Volume : 5 | Issue : 3 | March 2016 • ISSN No 2277 - 8179 | IF : 3.508 | IC Value : 69.48

Research Paper

Efficacy of Tranexamic Acid in Reducing Perioperative Blood Loss During Caesarean Section: A Placebo Controlled Double Blind Study

Medical Science

KEYWORDS :

Dr. Amrita Gupta	Lecturer,Deptt of Anaesthesia SNMC, AGRA
Dr Yogita Dwivedi	Asst. Proffessor,Deptt of Anaesthesia, S.N.M.C,AGRA
Dr. Vivek Shakya	P.G. student, Deptt of Anaesthesia, S.N.M.C., AGRA
Dr Uma Srivastva	Professor, Deptt of Anaesthesia S.N.M.C., AGRA
Dr Avanish Saxena	Proffessor, Deptt of Anaesthesia S.N.M.C., AGRA
Dr Atiharsh Mohan Agarwal	Lecturer,Deptt of Anaesthesia, SNMC,AGRA
Dr. Sandeep Mangla	PG Student, Deptt of Anaesthesia,SNMC,AGRA

ABSTRACT

Introduction: caeserian section is one of the most common surgeries in women of child bearing age. With this study we are emphasizing the effect of tranexamic acid in reducing blood loss after caeserian section.

Method: a total number of 102 parturients aged 20 -40 years with singleton fetus,38 or more weeks of pregnancy were selected for the study. They were divided into two groups – Group T who received 1 gm tranexamic acid diluted with 20 ml of 5 % dextrose which was given 20 min before skin incision. In Group P ,patient received 20 ml of 5 % dextrose. Hemodyanamic variables , amount of blood loss, apgar score and any adverse effects were noted.

Results: in this randomized controlled study , tranexamic acid significantly reduce the blood loss. Patients in Group T had higher mean hematocrit level postoperatively. haemodyamic variables were comparable in both the groups. No significant adverse effects were seen related to tranexamic acid administration.APGAR score was comparable in both the groups.

Conclusion: Tranexamic acid significantly reduce bleeding after caeseran section without increase in incidence of thromboembolic events.

INTRODUCTION

One of the most common surgeries done in women of child bearing age is cesarean section. In many areas of the world, 25-30 % incidence of cesarean section has been noted. One of the most common complications after cesarean section is primary and secondary postpartum haemorrhage[1]. Our maternal mortality ratio is 406/100000, it mainly due to haemorrhage[2].

Blood transfusion may be needed in 1 % of women with PPH after vaginal delivery but it is raised to 5 % after cesarean section.[3]

Tranexamic acid is a synthetic derivative of amino acid lysine that has antifibrinolytic effect. It reversibly block lysine binding sites in plasminogen molecule[4] and enhance patient own hemostatic mechanism[5, 6].

Tranexamic acid is used to decrease hemorrhage and the need of allogenic blood transfusion in many surgeries like cardiac, orthopaedic, liver transplantation[7,8,9,10,11].

We conducted a study to find out the effect of Tranexamic acid in reducing bleeding intraoperatively during cesarean section and postoperatively up to 2 hours. We also saw the requirement of blood transfusion in these patients and adverse effects of tranexamic acid.

MATERIAL AND METHOD

After institutional committee approval and the patient, the study was conducted on 102 parturients in department of Anaesthesia, S.N Medical College Agra from june 2013 to june 2015.The study include a pregnant women aged 20-40 year with singleton fetus, 38 or more weeks of gestation with uncomplicated pregnancy undergoing elective or emergent cesarean section. Parturients with severe pre-eclampsia, multiple pregnancy, previous PPH, APH, grand multiparity, polyhydramnios, anaemia (hemoglobin < 10gm%), on anticoagulants were excluded from the study. Randomization was done using computer generated random number table, concealed in sequentially numbered opaque envelop opened just before study. It was double blind study neither the provider nor the researcher know who is getting a placebo and who is getting the treatment to avoid information and calculation bias. After selection of patient study group (group T) patient received 1 gm tranexamic acid diluted with 20 ml of 5 % dextrose given 20 min before skin incision while placebo group (group P) received 20 ml of 5 % dextrose given 20 min before skin incision.

