SJIF Impact Factor: 6.711

WORLD JOURNAL OF ADVANCE HEALTHCARE RESEARCH

ISSN: 2457-0400
Volume: 8.
Issue: 11
Page N. 70-80
Year: 2024

Original Article www.wjahr.com

TRANEXAMIC ACID IMPACT ON THE PREVENTION OF HEMORRHAGE DURING AND AFTER CESAREAN SECTION IN PARTURIENTS AT RISK

Hadbi Mohamed*, Matouk Mohamed, Boutrid Hala, Benamane Raouf and Fellah Nadia

Algiers.

Article Received date: 05 September 2024 **Article Revised date:** 26 September 2024 **Article Accepted date:** 16 October 2024

***Corresponding Author: Hadbi Mohamed**

Algiers.

DOI: https://doi.org/10.5281/zenodo.18160629

ABSTRACT

Purpose: To assess the efficacy and safety of intravenous tranexamic acid in reducing blood loss during and after elective cesarean section in parturients at high risk for postpartum hemorrhage. **Methods:** We carried out a double-blind, randomized controlled trial involving 800 parturients at high risk of PPH scheduled for cesarean section. They were randomly assigned to receive 1 g of tranexamic acid or placebo 15 min before the surgical incision. The assessment of intraoperative and postoperative blood loss was based on the volumetric and gravimetric methods. The statistical software SPSS version 20 was used for the analysis. **Results:** Our results showed that tranexamic acid significantly reduced bleeding during and after cesarean delivery. The total blood loss in the study group (299 ± 113 ml) was significantly lower than that in the placebo group (503 ± 246 ml) ($p < 0.001$). The mean decrease in hemoglobin level was significantly lower in the tranexamic acid group than in the control group ($P= 0.0002$). It also reduced the incidence of PPH ($p = 0.0001$), the need for blood transfusion ($p = 0.04$), and additional uterotonic use ($p = 0.0007$) without major adverse effects. **Conclusion:** Preoperative administration of TXA is effective in reducing intraoperative and postoperative blood loss during high-risk cesarean section, without major side effects. This provides a potential intervention for improving maternal outcomes.

KEYWORDS: Tranexamic acid, parturients at risk of bleeding, cesarean section, postpartum hemorrhage.

INTRODUCTION

Postpartum hemorrhage (PPH) is a major cause of maternal morbidity and mortality worldwide, accounting for approximately 125,000 deaths per year, or almost 25 of all maternal deaths, 99 of which occur in low and middle-income countries.[1, 2, 3] Algeria is no exception to this scourge, which constitutes a real public health problem with an estimated maternal death rate of 48.5 per 100,000 live births, the main cause of which is PPH.[4] The World Health Organization and several learned societies define PPH as blood loss equal to or greater than 500 ml from the genital tract within 24 hours of cesarean or vaginal delivery.[5, 6, 7]

According to a report by Who, the global cesarean section rate almost tripled in a quarter of a century, rising from 6.7 in 1990 to 19.1 in 2014. The incidence of PPH associated with cesarean section is generally estimated to be twice that associated with vaginal delivery. As a result, the need to prevent high-risk cesarean sections has become a major concern in reducing the incidence of PPH and the occurrence of its severe form.[8, 9]

To date, administration of uterotonics, particularly oxytocin, remains the only recommended method for preventing PPH. However, in addition to this mechanical hemostasis improvement (uterine contraction), a complementary biochemical hemostat's effect could be enhanced by an anti-fibrinolytic drug, such as tranexamic acid (TXA), which has widely demonstrated its efficacy as a pharmacological means of perioperative blood sparing, notably in cardiac and orthopedic hemorrhagic surgery.[10] TXA was recently evaluated in the management of PPH; Woman's study demonstrated its value in reducing mortality, the need for invasive procedures, low cost, and few supposedly minor side-effects.[11] The prophylactic use of TXA to prevent PPH secondary to cesarean section has been extensively studied. However, limited data are available concerning its application in cesarean sections with a high risk of hemorrhage.

This study aimed to evaluate the efficacy of TXA in reducing both intra- and postoperative blood loss in

parturients with risk factors for hemorrhage during cesarean section.

MATERIALS AND METHODS

This was a prospective randomized, placebo-controlled study that was conducted between September 2019 and September 2021 at Bab El Oued University Hospital, Algiers City. After the approval of our hospital ethical committee, all participants have signed informed written consent. This trial involved 800 high-risk women who underwent elective cesarean sections.

Study Population

All consenting parturients, classified as ASA I or II, with one or more risk factors, undergoing a delayed emergency cesarean section (time from the surgical indication─to the incision > 15 min) or a scheduled cesarean section.

