ORIGINAL ARTICLE

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Role of Intravenous Tranexamic Acid before Elective Caesarean Section in Preventing Postpartum Hemorrhage

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ABSTRACT

Background: Post-partum hemorrhage is one of the most common obstetric emergencies. However, Tranexamic acid (TXA) is a medication used to treat or prevent excessive blood loss due to trauma, surgery and medical conditions including hemophilia and heavy menstrual bleeding. **Objective:** To determine the role of intravenous tranexamic acid before elective caesarean section in preventing postpartum hemorrhage at tertiary care hospital. **Study Design:** Randomized control trial. **Settings:** Obstetrics & Gynecology Department, Allied Hospital Faisalabad Pakistan. **Duration:** 6 months from March 02, 2019 to August 01, 2019. **Methodology:** After taking demographic information and informed consent, all the patients were randomly divided into two groups by using random number table. Group A patients received tranexamic acid (1gm/10ml TA diluted with 20ml of 5% glucose) and group B patients not received tranexamic acid (placebo). Blood loss was noted by measuring the total blood collected in kidney tray of 10" size during delivery of placenta till completion of caesarean section. All this information was recorded through study proforma. Data was entered and analyzed on SPSS version 21. **Results:** In our study the mean age of the patients was 29.90±6.06 years. The mean blood loss value of the patients was 387.27±89.56 ml. Statistically highly significant difference was found between the study groups with blood loss of the patients i.e. p-value=0.000. **Conclusion:** It has been proved in our study that the tranexamic acid is useful and effective drug to control the mean blood loss before delivery in females undergoing elective caesarean section as compared to placebo group.

Keywords: Caesarean section, Placebo, Tranexamic acid, Blood loss.

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INTRODUCTION

Post-partum hemorrhage is one of the most common obstetric emergency. It remains a leading cause of early maternal death accounting for about 300,000 deaths worldwide every year and of morbidity related to anemia, blood transfusions and hemorrhage related ischemic complications.[1] The incidence of caesarean delivery is increasing day by day and the average blood loss during caesarean delivery (1000ml) is double the amount lost during vaginal delivery (500ml).[2]

In Pakistan, the caesarean section rate is 25%.[3] The hematocrit falls by 10% and blood transfusion is required in 6% of patients undergoing caesarean delivery.[3] Thus obstetric hemorrhage during caesarean section can be life threatening. To reduce morbidity and mortality associated with obstetric hemorrhage various pharmaceutical, hematological and surgical techniques have been used to prevent PPH during caesarean section. Medications such as oxytocin, misoprostol, prostaglandins F2α and methysergide have been used to control bleeding after caesarean section.[4]

Tranexamic acid, a synthetic derivative of amino acid Lysine, is an antifibrinolytic that reversibly inhibits the activation of plasminogen thus inhibits fibrinolysis and reduces bleeding. This hemostatic drug is included in WHO list of essential medicines.[5] It has been used for various types of intra-operative and post-operative bleeding in Gynecology and Obstetrics, tranexamic acid has already been used to treat idiopathic menorrhagia and is effective and well tolerated when administrated orally.[6] Tranexamic acid can be used in addition to current prophylactic uterotonic drugs in the third stage of labour to reduce blood loss.[7] Some randomized controlled studies have shown that TXA reduces post-partum hemorrhage during caesarean section. The mean estimated blood loss was significantly lower in women treated with TXA compared with women in the other group in which only standard routine uterotonic drugs were used (499.9±206.4ml versus 600.7±215.7ml respectively; p <0.001).[2] Another trial has also showed that Tranexamic acid significantly reduced the quantity of blood loss from placental delivery to the end of LSCS which was 356.44±143.2ml in the TXA group versus 710.22±216.72ml in the placebo group (p < 0.001).[3] But in one trial, the mean blood loss was 336.7±151.2ml in the TXA group and 368.5±156.4ml in the control group. However, the amount of blood loss in the period from placental delivery to the end of CS did not differ between the TXA and control groups (p = 0.17).[8]

The rationale of this study is to compare mean blood loss with tranexamic acid versus placebo given before delivery in females undergoing elective caesarean section. In literature, controversial results have been observed. It is known that TXA is effective in controlling bleeding in many surgical procedures.