After taking the patient in OT, Pulse oximeter, ECG and NIBP were attached and IV line secured. After preloading with 500 ml of RL, each patient received spinal anaesthesia with 2.0- 2.2 ml of 0.5 % bupivacaine heavy at L 3- L 4 intervertebral space with 26 g spinal needle. The surgery was allowed to commence after adequate surgical anaesthesia. After delivery of baby 20 units inj. syntocinon was added to the IV drip and given at rate of 8 micro U/min. The following parameters were observed;-

1. Blood pressure & heart rate were monitored before tranexamic acid infusion, immediately before surgery & every 5 minutes till end of surgery then every 30 minutes for 2 hours in post anaesthesia care unit (PACU).
2. Measurement of amount of blood loss after delivery of placenta (soaked mops, pads, operation table sheets were weighed by electronic scale before and after surgery).
3. Hemoglobin, hematocrit levels, creatinine were obtained in all the patients before surgery and 24 hours post operatively. Special hematological investigations (PT, APTT, S. bilirubin, SGOT, Serum urea) were done only in patients undergoing elective cesarean section.
4. Uterine contractility, placental separation, neonatal condi-

Volume : 5 | Issue : 3 | March 2016 • ISSN No 2277 - 8179 | IF : 3.508 | IC Value : 69.48

tion were noted.

The quantity of blood loss was determined after delivery of placenta (soaked mops, pads, OT tables sheets) by electronic scale before and after surgery. The quantity of blood loss (mL) = (weight of the used material in both the periods – weight of materials prior to surgery) + the volume sucked in the suction bottle after placental delivery in ml.

Sample size justification:
Sample size was calculated using data from previous studies data from Cochrane systematic review that showed the risk of post-partum blood loss > 400 mL was 14.44% in women who received TXA, in contrast to 32.38% in women who did not [6], and EpiInfo version 7.0, setting the power at 80%, the two-sided confidence level at 95% and 10% patients drop rate. Calculation according to these values, the minimal number of women needed to produce a statistically acceptable figure was 51 in each group. Therefore, one hundred women were recruited in the beginning of the current study to be randomized into two groups.

Statistical analysis:
Data were collected, tabulated then statistically analyzed using the Statistical Package for Social Sciences (SPSS) computer software version 18. Numerical variables were presented as mean and standard deviation, while categorical variables were presented as number and percentage. Chi-square test was used for comparison between groups as regard qualitative variables. Student t-test was used for comparison between groups as regard quantitative variables. A difference with a P value <0.05 was considered statistically significant.

Results:
The subject characteristics in the two groups were similar with no statistically significant difference between age, weight, height, duration of surgery and the no. of elective/ emergency cesarean section. TABLE 1

No statistically significant difference in vital signs (heart rate, blood pressure, respiratory rate) at various time intervals during cesarean section was found between groups. TABLE 2

Mean estimated blood loss and the proportion of women who experienced an estimated blood loss > 500 ml were significantly lower in TA group than the placebo group (TA=359.13±75, placebo=479.93±87; p value <0.0001). No blood transfusion was required in tranexamic group while it was needed in 3 cases in group P. 17 % patient in placebo group experienced blood loss >500 ml while none was found in TA group.TABLE 3

Postoperative hemoglobin and hematocrit levels were significantly higher in TA group than placebo group (TA Hb =12.57 ± 1.33; placebo Hb= 11.74 ± 1.14, p value <0.002).No significant change in PT, aPTT, renal and liver function test was observed in either group. TABLE 4

Gastrointestinal side effects of tranexamic acid were found in 52 % of patients (nausea 34 %, vomiting 16 %, diarrhea 2 %. No episodes of thromboembolic events was observed in women who received tranexamic acid. TABLE 5

Neonatal APGAR score was comparable in both the groups.TABLE 6.

TABLE 1

Parameter	Group T Mean ± SD	Group P Mean ± SD	T value	P value
Age (years)	27.32 ± 4.33	26.88 ± 4.88	0.4769	0.6345
Weight (kg)	52.54 ± 7.86	53.5 ± 7.45	0.6268	0.5322
Height (cm)	152.56 ± 5.75	153.2 ± 6.0	0.5446	0.5873
Duration of surgery	70 min	75 min		
No. of elective cases	24	27		
No. of emergency cases	26	25		

TABLE 2
Preoperative:

