Can Tranexamic Acid Control Bleeding during and After Total Thyroidectomy? A Randomized Double-blind Clinical Trial Study

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ABSTRACT

Introduction: Head and neck operations are among the thyroid surgeries which are occasionally accompanied by blood loss (BL) during operation, tainting the operating field, and increasing the probability of damage to adjacent structures. Several studies have hitherto been conducted toward decreasing the BL that occurs during and after the operation. This study has been designed and executed with the objective of determining and comparing the effectiveness of tranexamic acid (TA) medication on controlling BL during and after total thyroidectomy. Materials and Methods: This study was carried out as a double-blind clinical trial on 83 patients affected with benign and malignant pathologies which were candidates for total thyroidectomy surgical operation, referred to the surgery department of Shahid Rahnemoun Hospital in Yazd, Iran, during a 1-year period. Patients were randomly divided into two groups including TA recipients, for which 20 mg/kg of TA was diluted to 20 cc with normal saline before surgery, and the control group which did not receive TA. The amount of BL during surgery was measured based on the blood gas value at the time of operation and post-surgery BL was measured based on the amount of blood collected in the Hemovac drain. The patients’ hemoglobin was also measured and recorded before surgery and 24 h after surgery. Results: Among the 83 studied patients, 42 patients received TA, whereas the other 41 did not receive this medication. BL during surgery in the TA receiving group was significantly less than the control group (P = 0.016). Post-operation BL in the TA receiving group was also less than the control group, although the difference was not statistically significant (P = 0.5). Moreover, the decline of hemoglobin level 24 h after surgery was not significant in the TA receiving group and the control group. Conclusion: According to the results of the present study, TA significantly reduces the amount of BL during the surgical procedure of total thyroidectomy. TA also results in a non-significant reduction of post-operation BL, whereas the hemoglobin level is not affected by it.

Key words: Blood loss, Total thyroidectomy, Tranexamic acid

INTRODUCTION

Head and neck surgeries are occasionally accompanied by severe blood loss (BL) during the procedure, requiring an emergency blood transfusion. Numerous strategies have been suggested to reduce the need for blood transfusion, one of which is the utilization of tranexamic acid (TA).¹ TA is a synthetic derivative of the amino acid lysine and a strong antifibrinolytic drug² that is 7–10 times stronger than epsilonaminocaproic acid and has limited side-effects.³ This drug has hitherto received great attention due to its mechanism of action and is used to reduce BL in heart surgeries, liver transplantations, orthopedic
surgery, and in arthroplasty and knee replacement procedures and to reduce BL after prostatectomy or tooth extraction. This drug is also used for treating idiopathic menorrhagia.\textsuperscript{[3]} Considering the anatomic structure of the thyroid gland and its adjacency to the vital element in the neck region, BL during thyroid surgery limits the surgeon’s vision and increases the possibility of damage to these structures which significantly increase mortality and morbidity during and after surgery. BL during surgery also prolongs the surgical procedure. In addition to BL during surgery, post-surgery BL is also one of the major complications of thyroidectomy that leads to the patient not being discharged and prolongation of the hospitalization period, the respiratory tract being jeopardized, and even reoperation in some cases.\textsuperscript{[4,5]} Some studies have hitherto been conducted on TA effectiveness in head and neck surgeries, as well as elective and emergency operations.\textsuperscript{[6,7]} but studies dedicated to thyroid surgeries have been very limited. The present study aims to investigate the impact of TA in controlling BL during and after thyroid surgery in Shahid Rahnemoun Hospital in Yazd, Iran during 2018 and 2019.

**MATERIALS AND METHODS**

The present study is a randomized double-blind clinical trial, conducted on 83 patients afflicted with benign and malignant thyroid pathologies and candidates for total thyroidectomy, referred to the surgery department of Shahid Rahnemoun Hospital in Yazd during a 1-year period. Patients of over 18-year old with multinodular goiter (MNG) and papillary thyroid carcinoma (PTC) that was candidates for the total thyroidectomy were admitted to the study. Moreover, the patient dissent, impaired coagulation profile, liver and kidney failure, heart and lung disorders, pregnancy, and history of thromboembolic events such as deep vein thrombosis, pulmonary embolism, myocardial infarction, stroke, and transient ischemic attack and the utilization of hemostatic agents such as Surgicel, PerClot powder, and Gelfoam during the surgical operation were criteria for leaving the study. Patients were randomly divided into two groups of TA recipients (T group) and the control group (C group). Fifteen minutes before induction, TA was infused intravenously in 5 min by the anesthesiologist, while the surgical team was not aware as to whether or not the injection has been performed. A 20 mg/kg dose of TA, diluted to 20 cc with normal saline, was injected for the group T patients. After establishing complete hemodynamic monitoring, the patients were injected with 5 cc/kg of Ringer’s serum, followed by receiving 2 g/kg of Fentanyl and 0.03 mg/kg of Midazolam and, 3 min after the injection of narcotics, and receiving 100% oxygen, anesthesia induction was performed using 2 mg/kg of Propofol and 0.5 mg/kg of Atracurium. Three minutes after induction and Atracurium injection, patients were intubated with a 6.5 or 7.5 mm tracheal tube and, after achieving hemodynamic stability, received 5 mg of morphine. Anesthesia was maintained with 1% Isoflurane and a combination of oxygen and N\textsubscript{2}O. At the end of the surgery, a Hemovac drain 12 was installed at the place of operation for all patients. After completion of the surgery, patients were first transferred to recovery and then to the surgery department and all patients were discharged from the hospital the day after surgery.

