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Efficacy of Intravenous Tranexamic Acid in Reducing Blood Loss after Elective Cesarean Section

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ABSTRACT

Background: Primary post-partum hemorrhage (PPH) is defined as blood loss greater than or equal to 500 ml within 24 hours after birth, while severe PPH is blood loss greater than or equal to 1000 ml within 24 hours.

Objective: was to determine the efficacy and safety of tranexamic acid in reduction of blood loss after the elective cesarean sections.

Patients and Methods: We performed a randomized, controlled study of 200 pregnant females who underwent elective CS. The patients had attended the Labor Ward in Al-Azhar University Maternity Hospital. 100 of them received tranexamic acid 20 minutes before beginning of anesthesia in addition to oxytocin after delivery of the baby; the other 100 patients received oxytocin only.

Results: In the 1st two hours post-partum vaginal bleeding was significantly less severe in study group than control group (p<0.019). There was nonsignificant difference between study and control groups as regards preoperative hemoglobin concentration (p=0.195), Postoperative hemoglobin concentration was significantly greater in study group than control group (p<0.001), Reduction in hemoglobin levels ware significantly less in study group than control group (p<0.001). There was nonsignificant difference between study and control groups as regards to preoperative hematocrite (p=0.967), Postoperative hematocrite levels were significantly higher in study group than control group (p0.015), Reduction in hematocrite levels ware significantly less in study group than control group (p<0.001).

Keywords: Cesarean section, lower segment cesarean section

INTRODUCTION

Cesarean section is defined as the delivery of a baby through a surgical abdominal incision. Cesarean section (CS) rates are increasing to as high as 25 to 30 % in many areas of the world [(1)].

Delivery by CS causes more complications than normal vaginal delivery. Infection can occur at the incision site, in the uterus and in other pelvic organs such as the bladder. blood loss in a cesarean delivery is greater than with vaginal deliveries. This can increase levels of anemia or a blood transfusion (1 to 6 women delivered by CS per 100 require a blood transfusion), increase the possibility of injury to organs such as the bladder or bowel. Scar tissue may travel inside the pelvic region causing blockage and pain. Adhesions also increases levels of future pregnancy complications such as placenta previa or placental abruption. Extended hospital stays and recovery time. There may be a negative reaction to the anesthesia given during a cesarean or negative reaction to pain medication given after the operation.

The increase of the Risk of additional surgeries: Includes possibility of hysterectomy, bladder repair or another cesarean. Risks and complications may occur to the baby e.g.; premature birth breathing problems, low APGAR scores and fetal injuries may occur [(2)]**.**

One of these common complications is primary or secondary postpartum hemorrhage (20%). It leads to the increase of maternal mortality and morbidity. Postpartum hemorrhage causes approximately 25% of worldwide maternal deaths (WHO Recommendations 2006) and also causes 12% severe anemia of survivors. In order to reduce maternal mortality and morbidity rates caused by bleeding, it is important to reduce the amount of bleeding during and after cesarean sections [(3)].

In severe cases, CS may cause obstetric hemorrhage, hysterectomy, admission to an intensive care unit, or maternal death. Medications, such as oxytocin, misoprostol, prostaglandin F2α, and tranexamic acid, have been used to control bleeding during and after CS [(4)]**.**

Tranexamic acid is a synthetic derivative of the amino acid lysine that has an antifibrinolytic effect through the reversible blockade of the lysine binding sites on plasminogen molecules. The intravenous administration of tranexamic acid has been routinely used for many years to reduce hemorrhage during and after surgical procedures like coronary artery bypass, oral surgery, orthotopic liver transplantation, total hip or knee arthroplasty, and urinary tract surgery [(5)]**.**

Tranexamic acid is very useful in reducing blood loss and incidence of blood transfusion in the surgeries. Tranexamic acid treatment is inexpensive and would be considered highly cost effective in high, middle- and low-income countries [(6)]**.**

AIM OF THE WORK

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The aim of the current study was to determine the efficacy and safety of tranexamic acid in reduction of blood loss after the elective cesarean sections.

PATIENTS AND METHODS

This randomized, controlled study included a total of 200 pregnant females who underwent elective CS, attending at the Labor Ward in Al-Azhar University Maternity Hospital. Approval of the ethical committee and a written informed consent from all the subjects were obtained. This study was conducted between May 2018 to December 2018.

All women fulfilled the inclusion criteria were enrolled in the study. The patients were randomized into 2 groups using a computer-generated randomization list, generated using medcalc© version 13(medcalc@ software, mariakirke, ostend, Belgium).