But its role in prevention of excessive blood loss, when used as prophylactic drug, has contradiction. So, we want to conduct this study to resolve this controversy. If it proves to be effective, we will recommend the use of this safe, cost-effective and easily available pharmacological therapy to prevent excessive blood loss and prevent post-partum hemorrhage and to reduce the morbidity and mortality associated with post-operative blood transfusions. This will help to improve our practice and guidelines for prevention of excessive blood loss and complications associated with excessive blood loss.

The objective of this study is to compare mean blood loss with tranexamic acid versus placebo given before delivery in females undergoing elective caesarean section.

METHODOLOGY

Study Design: Randomized control trial.

Settings: Obstetrics & Gynecology Department, Allied Hospital Faisalabad Pakistan.

Duration: 6 months March 02, 2019 to August 01, 2019.

Sample Size: Sample size of 200 cases; 100 cases in each group is calculated with 95% confidence level, 90% power of test and taking magnitude of mean blood loss i.e. 499.9±206.4ml with tranexamic acid and 600.7±215.7ml with placebo in females undergoing elective caesarean section.[16]

Sample Technique: Non-probability, consecutive sampling

Inclusion Criteria:

- All elective LSCS due to malpresentation and repeat LSCS in women of age 20 – 40 years having parity <5
- Singleton pregnancy (confirmed by Ultrasonography)
- Gestational age of ≥38 weeks (confirmed by LMP)

Exclusion Criteria:

- Placenta previa, abruption, Accreta, increta, percereta (on ultrasonography)
- Uterine fibroid, Polyhydramnios (AFI>24cm), Fetal macrosomia (on USG)
- Preeclampcia (BP≥140/90mmHg with proteinuria+1 on dipstick method)
- Coagulopathy (INR>2) or active thromboembolic state (on medical record)
- Hypersensitivity to tranexamic acid (history)

Data Collection Procedure: After taking Hospital ethical committee approval, 200 women who fulfilled inclusion criteria were enrolled from indoor of Obstetrics & Gynecology Department, Allied hospital Faisalabad. Informed consent was taken. Demographic details (name, age, gestational age, parity) were also obtained. All the patients were randomly divided into two groups by using random number table. Group A patients received tranexamic acid (1gm/10ml TA diluted with 20ml of 5% glucose) and group B patients not received tranexamic acid (placebo). Trial drug was slowly administered intravenously over a five-minute period at least 10 minutes prior to skin incision. After delivery, both groups received a 5 IU intravenous bolus of pre-prepared oxytocin and then 30 IU oxytocin in 500ml lactated Ringer's solution was infused at a rate of 125ml / h. Blood loss was measured from delivery of placenta till completion of caesarean section (i.e. closure of uterus and skin). Blood loss was noted by measuring the total blood collected in kidney tray of 10" in size during delivery of placenta till completion of caesarean section. All this information was recorded through study proforma.

Statistical Analysis: All the data was entered and analyzed by using SPSS V-21. Mean and standard deviation was calculated for all quantitative variables like age, gestational age and blood loss. Parity was presented as frequency. Independent sample t-test was used to compare mean blood loss between two groups. P-value≤0.05 was taken as significant.

