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Original Research Article

Efficacy of prophylactic use of tranexamic acid in reduction of blood loss in benign hysterectomy: a randomised controlled trial

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ABSTRACT

Background: Aim of current study was to determine the efficacy of tranexamic acid in the reduction of blood loss during hysterectomy for benign indications.
Methods: This is a randomized controlled trial in a tertiary care teaching hospital in Pondicherry. The study population was 108. Participants were allocated into 2 groups: Group A (N=54) and group B (N=54) based on computer generated random numbers. Group A (N=54) comprised of participants undergoing hysterectomy with prophylactic intravenous tranexamic acid (1 gram in 100 ml of 0.9% normal saline) which was further subdivided into A1 (N=27) and A2 (N=27) undergoing abdominal and vaginal hysterectomy respectively. Group B: comprised of participants undergoing hysterectomy without tranexamic acid, further subdivided into B1 (N=27) and B2 (N=27) undergoing abdominal and vaginal hysterectomy respectively. The mean blood loss during the intraoperative and post-operative periods was calculated and compared between the groups.
Results: Participants in Group A who received prophylactic tranexamic acid were found to have less blood loss compared to the control population in Group B. The difference between the means was statistically significant.
Conclusions: We concluded that tranexamic acid should be considered as prophylactic treatment for hysterectomy to reduce the risk of substantial blood loss and the need for blood transfusion and early recovery.

Keywords: Tranexamic acid, Hysterectomy, Blood loss, Intraoperative

INTRODUCTION

Hysterectomy accounts for the second most commonly performed surgery in gynecology after caesarean section. Hemorrhage is the most frequently encountered complication during surgery requiring blood transfusion in 1-2% of total hysterectomies performed worldwide.[1] Blood products are scarce and blood transfusion has several rare but significant adverse effects. World Health Organization (WHO) recently placed tranexamic acid (TXA) on the WHO model list of essential medicines critical to health care. The clinical randomization of an antifibrinolytic in significant haemorrhage trial, known as CRASH-2 is based on the rationale that originated from tranexamic acid use in elective orthopaedic, liver transplants, and cardiac surgeries where its use has evidence of reduction of blood transfusion rates.[2] In this study, the efficacy of prophylactic use of tranexamic acid in the reduction of blood loss in patients undergoing hysterectomy for benign indications has been evaluated.

METHODS

This prospective randomised controlled trial was conducted in a tertiary care hospital, in Pondicherry, from January 2020 to July 2021, after obtaining institutional human ethics committee approval. Inclusion criteria were

women undergoing hysterectomy for benign indications like fibroid uterus, abnormal uterine bleeding (AUB), adenomyosis, pelvic organ prolapse, benign adnexal mass, chronic pelvic pain, endometrial hyperplasia and cervical dysplasia who had an uterine size in weeks equal to or less than 14 weeks. Patients with history of hypersensitivity to tranexamic acid, bleeding/clotting disorders, thromboembolism, cardiovascular diseases, present unstable angina, renal diseases, seizure disorders and treatment with anticoagulants were excluded. A total of 108 patients were included in the study who were randomised into 2 groups i.e., case (A) N=54 and control (B) N=54 which were further subdivided into abdominal hysterectomy (A1 and B1) and vaginal hysterectomy (A2 and B2) subgroups respectively, each subgroup comprising of 27 patients. Pre operative haemoglobin estimation was done on the day before surgery. 1 gram of tranexamic acid was added to 100 ml of 0.9% normal saline and given as an intravenous infusion during the operation in the case group. Intraoperative blood loss was estimated by gravimetric methods by pre weighed drapes, sponges and abdominal pads with 1 gm=1 ml of blood. Post-op blood loss was calculated based on the number of vaginal pads used on post-op day 0 (based on pictorial blood assessment chart). Postoperative haemoglobin was assessed 48 hours from the day of surgery and additional factors such as the need for blood transfusion in the intra operative period and the patient's general condition were also assessed. The data was entered into Microsoft Excel and statistical analysis was carried out in SPSS software version 17.0. Qualitative variables were presented as frequency and percentages. Quantitative variables were presented as mean (standard deviation) or median (range) depending upon the distribution of data. Independent T test was used to find out the difference in blood loss between the two study groups. Intra-operative and post-operative complications were represented as percentage or proportions and the same was compared between the study groups using chi squared test. A p value of less than 0.05 was considered as statistically significant.