Inclusion criteria

Maternal age between 18 and 50 years, with a live fetus and a gestational age greater than 35 weeks, presenting one or more risk factors for PPH, such as:

- Age over 34 years
- Obesity: BMI greater than 30 kg/m2
- History of PPH, or caesarean section
- Anemia with a hemoglobin level ≤ 10.9 g/d
- Multiparity
- Uterine fibroid
- Preeclampsia
- Multifetal pregnancy
- Polyhydramnios
- Placenta previa
- Chorioamniotitis
- Macrosomia (weight ≥ 4 kg)

Exclusion criteria

- Presence of renal insufficiency
- History of venous or arterial thrombosis
- History of epilepsy
- History of known allergy to tranexamic acid
- Gestational age less than 35 AW
- fetal death Placental insertion anomaly of the accreta type

Sample size calculation

Estimation of sample size is based on the following assumption: it is a two arms of a randomized controlled trial. TXA estimated to reduce blood loss by 50% and with a power of 90% and significance level at 5%, the sample size needed was 396 per arm. We opted for a study of 800 cases divided into 2 arms of 400 cases each.

Trial procedure

We sealed a plan of interventions in closed envelopes, numbered under the randomization tables. The anesthetist, who was not involved in patient management or assessment, opened the selected envelope and prepared the drug. The obstetric surgeon, pregnant women and outcome assessor were all blinded to group allocation. They concealed randomization coding tables from investigators until the end of the study.

We equally assigned the parturients into two groups to receive 15 min before surgery: either 1 g of intravenous TXA dissolved in 20 ml of normal saline (study group; n = 400) or placebo 20 ml of normal saline (control group; n = 400).

We used the same technique for all women: spinal anesthesia, Pfannenstiel incision, transverse incision of the lower uterine segment, an umbilical cord clamping immediately after fetal extraction, uterine exteriorization, repair of the uterine incision, and layered closure of the abdominal wall.

Following hysterotomy, they aspirate amniotic fluid into the graduated "F" container (figure 1). As soon as they clamped the umbilical cord, participants in the 2 study groups received 10 IU of oxytocin, infused in 500ml of glucose solution 5% over 30 min. A maintaining dose followed this infusion (10 IU) for 2 hours. After extracting of the baby, the gynecologists will manually deliver the placenta (Figure 2) and aspirate the remaining intrauterine fluid into the “F” container.

Total bleeding volume is the sum of blood loss quantified in 3 steps, from the surgical incision to the first 24 hours of the postpartum period. The first stage (T1) extends from the surgical incision to the skin closure. During this period, we quantify blood loss by measuring the amount of blood accumulated in the graduated suction container "B" (figure 3) following the aspiration of intra-abdominal blood and that accumulated in the lateral gutters of the operating field (figure 4), in addition to weighing blood-soaked in compresses (soaked in blood - dry) (figure 5). Knowing that 1g of weight is equivalent to 1 ml of blood.[12] The second phase (T2) lasts from the end of the cesarean section until 2 hours post-op, during which we quantified blood loss using the gravimetric method of weighing adult diapers (soaked in blood-dry). The third time (T3) extends from the end of the 2nd postoperative hour to the end of the first 24 hours, during which blood loss we quantified in the same way as T2.

Neonatal parameters (Apgar at 1 min and 5 min, baby weight), duration of cesarean section, duration of hospitalization and side effects of TXA were recorded in the patient files. Biological data (complete blood count, kidney, liver) were recorded preoperatively and compared to those 48 hours postoperatively.

At discharge, phone interviews followed participants up to look for adverse drug reactions like seizures, thrombosis or renal failure. We collected all these data at D10, D30, and D42 postpartum. We collected final results at 42 days post-cesarean, with all outcomes assessed at the same

time. The trial ended on day 42 of the randomization of the last participant.

Statistical methods

We carried out data entry and analysis using the software SPSS version 20. We presented the continuous variables as mean and standard deviation, while the categorical variables as numbers and percentages. However, comparing across the groups using the Chi-square test for the qualitative variables and the student test for the quantitative variables. We have taken the alpha level as 5%. If any p value is less than 0.05, we have considered it significant.

RESULTS

There was no statistical difference between the two groups about the baseline characteristics of these participants, such as mean age, body mass index, and gestational age. As well as duration of operation, neonatal birth weight, neonatal outcome parameters such as 5 min Apgar, and neonatal intensive care unit admission (table 1).

Table 1: Baseline characteristics.

Parameters	TAX group	Placebo group	P value
Mean age (years)	34.2 ± 5.5	33.6 ± 5.7	0.13
BMI (kg/m^2)	31.6 ± 5.6	31.3 ± 4.8	0.42
Parity	1.71 ± 1.30	1.55 ± 1.24	0.075
Gestational age (weeks)	38.6 ± 1.2	38.8 ± 1.3	0.055
Cesarean duration (min)	52.8 ± 14.4	51.3 ± 15	0.14
New born			
Weight (grams)	3487.9 ± 611.8	3459.3 ± 561.1	0.41
Apgar at 5 min	9.18 ± 0.92	9.19 ± 0.88	0.87
NICU admission	11(2.7)	10 (2.5)	0.82

NICU : neonatal intensive care unit

In our study population, a history of cesarean sections dominated risk factors for PPH, followed by obesity, and then age over 35 years. The two groups were comparable in terms of the percentage of the hypothetical risk factors for PPH (table 2).

Table 2: Risk factors for postpartum hemorrhage.

