designed to inject tranexamic acid prior to the cesarean section because it reached peak concentration rapidly after injection[7,8].

According to the existing data and the authors' expertise, there were insufficient data about preoperative tranexamic acid in placenta previa that posed a high risk for massive hemorrhage.

Few RCTs evaluated the efficacy of prophylaxis tranexamic acid before cesarean section adjunct to intravenous oxytocin after delivery for prevent PPH in placenta previa. Abbas et al.[14] investigated the effect of prophylactic adjunctive tranexamic acid before cesarean section on operative blood loss in patients with placenta previa who underwent bilateral uterine artery ligation. According to the results of the present study, the supplementary use of tranexamic acid in individuals having bilateral uterine artery ligation because of placenta previa was associated with less blood loss.

In another RCT, Shady et al.[15] compared intravenous tranexamic acid before cesarean section and topical tranexamic acid application on the placental bed with placebo. The outcome showed that prophylactic tranexamic acid administered intravenously was effective in decreasing intra-operative blood loss by as much as 42% compared with placebo (p=0.0001).

Materials and Methods

The present study was a randomized double blind control trial conducted at Chonburi Hospital, a tertiary hospital in Thailand, between July 2021 and July 2022. The Institutional Ethical Review Board of Chonburi Hospital approved the study (study number 12/64/R/h1).

The present study performed in accordance with CONSORT 2010 standards checklist. The study protocol was entered into the Thai Clinical Trials Registry, Registration number TCTR 20220930003.

Before any patients were enrolled in the present trial, their informed written consents were obtained. The sample size estimation was calculated from

intraoperative blood loss from placenta previa patients at Chonburi Hospital in the year 2020, mean ± standard deviation (SD): 904±587 ml. A two-sample comparison of means was conducted with a two-sided test with 5% α error and 80% statistical power. It could be assumed that intervention could decrease blood loss intraoperatively by 50%, and according to Shady et al.[10], the blood loss decrease intraoperatively could be as high as 42%. The authors estimated a required sample size of 26 placenta previa patients per group and added 10% for loss of follow up, so required a sample size of 30 placenta previa patients per group.

The authors recruited all women diagnosed with placenta previa made by transabdominal or transvaginal ultrasound at gestational age (GA) of more than 28 completed weeks and cases undergoing cesarean delivery for placenta previa, composed of both elective cesarean section at term of 37+0 weeks, or emergency cesarean section due to placenta previa.

At Chonburi Hospital, the obstetricians planned to set elective cesarean sections for placenta previa at GA of 37 completed weeks and set emergency cesarean sections in placenta previa when presented with any condition that precluded expectant management such as active bleeding accompanied with unstable maternal vital signs and fetal distress. The authors collected both elective and emergency cases due to data from many cohort studies that revealed that operative blood loss was not different between elective and emergency cases[16,17].

Placenta previa diagnosed by the National Institutes of Health (NIH) classification is divided to placenta previa if the internal os was partially or completely covered by the placenta, or low lying if the placental edge lied within the 2-cm wide perimeter around the os and did not cover it[18]. All cases recruited required ultrasound confirmation conducted by a third-year resident or staff before the cesarean section.

Exclusion criteria included patients showing any sign of placental adherence on ultrasound before the procedure, patients with hepatic, cardiac, or renal disease, patients with tranexamic acid allergy, and patients with risk factors for venous thromboembolism (VTE) such as prior VTE, thrombophilia disease, hematologic cancer, immobilization, first degree relative history of VTE, or morbid obesity with body mass index (BMI) greater than 40.

Patients were randomized into two groups according to a randomization process using a block of four, with the codes T1 or T2 at a 1:1 ratio, prepared using a computer-generated randomization system. The allocated groups were concealed in serially-numbered sealed opaque envelopes that would only be opened after recruitment. Patient allocation was performed before going to the operation room and the patients were allocated to one of the two groups.

Group 1 patients received the drug labeled "T1" that was 1 g tranexamic acid of concentration as 250 mg/5 ml, 20 ml in 80 ml NSS intravenous drip in 10 minutes before the skin incision. Group T2 patients received the drug labeled "T2" that was normal saline solution (NSS) 100 ml intravenous drip in 10 minutes. The tranexamic acid drug and placebo were prepared by Chonburi Hospital 's pharmacist. Both T1 and T2 drugs were labeled with the name "tranexamic acid 1 g" in the same size of bottle package and the same color.