RESULTS

Total 200 patients were evaluated. The overall mean age of the patients was 29.90±6.06 years. However particularly mean age of the patients of TXA group was 29.53±5.81 years and in placebo group was 30.27±6.32 years. Average gestational age was 38.94±0.814 weeks were noted in TXA group 39.02±0.864 weeks was in placebo group. Parity 1-3 was commonest in groups as 74.0% in TXA group and 77.0% in control group, followed by 8.0% women were nulliparous in TXA group and 12.0% were in control group, while in TXA group 18.0% presented with parity >3 and 11.0% in control group, parity was statistically insignificant according to both groups (p=0.078). Table 1

Table 1: Demographic statistics of the patients n=200

Variables		Study Groups		p-value
		TXA	Placebo	
Age (years)	**Mean ±SD**	29.53±5.81	30.27±6.32	**0.463**
Gestational age (weeks)	**Mean± SD**	38.94±0.814	39.02±0.864	0.467
Parity (frequency/%)	**Nulliparous**	08(8.0%)	12(12.0%)	0.078
	1-3	74(74.0%)	77(77.0%)	
	>3	18(18.0%)	11(11.0%)	
	Total	100(100.0%)	100(100.0%)	

Mean blood loss in TXA group was 333.74±40.92 ml which is significantly lower in contrast to control group 440.80±93.064 ml, (p=0.001). Figure 1

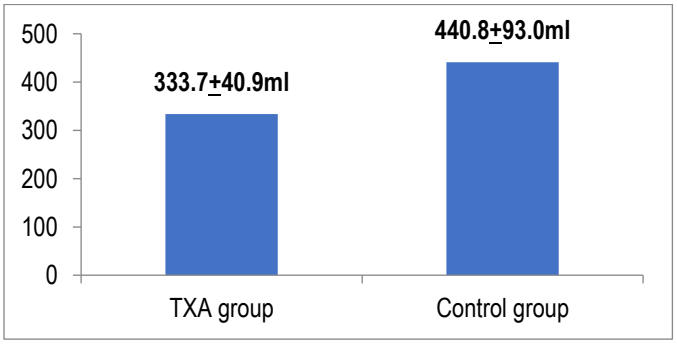

Figure 1: Comparison of average blood loss in both groups n=200

Independent t test=-10.531 p-value=0.001*

In TXA group patients having age ≤30 years, the mean of blood loss in TXA group was 329.19±42.62 ml, which was significantly lower as compared to placebo group 439.12±92.99 ml (p=0.001). Similarly, in patients having age >30 years, the average blood loss significantly decreased in contrast to controls (p=0.001). However, average of blood loss was significantly less in TXA group as compared to control groups, when assessed according to gestational age and parity p-values were quite significant. Table 2

Table 2: Comparison of blood loss with study groups stratified by age

Age	Study Groups	Blood Loss		p-value
		Mean	SD	
≤30 years	TXA	329.19	42.62	0.000*
	Placebo	439.12	92.99	
>30 years	TXA	339.77	38.21	0.000*
	Placebo	442.63	94.08	
Gestational age				
38 weeks	TXA	336.50	40.63	0.000*
	Placebo	471.50	93.28	
39 weeks	TXA	333.47	44.47	0.000*
	Placebo	415.00	78.99	
40 weeks	TXA	330.73	38.14	0.000*
	Placebo	429.37	95.95	
Parity				
Primi	TXA	327.27	35.93	0.000*
	Placebo	432.73	104.40	
Multi	TXA	336.51	42.82	0.000*
	Placebo	445.54	86.25	

DISCUSSION

This study was conducted at Obstetrics & Gynecology Department, Allied hospital Faisalabad to compare mean blood loss with TXA versus placebo given before delivery in females undergoing elective caesarean section.

Obstetric hemorrhage remains one of the major determinants of maternal death in both developed and developing countries. PPH is a common and potentially life-threatening complication of labour. Because of its weight as a leading cause of maternal mortality and morbidity, obstetric hemorrhage must be investigated for national guideline development.[9] Antifibrinolytic drugs, namely TXA have been recognized to decrease blood loss and transfusion needs in various elective surgeries.[10]

In this study the overall mean blood loss value of the patients was 387.27±89.56 ml. In our study the mean value of blood loss in TXA group was 333.74±40.92 ml and its mean value in placebo group was 440.80±93.064 ml. Statistically highly significant difference was found between the study groups with blood loss of the patients. i.e. p-value=0.000. Some of the studies are discussed below showing the results in favor of our study as.