Parameters	TXA group (%)	Placebo group (%)	P value (%)
Age > 35 ans	51.5	46.5	0.15
BMI > 30 kg/m^2	56	52	0.25
Previous PPH	3.5	2.8	0.64
Multifetal pregnancy	3	2.75	0.83
Anemia	29	28.2	0.81
low platelet count	9	8.8	0.9
chorioamnionitis	23	25.5	0.41
Hydramnios	31	34	0.36
Macrosomia	25.5	21	0.15
Previous CS	74.75	73.75	0.75
Placenta previa	2.8	2.3	0.65

CS : cesarean section

The mean intraoperative blood loss at T1 was 274.6 ± 113.5 ml in the TXA group and 450.9 ± 208.8 ml in the placebo group. P value < 0.001, showing a significantly more blood loss in the placebo group. Concerning postoperative mean blood loss at T_2 was 7 ± 4.3 ml in the TXA group and 13.37 ± 8.1 ml in the placebo group. P value < 0.001, showing significantly more blood loss in the placebo group. About the mean blood loss at T_3 was 17.5 ± 15.5 ml in the TXA group and 38.5 ± 29.2 ml in the "placebo" group. P value < 0.001, showing significantly more blood loss in the placebo group (table 3).

The incidence of moderate PPH (blood loss > 500 ml) was significantly lower in the TXA group with 7% compared to the control group with 36.1%, P value < 0.0001. Major PPH (bleeding between 1000 and 1500 ml) and massive PPH (greater than 1500 ml) were present only in the placebo group, with an incidence of 1.8% and 0.8%, respectively (Table 3).

Table 3: Primary outcomes.

Parameters	TXA	Placébo	P value
intraoperative bleeding volume (ml)	274.6 ± 113.5	450.9 ± 208.8	< 0.001
Postoperative bleeding volume 0 to 2 h (ml)	7 ± 4.3	13.4 ± 8.1	< 0.001
Postoperative bleeding volume 2 to 24 h (ml)	17.5 ± 15.56	38.5 ± 29.2	< 0.001
Volume < 300ml	260 (65%)	64 (16%)	< 0.001
300 ml < volume < 500 ml	113 (28.3%)	187 (46.8%)	< 0.001
500 < volume < 1000 ml	28(7%)	134 (33.5%)	< 0.001
1000 < volume < 1500 ml	0 (0%).	7 (1.8%)	//
Volume > 1500 ml	0 (0%).	3 (0.8 %)	//

The hemoglobin value showed a statistically significant less decrease in the ATX group compared to the placebo group when measured 48 hours after surgery. Consequently, more frequent incidence of anemia appears in the placebo group (Table 4). Similarly, the need for additional oxytocin was lower in the TXA group (6.8%) when compared to the placebo group (14%) (Table 4). In the same way, the need for the blood transfusions was significantly lower in the TXA group (0.25%) when compared to the placebo group (2%) (Table 4).

Table 4: Secondary outcomes.

Parameters	TXA	Placebo	P value
Preoperative Hb (g/dl)	11.50 ± 1.13	11.46 ± 1.12	0.61
Postoperative Hb 48h	10.94 ± 1.50	10.57 ± 1.29	0.0002
Postoperative anemia (%)	16.8%	33.8%	< 0.0003
Blood transfusion (%)	0.25%	2%	0.04
Need for additional oxytocin (%)	6.8	14	0.0007

Hb : hemoglobin

In the TXA group, more women than in the control group (16.8% vs. 1.4%, respectively) reported milder side symptoms, such as nausea, vomiting, and dizziness.

Regarding major side effects, we recorded no cases of venous thromboembolism complications in the treated group. However, we noted the occurrence of transient renal failure in four patients (1%) in the TXA group versus three cases (0.75%) in the placebo group, with no significant difference between the two groups (table 5). The evolution was spontaneously favorable in less than 10 days. During our study (D_0-D_{42}), we did not observe any incidents of death, additional surgery, or hospitalizations for intensive care.

Table 5: Comparative table by side effects.

Parameters	TXA n (%)	Placebo n (%)	P value
Minor			
Nausea	50 (12.5)	1 (0.3)	< 0.001
Vomiting	13 (3.3)	3 (0.8)	0.01
Dizziness	4 (1)	1 (0.3)	0.36
Major			
Renal failure	4 (1)	3 (0.75)	1
Thrombosis	0 (0%)	1 (0.3%)	//

The number of patients requiring hospitalization for over two days was lower in the TXA group (1.75%) than in the placebo group (4.5%), with a significant difference (P value = 0.024) (Table 6).

Table 6: Comparison of the two groups according to length of hospital stay.

Hospital stay	TXA	Placebo	P value
Mean	2.049 ± 0.49 D	2.06 ± 0.58 D	0.8
≤ 2 D	98.25 %	95.5 %	0.024
> 2 D	1.75 %	4.5 %	0.024

D : day

Figure 1: Amniotic fluid suction container "F".