Only the pharmacist knew which code (T1 or T2) was the tranexamic acid. The code was revealed at the end of the data analyses. Therefore, the outcome assessor, the surgeon, and the participants were all blind to the intervention. The standard technique for cesarean section was performed for all patients, under general anesthesia or spinal block anesthesia depending on the anesthesiologist's decision. The operator would be resident 3 covered by obstetric staff, while the drug T1 or T2 was administered intravenously and slowly in 10 minutes prior to skin incision at not over 100 mg per minute, by the anesthesia nurse.

After delivery of the placenta, all patients would receive an oxytocin intravenously according to Chonburi Hospital's standard guidelines for preventing PPH in the third stage of labor. The dosage was a total of 20 units divided as 17 units dissolved in 1,000 ml ringer lactate solution and 3 units given intravenously.

The primary outcome of the present study was intraoperative blood loss measured by the sum of the volume of blood in the suction bottle after the amniotic fluid was completely suctioned after placental delivery, adding the difference in weight of the dry for preoperative and soaked for postoperative gauze. The gravimetric method of measuring operative blood loss was used, assuming that density of blood is equivalent to water 1 g for 1 ml[19].

The outcome assessor, who was any doctor who did not participate in the surgery, weighed the gauze using a weighing machine that met the certificated standard by the Ministry of Commerce and could report the weight to three decimal places.

The secondary outcomes included the incidence

of PPH for blood loss more than 1,000 ml within 24 hours, measured by the difference in weight of the dry and soaked pampers at the postpartum unit measured by the nurse.

Other outcomes recorded were additional uterotonic drugs administered intraoperatively such as oxytocin greater than 20 unit that was standard protocol for all cesarean section cases in Chonburi Hospital, Methylergometrine, Misoprostol, additional surgical procedures performed intraoperatively such as uterine compression suture performed using the Hayman suture technique, uterine artery ligation, internal iliac artery ligation, and hysterectomy, combined additional intraoperative and postoperative blood transfusion of more than one unit, operative time, hospital length of stay, and postoperative 24 hours hematocrit.

Any side effects of tranexamic acid such as nausea, vomiting, headache, or myalgia were also recorded via questionnaire, 24 hours after the operation, recorded as "yes" if the patient had more than one episode of any symptom within 24 hours of the operation.

Serious side effects of tranexamic acid such as thromboembolism or pulmonary embolism were monitored by questionnaire asking patients about symptoms such as dyspnea, chest pain, hemoptysis, and persistent oxygen saturation below 90%. If any symptoms were presented, initial investigative chest X-ray, electrocardiogram (EKG) 12 lead, and arterial blood gas would be conducted to exclude other causes such as preeclampsia with severe features. When pulmonary embolism was suspected, the protocol called for a computed tomography pulmonary angiogram (CTPA) test and medicine consultation.

If any serious side effects occurred, the authors could report to the Institutional Ethical Review Board of Chonburi Hospital and stop enrolling the studied patient until the Board approves to continue the study.

The data were collected and statistically analyzed using Stata Statistical Software, version 16 (StataCorp LLC, College Station, TX, USA). Qualitative data such as type and location of placenta and type of anesthesia such as general anesthesia (GA) or spinal block (SB) were described as number and percentage, while Fisher's exact test was used to compare between groups. Quantitative data were described as mean (±SD) or median (minimum-maximum) depending on the normal or non-normal distribution of the variables. The two samples t-test was used for normally distributed variables and the Mann-Whitney U test was used for non-normally distributed variables. A p-value less than or equal 0.05 was considered statistically significant.

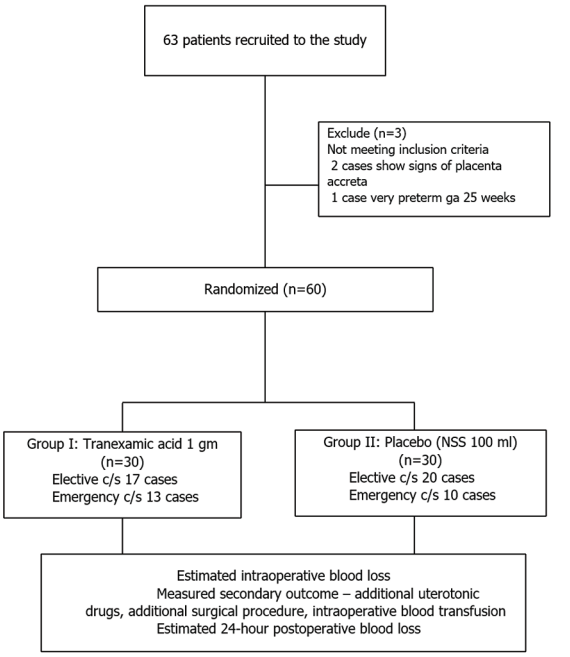

Figure 1. The study flowchart.