RESULTS

Age, BMI and associated co morbidities were comparable between the case and the control groups (Table 1).

Table 1: BMI comparison across groups.

BMI	Control group		Study group	
	N	%	N	%
18.5-24.9	20	37.0	23	42.6
25.0-30.0	23	42.6	27	50.0
More than 30	11	20.4	4	7.4
Total	54	100	54	100.0

Chi square p value=0.15 (Not significant).

The mean intraoperative blood loss in the study group was 259 ml which was 185.6 ml lesser than the control group and this ranged from 141.8 ml to 229.5 ml when TXA was administered during hysterectomy with a statistically significant p value of less than 0.001 (Table 2).

Table 2: Comparison of intra operative blood loss across the groups.

Groups	N	Mean (ml)	SD	Difference (ml)	95% CI	P value
Study	54	444.6	135.4	185.6	141.8-229.5	<0.001
Control	54	259.0	89.6			

Table 3: Comparison of post operative blood loss across the groups.

Groups	N	Mean (ml)	SD	Difference (ml)	95% CI	P value
Study	54	37	17.7	7.0	0.8-13.1	0.03
Control	54	30	14.4			

Table 4: Comparison of total blood loss across the groups.

Groups	N	Mean (ml)	SD	Difference (ml)	95% CI	P value
Study	54	479.8	19.4	192	146.1-237.9	<0.001
Control	54	287.8	12.5			

Table 5: Comparison of time taken for surgery across the groups.

Groups	N	Mean (ml)	SD	Difference (ml)	95% CI	P value
Study	54	103.3	36.9	27.3	13.9-40.7	<0.001
Control	54	76.1	33.1			

The reduction of intra-operative blood loss was by 233.5 ml in the abdominal hysterectomy (A1) and 131 ml in the vaginal hysterectomy (B1) subgroups respectively. The mean postoperative blood loss in the study group was 30 ml and in control group was 37 ml which was statistically significant with a p value of 0.03 (Table 3). The mean total blood loss in the study group was 287.8 ml which was 192 ml lesser than the control group, this difference being statistically significant with a p value of

less than 0.001 (Table 4). The reduction of total blood loss in the study group was 129 ml and 248 ml in the subgroups A1 and B1 respectively. In the case group, the intraoperative time was 76 mins whereas in the control group it was 10 minutes with a difference of 27 minutes between the groups and this was significant statistically (p<0.001) (Table 5). The reduction of intra operative duration was by 29 and 22 minutes in the A1 and B1 subgroups respectively. In the study group, 74.1% did not need any blood transfusion whereas only 46% did not need it in the control group. Only 7.4% needed 2 transfusions in the study group but in the control group, it was almost two times higher (16.7%) which was found to be statistically significant with a p value of 0.01(Table 6).

Table 6: Intraoperative blood transfusion across the groups.

Intra- operative blood transfusion	Control group		Study group	
	N	%	N	%
Yes	24	44.4	9	16.7
No	30	55.6	45	83.3
Total	54	100	54	100

Chi square p value=0.003 (Significant).

Postoperative complications were found to be comparatively less in study group (11.1%) and it was three times higher in the control group (11 vs. 35%) and this was significant with a p value of 0.003. Hypotension, tachycardia, and bradycardia were the intra-op complications in both the groups, whereas shivering was noted in the control group alone. In the study group, headache and fever were the main complications. In the control group in addition to the above, the incidence of UTI and wound gape were also noted.