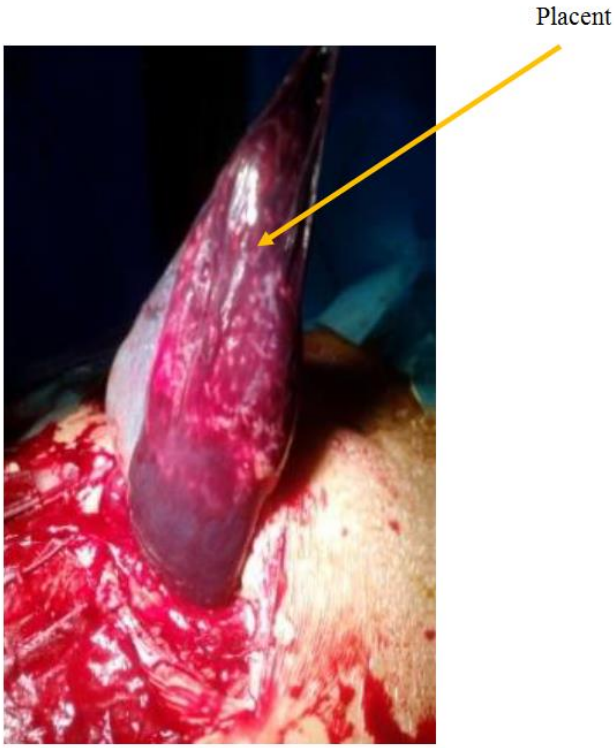

Figure 2: Manual delivery

Figure 3: blood suction container 'B'

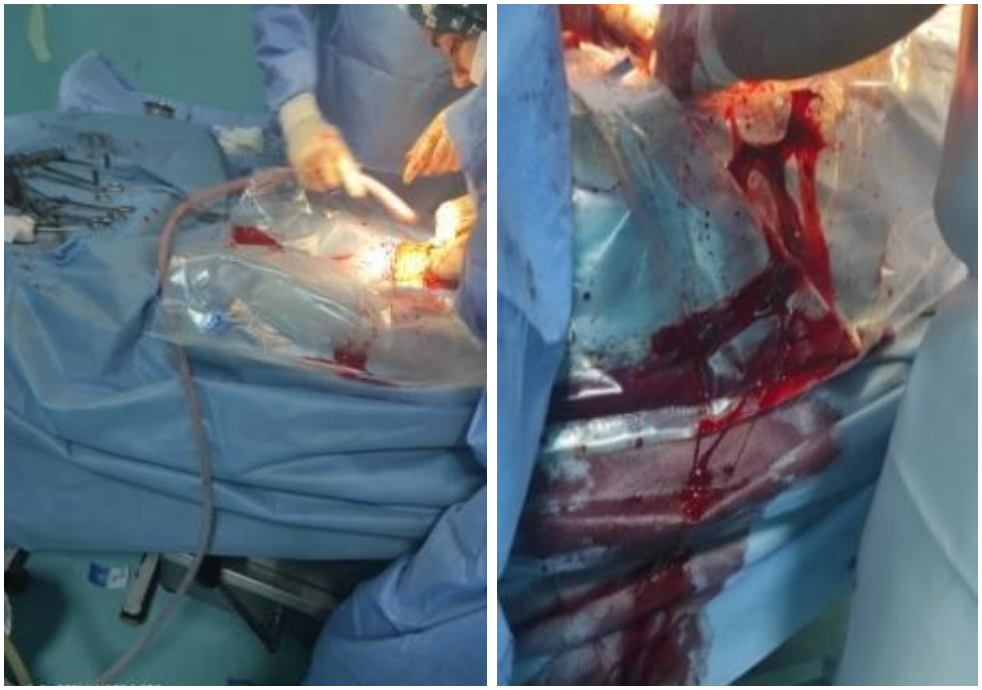

Figure 4: Operating fields with external blood accumulation gutters.

Figure 5: weight of blood-soaked compresses (a) / weight of dry compresses (b)

DISCUSSION

The pathophysiological process of bleeding has changed significantly since hyperfibrinolysis was found to be the exacerbating component, potentially rendering bleeding uncontrollable. Indeed, fibrinolysis is activated in response to any tissue trauma, surgical or otherwise. There is a correlation between the extent of lesions, the abundance of bleeding, and the intensity of fibrinolysis. Thus, during a cesarean section, fibrinolysis is initiated as soon as the surgical incision begins and increases as the placenta is delivered.

Tranexamic acid (TXA) is a synthetic lysine-derived antifibrinolytic that acts by competitively inhibiting plasminogen-fibrin binding, preventing plasminogen activation, and protecting fibrin from degradation and dissolution by plasmin.[13, 14]

The results of our study showed that preoperative administration of TXA in cesarean sections at risk of PPH reduced blood loss by 40.9% during both operative and postoperative periods. This result is consistent with several similar clinical trials, in which the percentage of blood savings ranged from 21.4 to 58% (table 7).

Our study's findings showed that giving TXA prior to cesarean sections in patients at risk of PPH decreased blood loss by 40.9% during both operative and postoperative periods. This outcome is in line with

several related clinical trials where the blood save percentage varied from 21.4 to 58% (table 7).