Group (A): received 1g of intravenous tranexamic acid in 200 mL of normal saline (study group; n=100).
Group (B): received no the tranexamic acid (control group; n=100).

The randomization list was concealed and accessed by sequentially numbered, opaque, sealed envelopes (SNOSE); immediately before intervention. The solution was prepared by an anesthetist who was not involved in patient's management or assessment.

Inclusion criteria: pregnant women undergoing cesarean delivery for many elective indications. Full term primiparas / multiparas. Singleton pregnancy being delivered by CS.

Exclusion criteria: Medical problems involving the heart, liver, kidney and brain diseases. Blood disorders. Allergy to tranexamic acid. History of thromboembolic disorders, abnormal placentation, severe pre-eclampsia, uterine anomalies and pathology. Multiple pregnancy, macrosomia. Polyhydramnios. Patients requiring blood transfusion due to anemia

All Patients were subjected to completed history taking and clinical examination and pre-operative investigations (complete blood count, prothrombin time, activated partial thromboplastin time, liver and kidney function tests).

In the study group patients. 20 minutes before taking the skin incision 1 g tranexamic acid (Kapron®, Amoun, Egypt) was given in 200 mL normal saline. After delivery of the neonate, 5 units of oxytocin (Syntocynon®, NOVARTIS, Egypt) in 500 ml normal saline was given by intravenous drip over 30 minutes.

Tranexamic acid injections were prepared by diluting 1g (10 mL) tranexamic acid with 200 ml of normal saline.

Tranexamic acid was not given in the control group patients. After delivery of the neonate, oxytocin was given as in the study group patents.

The blood loss was measured at 2 periods. following placental delivery to the end of the surgery (1st period), and from the end of the operation to 2 hours after birth(2nd period).

Uterine contractility, placental separation, neonatal manifestations, and side effects caused by tranexamic acid ware noted as nausea ,vomiting ,diarrhea ,thrombosis ,blurring of vision and hypotension.

Measuring blood loss

The amount of blood loss (mL)= (weight of the used towels in every period – weight of the towels prior to the surgeries) + the volume sucked in the suction bottle after placental delivery in mL. In addition, the pads used after completion of CS to two hours postpartum were separately assessed. Hemoglobin, hematocrit values were noted 24 hours after operation for both groups. Conversion of weight of towels by (g) to volume by (ml) by equation (1000 g = 962 ml). Heart rates, respiratory rates and blood pressure were checked and noted before the surgery, immediately after placental delivery and one and two hours after birth, respectively.

***Primary outcome measures*:** Amount of blood loss assessed during cesarean section (in ml) after placental delivery till end of the operation.

Secondary outcome measures: Vital data during first two post operative hours. Vaginal bleeding were assessed during first two post-operative hours. 24 hours post operative hemoglobin and hematocrit. Maternal and neonatal side effects of tranexamic acid.

Sample Size Justification Sample size was calculated using data from previous studies [7], data from Cochrane systematic review that showed the risk of post-partum blood loss > 400mL was 14.44% in pregnant women who received tranexamic acid (TXA), in contrast to 32.38% in women who were not [8] and EpiInfo version 7.0, setting the power at 80%, the two-sided confidence level at 95% and 10% patients drop rates. Calculation according to these values, the minimal number of women needed to produce a statistically acceptable figure were 98 in each group. Therefore, two hundred (200) were recruited at the beginning of the current study to be randomized into two groups.

Statistical analysis

Data were analyzed using Statistical Program for Social Science (SPSS) version 18.0. Quantitative data were expressed as mean± standard deviation (SD). Qualitative data were expressed as frequency and percentage.

The following tests were done: Independent-samples t-test of significance was used when comparing between two means. Chi-square (X2) test of significance was used in order to compare proportions between two qualitative parameters. Probability (P-value) – P-value <0.05 was considered significant. – P-value <0.001 was considered as highly significant. – P-value >0.05 was considered insignificant.