Shahid et al, found that TXA significantly reduced the quantity of blood loss from placental delivery to the end of LSCS and it also reduced the quantity of blood loss from the end of LSCS to 2 hours post-partum. Shahid et al, concluded that TXA can be used safely and effectively in women undergoing LSCS to reduce intra-operative blood loss.[3]

One more study by Leila Sekhavat et al concluded that TXA statistically reduces blood loss from end to 2 hours after CS and its use was not associated with any side effects or complications. They showed that the TXA significantly reduced the blood loss from the end of CS to 2 hours postpartum; 28.02 ± 5.53 ml in the tranexamic group versus 37.12 ± 8.97 ml in the control group (p = 0.000).[11]

Abdel Aleem and colleagues; concluded that the pre-operative use of TXA is associated with reduced blood loss during and after elective CS.[12] They enrolled seven hundred and forty women (373 in study group and 367 in control group). Mean total blood loss was 241.6 (SE 6.77) ml in the TXA group versus 510 (SE 7.72) ml in the control group.

A study by Amr H. Yehia et al[13] resulted that total blood loss from placental delivery till end of caesarean section was significantly less in TXA group compared to control (369.5 ± 198.0 versus 606.8 ± 193.0 ml; respectively). Also calculated vaginal bleeding during first 6 hours post-operative was significantly less in TXA group compared to control (85.0 ± 30.7 ml versus130.8 ± 49.3 ml, respectively). The incidence of PPH was significantly less in TXA group compared to control (31.1% versus 63.2%; respectively.

Six hundred and sixty women (660) women who underwent elective CS were included in Gungorduk and colleagues study to determine the efficacy and safety of TXA in reducing blood loss during elective CS. Gungorduk and colleagues found that TXA significantly reduced bleeding during CS and reduced the need for additional uterotonic agents.[2]

Two hundred and twenty-three (223) women (101 study group & 122 control) were included in Sentürk & colleagues double-blind trial. They found that TXA reduced intra-operative and post-operative blood loss and they did not observe any complications caused by TXA such as venous thromboembolism, gastrointestinal problems and hypersensitivity.[14]

TXA is an antifibrinolytic agent, and a recent systematic review of antifibrinolytic agents in PPH reported a reduction in blood loss of 92 ml (CI 76 to 109 ml).[15]

But on the other hand, in one trial, the mean blood loss was 336.7±151.2ml in the TXA group than 368.5±156.4ml in the control group. However, the amount of blood loss in the period from placental delivery to the end of CS did not differ between the TXA and control groups (p = 0.17).[8]

CONCLUSION

It has been proved in our study that the TXA is useful and effective drug to control the mean blood loss before delivery in females undergoing elective caesarean section as compared to placebo group.

LIMITATIONS

As this study is conducted only on elective LSCS so effect of drugs on emergency and complicated LSCS with placenta accreta spectrum are to be studied.

SUGGESTIONS / RECOMMENDATIONS

As TXA is very effective in prevention of primary PPH in low risk LSCS and this drug is also cost effective and with less side effect profile. So, I will suggest Government authorities to add this drug in EMOC (Emergency Obstetric Care) at all BHU's.

CONFLICT OF INTEREST / DISCLOSURE

There is no conflict of interest in this study.

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AUTHORSHIP CONTRIBUTION

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Dr. Amna Batool Senior Registrar of Gynecology & Obstetrics, Allied Hospital, Faisalabad Pakistan	Data Collection
Dr. Sehrish Maqsood Senior Registrar of Gynecology & Obstetrics, Allied Hospital, Faisalabad Pakistan	References Collection