Shah and colleagues achieved a 21.4% blood-saving rate. The quantification process followed the same protocol as our study. The difference was in the reduced sample size (800 versus 160) and the lower blood savings (204 versus 160 ml). Which may be explained by the duration of bleeding quantification, performed only after incision of the lower segment, and the higher oxytocin dose (20 IU versus 10 IU).[15]

In their study, Goswami et al. examined ninety anemic patients undergoing cesarean sections. They established three groups at random: group G1 (n = 30) received 10 mg/kg of TXA, group G2 (n = 30) received 15 mg/kg, and group C (n = 30) received a placebo. TXA resulted in blood savings of 28% in G1 and 49.7% in G2.[16] The saving percentage we got in our study was closer to that of G2 (40.5 versus 49.7%), which was explained because the TXA dose was close to ours (15 mg/kg). The difference lies in the reduced sample size (800 versus 90), the duration of bleeding quantification performed only after the incision of the lower segment, and the longer delay between TXA injection and surgical incision (15 versus 20 min).

According to Sujata et al., there was a 52% reduction in blood loss, with 877.7 ml in the placebo group and 422 ml in the TXA group. we can explain this result (excessive bleeding), Because the measurement technique is predicated only on the variation between the preoperative and 48-hour postpartum hemoglobin level. Although the reliability of this procedure remains highly controversial, particularly in the obstetrical field, knowing that pregnancy is characterized by peripartum variations in weight and volume, measuring hemoglobin in this situation is not a good reflection of blood loss. In addition, the absence of blinding biased the study (the anesthetist in charge of the study was aware of the group allocation).[17]

A recent study by Shalaby et al. found that the intraoperative saving rate (35 versus 39%) was comparable to our result. The difference with their trial lies in the small sample size (800 versus 160) and the extent of bleeding in both groups (896.81 ml in the placebo group and 583.23 ml in the TXA group), which may be explained by the presence of placenta praevia in 30% of cases.[18]

Table 7: Total blood loss according to studies.

Study	Sample (n)	Blood loss (ml)	Difference (ml)	Blood savings (%)	P value
Goswami	90	277.5±58.8 vs 554±89.6	276.5	49.7	< 0.001
Sujuta	60	422 ± 124.5 vs 877.7 ± 263	457.7	52	< 0.001
Shah	160	392.1±10.06 vs 498.7 ± 15.8	106.6	21.4	< 0.001
Shalaby	160	583.2 ±379.6 vs 896.8 ± 519.6	313.6	35	< 0.001
Our study	800	299 ± 113 vs 503± 246	204	40.5	< 0.001

Contrary to most studies, Gay and Xu report a small intraopetative bleeding reduction rate of 20 and 17%, respectively, without significant differences between the treated groups and the control groups. Conversely, the savings were higher in the postoperative period, at 40% and 45%, respectively, and the difference was statistically significant in favor of the treated groups. The reason for these outcomes can be attributed to the delay of TXA administration (after cord clamping).[19,20] This result of a greater reduction in bleeding postoperatively was found in our work and confirmed by several similar studies.[19, 20, 21, 22, 23, 24, 25, 26] (Table 8)

Table 8: Postoperative blood loss according to studies.

Study	Sample size (n)	Mean blood loss (ml)	Différence (ml)	Blood savings (%)	P value
Gai	180	42.7±40.4 vs 74.2±77	31	41.7	< 0.001
Xu	174	46.6±42.7 vs 84.7±80.2	38.1	45	< 0.001
Movafegh	100	67.1± 6.5 vs 141±33.9	74	52.5	< 0.001
Yahia	212	85±31 vs 131±49	46	35	< 0.001
Thavare	100	20.8±07.3 vs 39.5±12.5	18.6	47	< 0.001
Miliani	60	42.3±21.7 vs 63.2±48.8	21	33.2	< 0.001
Agarwal	72	115.5±15.8 vs 65.8±7.7	49.7	43	< 0.001
AbdAleem	740	33.8±21 vs 82.6 ± 34.5	48.83	59	< 0.001
Our study	800	37.1±20 vs 52±37.3	27.5	53	< 0.001

In our series, the incidence of PPH was 7%. 95% CI [4.79–9.82] in the TXA group and 34%. 95% CI [29.48–38.75] in the placebo group with a significant difference; P value < 0.001. These results are consistent with those

in the literature[26, 22, 27, 28, 29], the incidence of which was between 3.1 and 31.1% in the treated groups and 18 to 64% in the placebo groups (table 9). The disparity in the results can be explained by the heterogeneity between the study populations, the difference between the sample sizes, as well as by the divergence of the working methods, particularly in the choice of TXA doses, the moment of its injection, and also by the methods for measuring blood loss.

Table 9: Incidence of PPH, according to studies.

Study	Sample (n)	PPH Incidence (%)		P value
		TXA	Placebo	
Abd-Aleem	740	3.1	48.8	0.0001
Yahia	212	31.1	63.2	0.0001
Lakshmi	120	3.3	60	0.0001
Mishra	100	4	18	0.025
Navya	150	4	64	0.0001
Our stady	800	7	34	0.0001

New cases of post-operative anemia accounted for 25.4% of the total study population. Its incidence was lower in the TXA group by 16.75% compared to the placebo group by 33.8%, with a significant difference (P value < 0.0001). The average hemoglobin level was 10.94 ± 1.5 g/dl in the TXA group versus 10.57 ± 1.29 g/dl in the placebo group, with a significant difference (P value < 0.002). The hemoglobin saving was 0.33 g/dl. This result is like those in the literature, where the average hemoglobin saved varied from 0.1 g/dl to 1 g/dl[30, 26, 31, 18, 28, 32, 15] (table 10).