RESULTS

Table (1): Descriptive data of the group (A) study group and group (B) control group.
This table should be table number (1)

	Group (A) Study group				Group (B) Control group			
Descriptive data	**Min.**	**Max.**	**Mean**	**±SD**	**Min.**	**Max.**	**Mean**	**±SD**
Age (years)	18	39	27.81	5.07	19	40	28.32	4.65
BMI (kg/m^2)	23	35.8	29.24	3	16.7	35	29.55	3.08
GA (weeks)	37	40	38.19	0.7	37	41	38.22	1.1
Systolic BP (preoperative)	100	140	117.84	9.4	100	130	117.63	7.98
Diastolic BP (preoperative)	60	90	74.54	6.19	60	80	75	5.29
Systolic BP (postoperative)	100	130	114.59	6.01	100	120	109.74	8.16
Diastolic BP (postoperative)	60	80	74.66	5.75	60	88	70.63	7.48
HR (BPM) (preoperative)	65	110	85.01	10.18	65	110	85.8	8.7
HR (BPM) (postoperative)	70	105	83.14	7.21	75	120	96.12	10.66
Hb. (g/dl) (preoperative)	9.8	15	12.16	1.28	9.5	15	11.9	1.24
Hb. (g/dl) (postoperative)	9.2	14	11.44	1.24	8.1	14.2	10.55	1.18
HCT% (preoperative)	30	45	37.07	3.54	27	49	37.1	4.13
HCT% (postoperative)	25	43	34.47	3.74	23	42	32.91	3.97
Blood loss 1st period (ml)	180	840	386.55	104.98	220	850	507.76	152.14
Blood loss 2nd period (ml)	10	270	114.73	53.82	10	320	139.67	73.35
Total blood loss (ml)	220	1030	501.28	119.2	295	1140	647.43	178.77

Table (2): Comparison between group A and group B as regard demographic data.

Demographic data	Group (A)		Group (B)			t-test
Mean	±SD	Mean		±SD	t	p-value
Women Age (years)	27.81	5.07	28.32	4.65	-0.636	0.526
BMI (kg/m2)	29.24	3.00	29.55	3.08	-0.624	0.533
GA (weeks)	38.19	0.70	38.22	1.10	-0.228	0.820
Duration of l.S C.S(min)	42.65	8.57	43.28	21.87	0.268	0.788

This table shows no statistically significant difference between groups as regard demographic data, using Independent sample t-test with p-value >0.05 NS

Table (3): Comparison between group A and group B as regard parity.

Parity	**Group (A)**		**Group (B)**	
	No.	**%**	**No.**	**%**
P0	22	22.0	14	14.0
P1	32	32.0	29	29.0
P2	31	31.0	37	37.0
P3	4	4.0	7	7.0
PG	11	11.0	13	13.0
Total	100	100.0	100	100.0
x2	3.299			
p-value	0.271			

This table shows no statistically significant difference between groups as regard parity using Chi-square test with p-value >0.05 NS

Table (4): Comparison between group A and group B as regard blood pressure and heart rate.

Blood pressure	Group (A)		Group (B)		t-test	
	Mean	±SD	Mean	±SD	t	p-value
Systolic BP (preoperative)	117.84	9.40	117.63	7.98	0.145	0.885
Diastolic BP (preoperative)	74.54	6.19	75.00	5.29	-0.490	0.625
Systolic BP (2hrs postoperative)	114.59	6.01	109.74	8.16	4.142	**<0.001**
Diastolic BP (2hrs postoperative)	74.66	5.75	70.63	7.48	3.693	**<0.001**
HR (BPM) (preoperative)	85.01	10.18	85.80	8.70	-0.511	0.610
HR (BPM) (2hrs postoperative)	83.14	7.21	96.12	10.66	-8.712	**<0.001**

This table shows statistically significant difference between groups as regard systolic and diastolic Blood pressure postoperative, using Independent sample t-test with p-value <0.001 HS, the rest have insignificant. Also, statistically significant difference between groups as regard heart rate postoperative.

Table (5): Comparison between group A and group B as regard Hemoglobin (Hb) and Hematocrite(HCT%).

	Group (A)		Group (B)		t-test	
	Mean	±SD	Mean	±SD	t	p-value
Hb. level (g/dl) (preoperative)	12.16	1.28	11.90	1.24	1.302	0.195
Hb. Level (g/dl) (24hrs postoperative)	11.44	1.24	10.55	1.18	4.511	**<0.001(HS)**
HCT% level (preoperative)	37.07	3.54	37.10	4.13	-0.041	0.967
HCT% level (24hrs postoperative)	34.47	3.74	32.91	3.97	2.470	**0.015 (S)**

This table shows highly statistically significant difference between groups as regard Hb. (g/dl) postoperative, using Independent sample t-test with p-value <0.001 HS, while Hb. (g/dl) preoperative non-significant, also statistically significant difference between groups as regard HCT% postoperative.

Table (6): Comparison between group A and group B as regard blood loss.