Parameters	Group	At 5 min	At 10 min	At 15 min	At 20 min	At 30 min	At 45 min	At 60 min	P value
Heart Rate	Group T (mean ± SD)	86.62 ± 6.83	89.16 ± 7.41	86.24 ± 5.42	86.10 ± 6.04	87.08 ± 6.25	87.08 ± 6.36	86.12 ± 6.57	0.2121
	Group P (mean ± SD)	82.62 ± 6.72	87.16 ± 5.29	87.68 ± 5.07	83.94 ± 6.20	85.92 ±5.85	85.24 ± 5.24	87.94 ± 4.44	
Systolic BP	Group T (mean ± SD)	117.50 ± 6.36	117.98 ± 7.50	120.16 ± 7.41	120.84 ± 8.58	118.56 ± 7.07	117.26 ± 5.37	118.52 ± 6.54	0.7184
	Group P (mean ± SD)	118.40 ± 7.41	117.50 ± 6.36	120.72 ± 8.90	120.22 ± 7.84	117.70 ± 6.70	121.04 ± 8.22	118.06 ± 7.13	
Diastolic BP	Group T (mean ± SD)	78.00 ± 4.99	76.76 ± 5.22	76.86 ± 6.07	76.36 ± 6.29	77.16 ± 5.65	77.04 ± 5.05	77.88 ± 5.33	0.8248
	Group P (mean ± SD)	76.84 ± 4.86	78.00 ± 4.99	77.28 ± 6.50	76.12 ± 5.90	77.06 ± 4.74	76.92 ± 6.72	77.12 ± 4.71	

Table 2

Parameters	Group	At 30 min	At 60 min	At 90 min	At 120 min	P value
Heart Rate	Group T (mean ± SD)	82.84 ± 7.22	86.24 ± 5.42	86.44 ± 6.22	83.82 ± 6.66	0.0157
	Group P (mean ± SD)	7.34 ± 6.42	89.66 ± 4.87	91.38 ± 4.24	87.96 ± 4.52	
Systolic BP	Group T (mean ± SD)	116.46 ± 7.38	120.96 ± 8.07	120.50 ± 6.98	116.98 ± 6.07	0.9039
	Group P (mean ± SD)	118.22 ± 17.02	117.92 ± 16.63	122.00 ± 8.75	117.80 ± 17.41	
Diastolic BP	Group T (mean ± SD)	76.28 ± 4.91	76.70 ± 6.63	76.80 ± 5.96	79.28 ± 10.98	0.6020
	Group P (mean ± SD)	76.62 ± 6.12	77.72 ± 5.60	77.76 ± 6.66	75.32 ± 5.69	

Postoperative:

Parameters		Group T (n=51)		Group P (n=51)	
		Before (Trenexa)	After (Trenexa)	Before placebo	After placebo
Spo2	Mean ± SD	98.16 ± 1.23	98.02 ± 1.05	98.28 ± 1.16	98.16 ± 0.93
	p-value	0.5419 NS		0.5696 NS	
RR	Mean ± SD	15.27 ± 2.64	14.78 ± 2.03	15.20 ± 2.65	14.72 ± 2.05
	p-value	0.3009		0.3137	

TABLE 3

	Intraoperative Blood loss (ml)		Post-operative Blood loss (ml)		Total blood loss (ml)	
	Group T	Group P	Group T	Group P	Group T	Group P
Mean	337.09	472.39	22.04	25.54	359.13	497.93
SD	74.52	82.33	2.98	8.11	74.91	86.83
t-value	8.6154		2.8644		8.5585	
p-value	<0.0001		<0.0051		<0.0001	
95% confidence intervals	104.13 to 166.47		1.057 to5.94		106.61 to 170.99	

TABLE 4

	Preoperative		Postoperative		
Parameters	**Group T (n=51)**	**Group P (n=51)**	**Group T (n=51)**	**Group P (n=51)**	**P value**
Haemoglobin	11.03 ± 1.01	11.34 ± 1.04	10.43 ± 1.02	9.8 ± 0.98	< 0.002
Haematocrit	32.43 ± 4.74	34.37 ± 2.97	31.28 ± 3.05	29.40 ± 2.77	< 0.0017
PT	12.35 ± 1.37	12.87 ± 1.43	13.01 ± 1.80	12.91 ± 1.43	0.7591
APTT	33.25 ± 3.20	33.35 ± 3.13	33.47 ± 3.12	33.11 ± 3.10	0.5647
Platelets	2.41 ± 0.62	2.49 ± 0.69	2.28 ± 0.58	2.36 ± 0.63	0.5104
S. bilirubin	0.51 ± 0.31	0.52 ± 0.32	0.48 ± 0.26	0.47 ± 0.24	0.8420
SGOT	20.43 ± 5.89	21.76 ± 7.06	20.12 ± 5.76	21.36 ± 6.23	0.3040
SGPT	26.53 ± 6.34	26.70 ± 6.11	27.63 ± 6.92	27.96 ± 6.20	0.8022
BUN	18.61 ± 5.04	16.24 ± 3.54	20.49 ± 6.71	19.88 ± 5.68	0.6248
S. Creatinine	0.82 ± 0.21	0.77 ± 0.15	0.77 ± 0.16	0.75 ± 0.15	0.5206