Table 10: Comparison with studies on hemoglobin saving.

Study	Sample (n)	Risk factors	Evaluation time	Hémoglobin gain	P value
Medhi	174	+	24 h	0.33	0.001
Abd-Alim	740	—	24h	0.55	0.001
Manal	200	—	24h	0.5	0.001
Shalaby	160	+	24h	1	0.001
Mishra	100	—	24h	0.1	0.001
Gungorduk	660	—	48h	0.2	0.001
Shah	160	+	24	0.48	0.001
Our stady	800	+	48h	0.33	0.0002

We observed the need for additional uterotonic in 6.8% of parturients in the TXA group versus 14% in the placebo group, with a significant difference, P value = 0.0007. The uterotonic save was 7.2%; this figure is comparable to those found in the literature[17, 25, 31, 35, 32, 27] where savings ranged from 6 to 40% (table 11).

Table 11: Comparison according to studies on oxytocin saving.

Study	Sample (n)	Risk factors	Additionnel oxytocin			P value
			TXA (%)	Placébo (%)	Epargne (%)	
Sujuta	60	+	23	83	60	< 0.001
Agarwel	72	—	0	11.1	11.1	0.115
Manal	200	—	3	12	9	0.015
Ifunanya	160	+	7.4	33.3	25.9	< 0.0001
Gungorduk	660	—	8.5	14.5	6	0.02
Lakshmi	120	+	5	15	10	0.067
Our study	800	+	6.8	14	7.2	< 0.001

The transfusion requirement was lower in the TXA group (0.25%) compared to the placebo group (2%). The difference was significant, with a P value of 0.04. Some studies have reported similar results[17, 34, 35, 30, 28, 33, 22, 16, 18], especially in populations at risk of PPH (table 12).

Table 12: Transfusion needs according to studies.

Study	Sample (n)	Risk factors	Blood transfusion		P value
			TXA n (%)	Placébo n (%)	
Sujuta	60	+	1 (3%)	4 (10%)	0.35
Obi	120	+	2 (3.5%)	5 (8.6%)	0.26
Abdel Nour	160	+	1 (1.25%)	5 (6.25%)	0.071
Medhi	174	+	2 (2.3%)	10 (5.7%)	0.0362
Mishra	100	_	2 (4%)	5 (10%)	0.43
Ifunania	164	+	5 (6%)	12 (14.3%)	0.03
Yahia	212	_	0	2 (1.8%)	0.47
Goswami	90	+	2 (6.6%)	0	0.02
Shalaby	160	+	1(1.25%)	5 (6.25%)	0.071
Our study	800	+	1 (0.25%)	8 (2%)	0.04

With a frequency of 12.5%, nausea was the most common minor adverse event, followed by vomiting with 3.3% and dizziness with 1%. The comparison with the placebo group found a significant difference except for dizziness (P value = 0.36). Our study's findings are in line with those found in the literature.[25, 30, 31, 32] (table 13).

Table 13: Minor side effects of ATX according to studies.

Paramètres	Xu (%)	Agarwal (%)	Medhi (%)	Manel (%)	Gongurduk (%)	Our study (%)
Vomiting	5.5	11.1	7	8	13.3	3.3
Dizzeness	5.6	0	0	0	2.7	1
Nausea	5.5	12.5	10.3	18	15	12
Total	16.6	23.6	17.3	26	31	16.8

We did not find any instances of major side effects in the treated group related to thromboembolism complications. The lack of an increase in thromboembolic risk has been corroborated by large studies as ATACAS (n = 4662), WOMAN (n = 2060), and CRASH-2 (n = 2021)[174, 184, 190, 191].

We noted the occurrence of transient renal failure in 4 patients (1%) in the TXA group, versus 3 cases (0.75%) in the placebo group, with no significant difference between the two groups. The evolution was spontaneously favorable in less than 10 days. The causal role of TXA in the onset of renal failure has never been confirmed because this complication appears in privileged situations such as low flow, hemorrhages, help syndrome, or severe preeclampsia[36], particularly when high and extended doses of TXA are involved.

CONCLUSION

Our randomized, double-blind, controlled study is one of the first to investigate the use of TXA to prevent excessive bleeding in cesarean sections at high risk of PPH. We assessed blood loss using two widely used and highly reliable methods. Our main results show that preoperative TXA administration was safe and effective in reducing blood loss during and after cesarean sections. In addition, this procedure was associated with a reduction in the incidence of postpartum hemorrhage and anemia, as well as oxytocin and blood transfusion consumption.

DECLARATIONS

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The ethics committee of the University Hospital " Lamine Debaghine" of Bâb El Oued city of Algiers has given its favorable opinion for the feasibility of this study on 30 /06/ 2019. Approval ID: 133/2019. All participating women have signed an informed written consent after explaining the risks and benefits of the study.