Results

Sixty-three patients were recruited to participate but excluded two cases with ultrasound findings that showed signs of placenta accrete spectrum and one case whose GA was less than 28 complete weeks. Baseline characteristics between the groups did not differ for BMI, GA, number of elective and emergency cases, or type and location of placenta between groups, as shown in Table 1.

The primary outcome was that patients in the tranexamic acid group showed significantly lower intraoperative blood loss compared with the placebo group at 349.5 ml (range of 168 to 2,200) versus 619 ml (range of 288 to 3,243), $p<0.001$.

Secondary outcomes were that the tranexamic acid group showed significantly lower incidence of PPH with a blood loss greater than 1,000 ml within 24 hours of delivery for 4 (13.33%) versus 10 (33.33%), $p=0.030$, decreased PRC transfusion of more than one unit for 5 (16.67%) versus 13 (43.33%), $p=0.047$, and decreased additional Methylergometrine as a uterotonic drug intraoperative for 26 (86.7%) versus 14 (46.7%), $p=0.001$. Other secondary outcomes such as operative time, other uterotonic drugs such as Methylergometrine or Misoprostol, or additional surgical procedures were all decreased in the

Table 1. Baseline characteristics of patients in the study group

Characteristics	Tranexamic acid group (n=30)	Placebo group (n=30)	p-value
Age (years); mean±SD	34.7±4.5	32.7±5.0	0.115
BMI; mean±SD	27.6±4.1	26.2±4.2	0.214
Gravida; n (%)			0.124
1	11 (36.7)	7 (23.3)	
2	14 (46.7)	15 (56.7)	
3	1 (3.3)	5 (16.7)	
4	3 (10.0)	0 (0.0)	
5	1 (3.3)	1 (3.3)	
Gestational age; n (%)			0.421
>37 week,	18 (60.0)	21 (70.0)	
34 to 36^{+6} week	5 (16.7)	6 (20.0)	
<34 week	7 (23.3)	3 (10.0)	
Hct preoperative; mean±SD	33.9±3.7	34.2±3.4	0.750
Surgery; n (%)			0.596
Elective	17 (56.7)	20 (66.7)	
Emergency	13 (43.3)	10 (33.3)	
Anesthesia technique; n (%)			0.795
General anesthesia	14 (46.7)	12 (40.0)	
Spinal block	16 (53.3)	18 (60.0)	
Previous CS x1; n (%)	24 (80.0)	23 (76.7)	1.000
Abortion; n (%)	5 (16.7)	6 (20.0)	1.000
History of dilatation & curettage; n (%)	2 (6.7)	2 (6.7)	1.000
Type of placenta previa; n (%)			1.000
Placenta previa	23(76.7)	23 (76.7)	
Low lying	7 (23.3)	7 (23.3)	
Placental location; n (%)			1.000
Anterior	11 (36.7)	12 (40.0)	
Posterior	19 (63.3)	18 (60.0)	
Fetal presentation; n (%)			0.656
Cephalic	25 (83.3)	22 (73.3)	
Breech	1 (3.3)	3 (10.0)	
Transverse	4 (13.3)	5 (16.7)	
Twin pregnancy; n (%)	1 (3.3)	1 (3.3)	1.000
Hypertensive disease*, n (%)	2 (6.7)	3 (10.0)	1.000
Preeclampsia with severe features; n (%)	0 (0.0)	2 (6.7)	0.495
GDMA1; n (%)	6 (20.0)	5 (16.7)	1.000
Myoma uteri; n (%)	1 (3.3)	1 (3.3)	1.000
Fetal growth restriction; n (%)	2 (6.7)	1 (3.3)	1.000
Maternal HIV; n (%)	1 (3.3)	0 (0.0)	1.000
Maternal hepatitis B carrier; n (%)	1 (3.3)	1 (3.3)	1.000

SD=standard deviation; BMI=body mass index; CS=cesarean section; Hct=hematocrit; GDMA1=gestational diabetes mellitus type 1; HIV=human immunodeficiency virus

* Chronic hypertension, gestational hypertension, preeclampsia

tranexamic acid group, but the difference did not reach statistical significance, as shown in Table 2.