DISCUSSION

Shikha et al in a retrospective study found that the mean blood loss estimated in TXA group was 412.18±103.1 ml and 585.22±138.9 ml in the placebo group with a significant reduction of the mean blood loss in the case group.[3] A study conducted by Arthi et al in concluded that the estimated blood loss in the TXA and control groups were 360.16±107.1 ml and 540.22±121.9 ml respectively with a significant reduction in mean blood loss in the case group.[4] In another study conducted in Denmark, the primary outcome of intraoperative blood loss was reduced in the TXA group compared to the control group when estimated subjectively by the surgeons and objectively, by weight (98.4 ml versus 134.8 ml, with p value <0.006 and 100.0 ml versus 166.0 ml, with p value of less than 0.004). In their secondary outcome they stated that the total blood loss of more than 1000 ml was 2 (1.2%) in the TXA group and 4 (2.4%) in the placebo group with a p value of 0.685, a RR of 0.56, and a 95% CI of 0.10-2.97. Total blood loss (TBL) of more than 500 ml was 6 (3.6%) in the TXA group and 21 (12.6%) in the placebo group with p value of 0.003 and a RR of 0.29 with a 95% CI of 0.12-0.70. The incidence of blood loss of more than 500 ml was also significantly found to be reduced (6 versus 21, with p value less than 0.003).[5] These results were inconcordance with our present study. Regarding need for blood transfusion, a study by Shikha et al found that in the TXA group, 2% of patients required a single unit of packed red blood cell transfusion compared to 6% in the placebo group which was statistically significant.[3] A randomized double blinded placebo-controlled trial conducted at Denmark stated that the relative risk of having blood transfusions in the TXA group (2/164) when compared to the control group (7/167) was 0.29 (95% CI, 0.06-1.38) which was lower in the TXA group.[5] In their study, Arthi et al noted that 12% of participants required single unit of packed red blood cell transfusion in the case group compared to 42% of participants in the control group which was statistically significant.[4] In the present study, 74.1% of patients in the case group did not need any blood transfusion whereas only 46% did not need it in the control group which was significant statistically.

As for the intraoperative time, Shikha et al stated that the operating time was found to be significantly shorter in the tranexamic acid group in comparison to the placebo group (102.86 minutes versus 138.64 minutes).[3] Similarly, Arthi et al concluded that the group of patients operated after administration of tranexamic acid had a significant shorter time of surgery (127.86 minutes versus 148.64 minutes).[4] Likewise, Toposee et al in their study published in the year 2016 stated that the duration of surgery was 114±42.9 minutes in the TXA group and 118±50.2 minutes in the control group with p value of 0.38.[5] In the present study, the intraoperative time was 76 mins in the case group whereas in the control group it was 103.3 minutes with a difference of 27 minutes between the groups which was significant statistically (p<0.001). Arthi et al concluded that incidence of minor adverse effects like vomiting, nausea, and diarrhoea in both groups were comparable and no major adverse events were noted.[4] Shikha et al noted the incidence of minor side effects like nausea, vomiting, diarrhoea, headache and dyspepsia, in a few number of patients in the tranexamic acid group but there was no incidence of thromboembolic events in any of the patients in both groups.[3] Similar results were obtained by Topsoee et al and Shady et al in their studies.[5,6] Postoperative complications were found to be comparatively in the present study group (11.1%) and it was three times higher in the control group (11 vs. 35%) which was significant with a p value of 0.003.

Limitations

The limitations of our study are absence of blinding for the observer which could have been eliminated by using a placebo for the control group. The numbers of patients were also limited in the study and control groups as it was a time bound teaching institution-based study.

CONCLUSION

It was concluded from the present study that TXA should be considered as a prophylactic treatment before elective hysterectomy to reduce the risk of substantial blood loss and the need for blood transfusion. It is especially helpful in developing nations like India where there is a huge burden of anaemia and the availability of resources are limited.

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