TABLE 5

Effects	Group 1 (n=51)	Group 2 (n=51)
Nausea	17(34%)	13 (26%)
Vomiting	8 (16%)	8 (16%)
Diarrhoea	1 (2%)	1 (2%)
Agitation	0	0
Shivering	0	0
Others	0	0

TABLE 6

Parameters	Group T (n=51)	Group P (n=51)	p-value
Birth weight (gm)	2857.23 ± 276.21	2945.43 ± 287.46	0.1209
Apgar at 1 min	8.2 ± 0.7	8.3 ± 0.9	0.11
Apgar at 5 min	9.0 ± 0.5	9.1 ± 0.5	0.3198
Neonatal jaundice (no.)	9	8	-
NICU admission (no.)	1	1	-

DISCUSSION :

Obstetric hemorrhage is the leading cause of maternal morbidity[12].various measures have been used to prevent PPH particularly pharmacologic agents. Tranexamic acid is a strong antifibrinolytic drug that inhibit binding of lysine on plasminogen molecules. It also increases capacity of patients own hemostatic system. Therefore fibrinolysis or clot interruption is inhibited. Whenever the placenta separates from the uterine wall during delivery, there is increase in fibrinolytic activity[13]. So early administration of antifibrinolytic seems to be reasonable for management of PPH.[14] Since then TXA has been widely used to treat heavy menstrual bleeding[15] and also decreases blood transfusion by one hand[16,17].

We calculated the difference in preoperative and postoperative hematocrit levels to estimate blood loss[18]. Like other studies , in our study also total blood loss in Group T (359.13± 74.91) was significantly less than group P (497.93± 86.83) (p value < 0.0001). TA group had higher mean hemoglobin and hematocrit level as compared to placebo after cesarean section.No blood transfusion is needed in Group T while it was needed in three cases in placebo group. 17 % of patients in placebo group experienced blood loss > 500 ml while no case was found in TA group. Our results are in agreement with many previous studies[18,19,20,21,22].

In our study no significant abnormal vital signs were observed following tranexamic acid administration, nor did we observe abnormalities in CBC, PT, aPTT, renal, liver function. Moreover there was no difference between the two groups in term of neonatal abnormalities. APGAR score at 1 min and 5 min was similar in both the groups.

In our study 30 % of the patients experienced gastrointestinal side effects. Gait et al[20] and Gohel et al[23]also reported mild adverse reactions with tranexamic acid.

No thromboembolic event was seen in our study. Antifibrinolytic cause increase in thrombotic event , but many studies showed no increase in thromboembolic events after TA[18].

Volume : 5 | Issue : 3 | March 2016 • ISSN No 2277 - 8179 | IF : 3.508 | IC Value : 69.48

Conclusion

This randomized study demonstrated that TA significantly reduced bleeding after Cesarean Section, the percentage of patients with blood loss > 500 mL, and additional use of uterotonic agents. Additionally, no increase in the incidence of thromboembolic events was observed. Thus, our results suggest that TA can be used safely and effectively to reduce bleeding resulting from Cesarean Section.

The current double-blind randomized trial concluded that TXA can be used safely without any maternal or neonatal side effects to reduce blood loss during and after Cesarean Section. The reduced blood loss during and after Cesarean Section following TXA administration was associated with improvement of postoperative hemoglobin, hematocrit values and with reduction of post-partum need for iron replacement.