CONSENT FOR PUBLICATION

Not applicable.

AVAILABILITY OF DATA AND MATERIALS

All data are available under reasonable request.

COMPETING INTERESTS

The authors report no declarations of interest.
No author is part of the team Editoriel system as an Editor or reviewer.

FUNDING

The authors have no sources of funding to declare for this manuscript.

AUTHORS' CONTRIBUTIONS

Hadbi Mohamed developed the idea and the design of the study. Matouk Mohamed and Boutrid Hala revised literature, collected the data. Then Benamane Raouf with

Nadia Fellah analyzed the data. Hadbi Mohamed wrote and critically revised the manuscript. All authors read and approved the final version of the manuscript.

ACKNOWLEDGEMENT

I thank all the staff of the Gharafa clinic, particularly the AMARs, the instrumentalists, the anesthesia and gynecology residents. and the laboratory team and their head Dr Souad Ziouche without forgetting the epidemiology team of the hospital and their head Professor Hamchaoui, Pr Zanoun and Dr Belaoudmou.

Abbreviations

ASA: American Society of Anesthesiologists classification
TXA: tranexamic acid; PPH, postpartum hemorrhage
WHO: World Health Organization
AW: amenorrhea weeks
BMI: body mass index
NICU: neonatal intensive care unit
CS: cesarean section
D: day.

REFERENCES

1. Say L, Chou D, Gemmill A, et al. Global causes of maternaldeath: a WHO systematicanalysis. Lancet Glob Health, 2014; 2(6): e323-e333.
2. Knight M, Kenyon S, Brocklehurst P, et al. Saving Lives, Improving Mothers' Care - Lessons learned to inform future maternity care from the UK and Ireland Confidential Enquiries into Maternal Deaths and Morbidity 2009–12. Oxford: University of Oxford, 2014.
3. Say L, Pattinson R, Gülmezoglu A. WHO systematic review of maternal morbidity and mortality: the prevalence of severe acute maternal morbidity (near miss). Biomed Central Reproductive Health, 2004; 1(1): 3.
4. Bounabi S. Journée d'étude sur la mortalité maternelle Plaidoyer pour des accouchements sans risques.09 décembre 2020. https://www.reporters.dz
5. Royal College of Obstetricians and Gynaecologists. Postpartum haemorrhage, prevention and management of postpartum hemorrhage (Green-top Guideline 52); 2011.
6. Sentilhes L, Goffinet F, Vayssiere C. Post-partum hemorrhage: Guidelines for clinical practice - Method and organization. Journal de gynécologie, obstétrique et biologie de la reproduction, 2014 Dec; 43(10): 933-5.
7. World Health Organization. WHO recommendations for the prevention and treatment of postpartum.haemorrhage. Geneva: World Health.Organization.Department.of.making pregnancysafer; 2014 http://apps.who.int/iris/bitstream/10665/75411/1/9789241548502 eng.pdf.
8. WHO. Recommendations on non-clinical interventions to reduce unnecessary caesarean section. Geneva, Switzerland: World Health Organization; 2018.
9. Parant O, et al. Spécificités obstétricales et anesthésiques de la prise en charge d'une hémorragie du post-partum (HPP) associée à la césarienne. J GynaecolObstet Biol Reprod (Paris), 0368-2315/© 2014 Elsevier Masson SAS. JGYN-1133; No. of Pages 19.
10. Ker K, Prieto-Merino D, Roberts I. Systematic review, meta-analysis and meta-regression of the effect of tranexamic acid on surgical blood loss. Br J Surg., 2013; 1271–1279.
11. WOMAN Trial Collaborators. Effect of early tranexamic acid administration on mortality, hysterectomy, and other morbidities in women with post-partum haemorrhage (WOMAN): an international, randomised, double-blind, placebo-controlled trial-Lancet, 2017 May 27; 389(10084): 2105-16.
12. Jaiprakash Sahu and Nalini Mishra. Role of intravenous tranexamic acid in reducing blood loss during caesarean section: Study at tribal-dominated area hospital in Chhattisgarh, India- J. Obstet. Gyneacol. Res., 2019- doi: 10.1111/jog.13915.
13. Hibbs SP, Roberts I, Shakur-Still et al. Post-partum haemorrhage and tranexamic acid: a global issue. Br J Haematol, 2018; 180: 799-807].
14. Clarisse P, Domitille D, Alessandro C. Acide tranexamique dans la priseen charge de l'hémorragie du postpartum: connaissances actuelles. Rev Med Suisse, 2018; 14: 1861-5].
15. Shah P, Agrawal A, Chhetri S et al. Tranexamic acid in prevention of postpartum hemorrhage in elective cesarean section. Int J Reprod Contracept Obstet Gynecol., 2019; 8(2).
16. Goswami U, Sarangi S, Gupta S et al. 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 J Anaesth., 2013; 7: 427-31.
17. Sujuta N, R. Tobin, R. Kaur et al, Randomized controlled trial of tranexamic acid among parturients at increased risk for postpartum hemorrhage undergoing cesarean delivery, Int J Gynecol Obstet (2016), http://dx.doi.org/10.1016/j.ijgo.2015.09.032.
18. Shalaby. M-A, Maged A-M, Al Asmar A.et al. Safety and efficacy of preoperative tranexamic acid in reducing intraoperative and postoperative blood loss in high-risk women undergoing cesarean delivery: a randomized controlled trial. BMC Pregnancy and Childbirth, 2022; 22: 201. https://doi.org/10.1186/s12884-022-04530-4.
19. Gai. M-Y, Wub. L-F, Suc. Q-F et al. Clinical observation of blood loss reduced by tranexamic acid during and after caesarian section: a multi-center, randomized trial. European Journal of Obstetrics & Gynecology and Reproductive Biology, 2004; 112: 154–157.