There was no significant difference in side effects within 24 hours of the operation between the two groups. The authors collected data of side effects including nausea, vomiting, headache, myalgia, and fatigue, and while the data showed more reported side effects in the tranexamic acid group, the difference was not statistically significant, as shown in Table 3. There were no reports of side effects of suspected

Table 2. Primary and secondary outcomes among study groups

Outcomes	Tranexamic acid group (n=30)	Placebo group (n=30)	p-value
Intraoperative blood loss; median (min-max)	349.5 (168-2,200)	619 (288-3,243)	<0.001
PPH blood loss >1,000 ml postpartum; n (%)	4 (13.3)	10 (33.3)	0.030
Operative time (hour); mean±SD	1±0.39	1.067±0.43	0.589
PRC transfusion >1 unit; n (%)	5 (16.7)	13 (43.3)	0.047
Additional uterotonic drugs; n (%)	21 (70.0)	27 (90.0)	0.104
Syntocinon >20 unit	13 (43.3)	19 (63.3)	0.195
Methylergometrine	14 (46.7)	26 (86.7)	0.002
Misoprostol	1 (3.3)	2 (6.7)	1.000
Additional surgical procedure; n (%)	3 (10.3)	8 (26.7)	0.181
Uterine compression suture (Haymann suture)	0	2 (6.7)	0.492
Condom balloon tamponade	2 (6.7)	4 (13.3)	0.671
Uterine artery ligation	1 (3.3)	4 (13.3)	0.353
Internal iliac artery ligation	0	1 (3.3)	1.000
Hysterectomy	0	0	
Additional uterotonic drugs post-operation; n (%)	1 (3.3)	13 (43.3)	<0.001
Hct 24 hours post-operative; mean±SD	32.8±4.26	31.5±3.41	0.196
Duration of hospital stay; mean±SD	2.3±0.66	2.1±0.30	0.141

SD=standard deviation; PPH=postpartum hemorrhage; PRC=packed red cell; Hct=hematocrit

Table 3. Side effects reported for tranexamic acid within 24 hours postpartum

Side effect	Tranexamic acid group (n=30); n (%)	Placebo group (n=30); n (%)	p-value
Nausea	15 (50.0)	7 (23.3)	0.060
Vomiting	10 (33.3)	4 (13.3)	0.125
Headache	6 (20.0)	6 (20.0)	1.000
Myalgia	1 (3.3)	2 (6.7)	1.000

thromboembolism or pulmonary embolism in the present study.

Discussion

Tranexamic acid is an antifibrinolytic agent. It is widely used as a treatment in reducing hemorrhage and lowering transfusion requirements and its use has been well established in various elective surgery procedures with a good safety profile. It is classified as pregnancy category B[6].

Several RCTs reported good effects of tranexamic acid for the treatment of PPH. The WOMAN trial[20], assessed the effect of tranexamic acid for treatment in 20,060 women who were diagnosed with PPH, randomized to 1 g tranexamic acid or a placebo. The results concluded that tranexamic acid significantly reduced death due to bleeding with no adverse effects.

According to the WOMAN trial, tranexamic acid appears to be a promising medication for the treatment of PPH. Now, the recommendation from many guidelines is to start giving tranexamic acid as soon as PPH is diagnosed, by giving 1 g over 10 minutes within three hours of cesarean or vaginal delivery. If bleeding persisted after 30 minutes or stops and restarts within 24 hours of the first dose, a second dose may be administered[11-13].

Furthermore, many RCTs evaluated the role of tranexamic acid for prevention of PPH. Ahmed et al.[21] conducted a systematic review and meta-analysis of 17 RCTs with 7,122 patients, that inspected the efficacy of prophylactic tranexamic acid among women undergoing vaginal delivery. The findings revealed that prophylactic tranexamic acid in all cases during active management of the third stage of labor was associated with a significant decrease in postpartum blood loss.

For cesarean delivery, Sentilhes et al.[22] conducted TRAAP2 trial, Tranexamic Acid for Preventing PPH Following a Cesarean Delivery, and recruited 4,551 patient that received prophylactic tranexamic acid after birth compared with placebo along with prophylaxis uterotonic drug, which resulted in decrease rate of PPH.

However, there is no recommendation for the role of prevention in tranexamic acid use, due to limited evidence to support such a role for tranexamic acid in prophylaxis for PPH, especially in the context of placenta previa that is the main cause of PPH.

There were some RCTs that evaluated efficacy of prophylaxis tranexamic acid before cesarean

section for placenta previa. Abbas et al. investigated the effect of prophylactic adjunctive tranexamic acid on operative blood loss during cesarean section in patients with placenta previa that underwent bilateral uterine artery ligation. According to the results of the present study, the supplementary use of tranexamic acid in individuals having bilateral uterine artery ligation because of placenta previa is associated with less blood loss[14].