REFERENCES

1. Abou Zahr C. Harvard School of Public Health on behalf of the World Health Organization and the World Bank; Boston (United States of America), Geneva, (Switzerland) ;: 1998 : (41) ,165-189.
2. Payal Ray et al. A Study on Effectiveness of Tranexamic Acid as an Anti-fibrinolytic Agent to Reduce the Intraoperative and Immediate Post-operative Bleeding During Caesarean Section. J Clin Biomed Sci 2014; 4(2):272-75.
3. Soltani S, Mirteimouri M, Movahedian A, Chalakinia N. Preventive and therapeutic effect of tranexamic acid on postpartum bleeding.Rev Clin Med.2015;2(1):37-41.
4. Williams-Johnson J, McDonald A, Strachan GG, Williams E. Effects of tranexamic acid on death, vascular occlusive events, and blood transfusion in trauma patients with significant haemorrhage (CRASH-2): A randomised, placebo-controlled trial. West Indian Med J. 2010;59:612–24.
5. Bolton TJ, Randall K, Yentis SM. Effect of the confidential enquiries into maternal deaths on the use of syntocinon at caesarean section in the UK. Anaesthesia 2003;58:277–279.
6. Prentice A. Fortnightly review. Medical management of menorrhagia. BMJ 1999;319:1343–1345.
7. Caglar G, Tasci Y, Kayikcioglu F, Haberal A. Intravenous tranexamic acid use in myomectomy: A prospective randomized double-blind placebo controlled study. Eur J Obstet Gynecol Reprod Biol. 2008;137:227–31.
8. Ghojazadeh M, Azar ZF, Saleh P, Naghavi-Behzad M, Azar NG. Knowledge and attitude of Iranian University students toward Human Papilloma Virus. Asian Pac J Cancer Prev. 2012;13:6115–9.
9. Ghojazadeh M, Naghavi-Behzad M, Azar ZF, Saleh P, Ghorashi S, Pouri AA. Parental knowledge and attitudes about Human Papilloma Virus in Iran. Asian Pac J Cancer Prev. 2012;13:6169–73.
10. Kagoma YK, Crowther MA, Douketis J, Bhandari M, Eikelboom J, Lim W. Use ofantifibrinolytic therapy to reduce transfusion in patients undergoing orthopedic surgery: A systematic review ofrandomized trials. Thromb Res. 2009;123:687–96.
11. Massicotte L, Denault AY, Beaulieu D, Thibeault L, Hevesi Z, Roy A. Aprotinin versus tranexamic acid during liver transplantation: Impact on blood product requirements and survival. Transplantation. 2011;91:1273–8
12. Ferrer P, Roberts I, Sydenham E, Blackhall K, Shakur H. Anti-fibrinolytic agents in post partum haemorrhage: a systematic review. BMC Pregnancy Childbirth 2009;9:29
13. Hellgren M. Hemostasis during normal pregnancy and puerperium. Semin Thromb Hemost. 2003;29:125-130.
14. Dunn CJ, Goa KL. Tranexamic acid: a review of its use in surgery and other indications.Drugs.1999;57:1005-1032.
15. Lukes AS, Kouides PA, Moore KA. Tranexamic acid: a novel oral formulation for the treatment of heavy menstrual bleeding. Womens Health 2011; 7:151-8.
16. Caglar GS, Tasci Y, Kayikcioglu F, Haberal A. Intravenous tranexamic acid use in myomectomy: a prospective randomized double-blind placebo controlled study. Eur J Obstet Gynecol Reprod Biol 2008; 137:227-31.
17. Mayur G, Purvi P, Ashoo G, Pankaj D. Efficacy of tranexamic acid in decreasing blood loss during and after caesarean section: a randomized case controlled prospective study. J Obstet Gynecol India 2007; 57:227-30.
18. Gungorduk K, Yıldırım G, Asıcıoğlu O, Gungorduk OC, Sudolmus S, Ark C. Efficacy of intravenous tranexamic acid in reducing blood loss after elective cesarean section: a prospective, randomized, double-blind, placebo-controlled study. Am J Perinatol 2011; 28(3): 233-240.
19. Abdel-Aleem H, Alhusaini TK, Abdel-Aleem MA, Menoufy M, G ülmezoglu AM. Effectiveness of tranexamic acid on blood loss in patients undergoing elective cesarean section: randomized clinical trial. J Matern Fetal Neonatal Med 2013; 26(1):1705-1709.
20. Gai MY, Wu LF, Su QF, Tatsumoto K. Clinical observation of blood loss reduced by tranexamic acid during and after caesarian section: a multi-center, randomized trial. Eur J Obstet Gynecol Reprod Biol 2004;112:154–157.
21. Xu, J., Gao, W., Ju, Y. Tranexamic acid for the prevention of postpartum hemorrhage after cesarean section: a double-blind randomization trial. *Arch Gynecol Obstet*. 2013;287:463–468.
22. Yang, H., Zheng, S., Shi, C. Clinical study on the efficacy of tranexamic acid in reducing postpartum blood lose: a randomized, comparative, multicenter trial. 2001;36:590–592.
23. Gohel M, Patel P, Gupta A, Desai P. Efficacy of tranexamic acid in decreasing blood loss during and after caesarean section: a randomized case controlled prospective study. J Obstet Gynaecol India 2007;57:228–230