20. Xu .J, W. Gao, Y. Ju et al. Tranexamic acid for the prevention of postpartum hemorrhage after cesarean section: a double-blind randomization trial. Arch Gynecol Obstet., 2013; 287: 463–468. DOI 10.1007/s00404-012-2593-y.
21. Movafegh. A, Eslamian. L, Dorabadi. A. Effect of intravenous tranexamic acid administration on blood loss during and after cesarean delivery. International Journal of Gynecology and Obstetrics, 2011; 115: 224–226.
22. Yehia A-H, Koleib M-H, Abdelazim I-A et al. Tranexamic acid reduces blood loss during and after cesarean section: A double blinded, randomized, controlled trial. Asian Pacific Journal of Reproduction, 2014; 3(1): 53-56.
23. Thavare M-G, Patil A-S. Effect of Intravenous Tranexamic Acid on Blood Loss During and After Caesarean Section. MVP Journal of Medical Sciences, January-June 2019; 6(1): 93-99.
24. Miliani. F, Haryalchi. K, Sharami. S-H, Atrkarroshan. Z. Prophylactic Effect of Tranexamic Acid on Hemorrhage During and After the Cesarean Section. I J W H and R S, January 2019; 7(1): 74–78.
25. Agarwal N, Lahiri A. Role of Prophylactic Tranexamic Acid in Reducing Blood Loss during and After Lower Segment Caesarean Section. Ann Clin Med Res., 2021; 2(1): 1021.
26. Abdel-Aleem. H. Alhusain. T-K, Abdel-Aleem. M-A et al. Effectiveness of tranexamic acid on blood loss in patients undergoing elective cesarean section: randomized clinical trialJ Matern Fetal Neonatal Med, 2013; 26(17): 1705–1709. DOI: 10.3109/14767058.2013.794210.
27. Lakshmi. SJ D, Abraham. R, Role of Prophylactic TXA in Reducing Blood Loss During Elective Cesarean Section. Journal of Clinical and Diagnostic Research., 2016 Dec; 10(12): QC17-QC21.
28. Mishra. N. Role of intravenous tranexamic acid in reducing blood loss during caesarean section: Study at tribal-dominated area hospital in Chhattisgarh, India. © 2019 Japan Society of Obstetrics and Gynecology, doi:10.1111/jog.13915.
29. Navya. B, Shenoy. H, Sreedhar. G et al Efficacy of intravenous tranexamic acid at reducing blood loss during elective caesarean section in a tertiary care hospital in North Kerala January 2022 International Journal of Health and Clinical Research, 2022; 5(2): 194-200.
30. Medhi R et al. Int J Reprod Contracept Obstet Gynecol., 2017 Aug; 6(8): 3423-3427.
31. Manel. F.A. Role of intravenous tranexamic acid on cesarean blood loss: a prospective randomized study. MOJ Womens Health., 2019; 8(3): 226–230. DOI: 10.15406/mojwh.2019.08.00241)
32. Gungorduk. K., Gokhan M-D et al. Efficacy of Intravenous Tranexamic Acid in Reducing Blood Loss after Elective Cesarean Section: A Prospective, Randomized, Double-Blind, Placebo-Controlled Study. Am J Perinatol., 2011; 28: 233–240.
33. Ifunanya N-J, Chukwu I-C, Nobert O-C et al. Tranexamic Acid versus Placebo for Prevention of Primary Postpartum Haemorrhage among High Risk Women Undergoing Caesarean Section in Abakaliki: A Randomized Controlled Trial. Open Journal of Obstetrics and Gynecology, 2019; 9: 914-922.
34. Obi V-O, Meora O-U-J, Dimejesi I-B-O et al. Efficacy of intravenous tranexamic acid at reducing blood loss during elective caesarean section in Abakaliki: A double blind randomized placebo controlled trial. African Journal of Medical and Health Sciences. April 2019 ; 18(2): 10-17.
35. Adel Nour D, El Husseiny T, Osman N-K. Efficacité and safety of preoperative intravenous tranexamic Acid to reduce blood loss during and after electiive lower segment cesarean delivery. ISSN: 2090-7265, May 2021; 11(2). DOI:10.21608/ebwhj. 2021.74846.1133.
36. Frimat M, Provot F, Hertig A. In reply to risk of tranexamic acid for treatment of postpartum hemorrhage. Am J Kidney Dis., 2017; 69: 160-1.