Another RCT by Shady et al. compared intravenous tranexamic acid before cesarean section in placenta previa with topical tranexamic acid application on the placental bed, whereby the outcome showed that prophylactic tranexamic acid administered both topically on the placental bed and intravenously was effective in reducing intraoperative blood loss[15].

From the present study, the authors also concluded that adjunct intravenous administration of tranexamic acid before cesarean section to prophylactic intravenous oxytocin after placental delivery effectively reduced intraoperative blood loss. During delivery, when the placenta detaches from the uterine wall, activation of the fibrinolytic system causes rapid degradation of fibrinogen to fibrin along with an increase of plasminogen activators and fibrin degradation products that lead to hemorrhage[23]. Physiologic and hemostatic changes occur sequentially to reduce bleeding such as increased platelets, coagulation factor release, and generated myometrial contraction[24]. In placenta previa, the lower uterine segment's smooth muscle may fail to contract properly due to its characteristic of poorly contracted area, which can cause the placental implantation site to bleed excessively[3]. Tranexamic acid can be used to facilitate the hemostatic process, inhibit fibrin degradation, and promote hemostasis adjunct to prophylactic oxytocin administration in the third stage of labor that enhances myometrial contraction[5].

Its concentration reached its peak in the plasma rapidly following administration[7,8], so it is reasonable to add the drug before the cesarean section.

Tranexamic acid also decreased the incidence of PPH, reduced blood transfusion greater than one unit, and reduced the use of some uterotonic drugs such as Methylergometrine with statistical significance, but did not reduce the use of other uterotonic drugs.

Other outcomes such as additional surgical procedures including uterine compression suture, uterine artery ligation, and internal iliac artery ligation were all decreased in the tranexamic acid group but not to an extent that reached statistical significance. There were no cases resulting in hysterectomy or death in the present study. Because of the small sample size, however, the study was not sufficiently powered to evaluate the secondary outcomes.

In the present study, eight patients (26.7%) from the placebo group received an additional surgical procedure to decrease blood loss including uterine artery ligation and internal iliac artery ligation. No patients from the tranexamic group received these procedures.

Table 3 shows the side effects of nausea, vomiting, myalgia, and headache within 24 hours of the operation. The outcome showed no difference in adverse effects of tranexamic acid between the two groups. The patients who received tranexamic acid reported side effects of nausea in 15 (50%) versus 7 (23.33%) and vomiting in 10 (33.33%) versus 4 (13.33%), but these results were not statistically significant. The outcome was consistent with earlier RCTs that taking tranexamic acid prior to a cesarean section had no significant adverse effects[14,15].

No case reported of the adverse effects of thromboembolism, deep vein thrombosis, or pulmonary embolism in the present study.

Strength and limitation

This is the first trial to examine the potential benefits of supplementary 1 g tranexamic acid intravenously before cesarean section to prophylactic intravenous oxytocin after placental delivery in placenta previa. The baseline characteristics of patients in the two groups were well balanced.

The surgeon and outcome assessors were totally blinded to the use of the placebo performed by the pharmacist so there was no assessment bias or performance bias.

However, the limitation of the present study was having many surgeons performing the cesarean sections. Although the surgeons must be chief residents covered by obstetrics staff in all cases, each surgeon would still have different surgical skills and decisions for the management of PPH.

Another limitation was that the present study did not collect neonatal outcome data such as Apgar scores or neonatal complications because there are many other factors that affect neonatal outcomes, such as preterm gestation, or hypotension of the mother due to active bleeding, so further study to assess effects upon the fetus is needed.

Finally, one further limitation was the small sample size since it was a single center RCT.

Therefore, it was not designed with sufficient power to evaluate the secondary outcomes. Further trials with a larger sample size are recommended.

Conclusion

Prophylactic supplementary administration of 1 g tranexamic acid intravenously before cesarean section to prophylactic intravenous oxytocin after placental delivery is found to effectively reduce intraoperative blood loss, and incidence of PPH in placenta previa cases without any adverse effects.

What is already known on this topic?

Tranexamic acid is recommended for the treatment of PPH. However, there is no recommendation for the role of prophylaxis in tranexamic acid use, even in high risk for PPH cases such as placenta previa.

What this study adds?

Prophylactically adjunct intravenous Tranexamic acid before cesarean section effectively reduces intraoperative blood loss and decrease incidence of PPH in placenta previa.

Conflicts of interest

The authors declare no conflict of interest.

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