	Group (A)		Group (B)		t-test	
	Mean	±SD	Mean	±SD	T	p-value
Blood loss in 1st period (ml) (from placental delivery till end of operation)	386.55	104.98	507.76	152.14	-5.665	**<0.001(HS)**
Blood loss in 2nd period (ml) (from end of operation till 2 hrs postoperative)	114.73	53.82	139.67	73.35	-2.369	**0.019(S)**
Total blood loss (ml)	501.28	119.20	647.43	178.77	-5.875	**<0.001(HS)**

This table shows statistically significant difference between groups as regard blood loss 1st and 2nd periods and total blood loss **with difference [146.15 ml (22.6%)] blood loss** in group (A) less than group (B), using Independent sample t-test.

Table (7): Comparison between group A and group B as regard intraoperative events.

Intraoperative events	Number of cases		Chi-square	
	Group (A)	Group (B)	X2	P-value
Accessory hemostatic Sutures of the uterine incision	33	38	0.546	0.460
Uterine artery injury or ligation	2	3	0.205	0.651
Broad ligament hematoma	0	0	0.000	1.000
Blood transfusion	0	1	1.005	0.316
Hysterectomy	0	0	0.000	1.000

This table shows no statistically significant difference between groups as regard intraoperative events, using Chi-square test, with p-value >0.05 NS

Table (8): Differences between preoperative and postoperative data as regard all parameters in group (A).

Parameters	Group (A)		Paired Difference		Paired Sample t-test	
	Mean	±SD	Mean	±SD	T	p-value
Systolic Bpr (preoperative)	117.84	9.40	3.24	10.08	2.77	0.007 (S)
Systolic Bpr (2hrs postoperative)	114.59	6.01				
Diastolic Bpr (preoperative)	74.54	6.19	-0.12	8.07	1.08	0.896
Diastolic Bpr (2hrs postoperative)	74.66	5.75				
HR (BPm) (preoperative)	85.01	10.18	1.88	9.07	-0.76	0.079
HR (BPm) (2hrs postoperative)	83.14	7.21				
Hb. (g/dl) (preoperative)	12.16	1.28	0.73	0.58	10.77	<0.001 (HS)
Hb. (g/dl) (24hrs postoperative)	11.44	1.24				
HCT% (preoperative)	37.07	3.54	2.61	2.26	9.94	<0.001 (HS)
HCT% (24hrs postoperative)	34.47	3.74				
Blood loss 1st period (ml)	386.55	104.98	271.82	116.73	20.03	<0.001 (HS)
Blood loss 2nd period (ml)	114.73	53.82				

This table shows statistically significant difference between preoperative and postoperative as regard systolic Blood pressure, Hemoglobin, HCT% and blood loss, the rest have insignificant, using Independent sample t-test, in group (A).

Table (9): Differences between preoperative and postoperative as regard all parameters data in group (B).

Parameters	Group (B)		Paired Difference		Paired Sample t-test	
	Mean	±SD	Mean	±SD	t	p-value
Systolic Bpr (preoperative)	117.63	7.98	7.89	9.84	6.99	<0.001 (HS)
Systolic Bpr (2hrs postoperative)	109.74	8.16				
Diastolic Bpr (preoperative)	75.00	5.29	4.37	8.18	4.658	<0.001 (HS)
Diastolic Bpr (2hrs postoperative)	70.63	7.48				
HR (BPm) (preoperative)	85.80	8.70	-10.32	10.17	-8.84	<0.001 (HS)
HR (BPm) (2hrs postoperative)	96.12	10.66				
Hb. (g/dl) (preoperative)	11.90	1.24	1.35	0.56	21.21	<0.001 (HS)
Hb. (g/dl) (24hrs postoperative)	10.55	1.18				
HCT% (preoperative)	37.10	4.13	4.19	2.51	14.53	<0.001 (HS)
HCT% (24hrs postoperative)	32.91	3.97				
Blood loss 1st period (ml)	507.76	152.14	368.09	158.41	20.26	<0.001 (HS)
Blood loss 2nd period (ml)	139.67	73.35				

This table shows statistically significant difference between preoperative and postoperative as regard all parameters, using Independent sample t-test, with p-value <0.001 HS in group (B).
Comparison between table (11) and table (12) shows: Decrease of haemoglobin in group A is less than group B. Decrease of blood pressure (systolic and diastolic) in group A is less than group B. Decrease in hematocrite in group A is less than group B. Amount of blood loss in group A is less than gro

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