The amount of BL during surgery was calculated by estimating the number of gauzes with the standard size of 10 cm × 10 cm that were completely soaked with blood during surgery. Each completely blood-soaked gauze holds 20 cc of blood, the amount of which was obtained by weighing a completely blood-soaked gauze and comparing it to the dry weight of the gauze. The amount of BL 24 h after surgery was calculated by measuring the amount of blood collected in the Hemovac drain, installed at the time of operation. Before surgery and 24 h after surgery, the amount of BL at the time of surgery and during the hospitalization period as well as the hemoglobin level was assessed in all patients and the results were statistically analyzed using SPSS software. $P < 0.05$ was determined as the level of significance.

**RESULTS**

In the present study, 83 patients were evaluated in two groups, 20 (24.1%) of which were male and 63 (75.9%) were female, and considering $P = 0.565$, there was no significant difference between the two evaluated groups. Regarding the average age of the patients, the control group had an average age of 47.85±14.1, while the average age of the experimental group was 46.16±11.3, and $P = 0.55$ shows no significant difference regarding the average age in the two evaluated groups. In terms of the amount of patients’ BL during surgery in the two evaluated groups, the experimental group (TA) with an average BL of 25.27±9.52 cc and the control group with an average BL of 34.58±14.06 cc was reported, which considering $P = 0.016$ obtained from the $t$-test, a statistically significant difference was observed between the two groups, indicating that the group treated with TA had lost significantly less blood during surgery in comparison to the control group. Regarding the amount of BL after surgery, the average BL based on the volume of blood collected in the Hemovac drain was 32.5±4.15 cc for the experimental group and 35.48±4.88 cc for the control group, which considering $P = 0.5$ obtained from the $t$-test, there was no significant difference between the two groups. According to the type of pathology [Table 1] in the two studied groups, BL during surgery was an average of 24.46±4.12 cc in the PTC group and 26.47±4.14 cc in the MNG group, which considering $P = 0.748$ obtained from the $t$-test, there was no significant difference between the two groups of patients – in terms
of pathology types in the group receiving TA – regarding BL during surgery. The amount of BL after surgery in the TA-receiving group was 35.4±5.68 cc in the patients with PTC pathology and 33.8±4.2 cc in the patients with MNG pathology, which considering \( P = 0.619 \) obtained from the \( t \)-test, no significant difference was observed between the two groups. As for the control group, BL during surgery was 34.16±3.49 cc in the PTC group and 35.01±4.95 cc in the MNG group and considering \( P = 0.845 \), there was no significant difference between the two evaluated groups. No significant difference was observed in terms of BL after surgery. The pre-surgery hemoglobin levels [Table 2] were 13.08±1.53 mg/dl in the TA-receiving group and 13.53±1.44 mg/dl in the control group and considering the obtained \( P = 0.156 \), there was no significant difference between the two groups. Furthermore, the post-surgery hemoglobin levels were 12.22±1.42 mg/dl in the TA-receiving group and 12.52±2.36 mg/dl in the control group which, considering the obtained \( P = 0.492 \), were not significantly different.

**DISCUSSION**

TA is an inexpensive and relatively safe antifibrinolytic drug that is used in various surgical operations to reduce BL during and after the procedure. This drug blocks the fibrinolysis process by inhibiting plasmin. TA is considered one of the safest drugs with minimal side-effects. Very rare cases of orthostatic hypotension and thromboembolism have been reported as a result of using this drug that have not yet been proven by any research studies.\[^9\] According to the results of the present study, the authors have discovered that TA drastically reduces BL during total thyroidectomy and this reduction is statistically significant. Even though TA slightly reduced BL during 24 h after total thyroidectomy, this reduction was not statistically significant. According to the conducted research, it is also obvious that prescribing TA before surgery does not have an observable effect on preventing hemoglobin declination after surgery. Research by Das *et al.* conducted as a double-blind case–control study on 80 patients undergoing head and neck cancer surgeries revealed a significant difference of the hemoglobin level before and after surgery in the two groups of TA-receiving and control, which is not consistent with the results of the present study. The amount of BL during and after surgery in the two groups studied by Das was also significantly different which is consistent with the present study regarding the case of BL during surgery. It is notable that Das’s study only admitted the patients affected with malignant pathologies and comprehensive neck dissections had been performed in the majority of operations.\[^9\] Conducting a systematic review in 2018, De Vasconcellos *et al.* investigated the effect of TA on the amount of BL during rhinoplasty surgery and according to the results of this study, BL during surgery in the TA-receiving group was significantly less than the control group, which is consistent with the results of the present study.\[^10\] In a study conducted by Kalkarni *et al.* in 2016 on 240 patients undergoing head and neck cancer surgeries, one group of patients was injected with 10 cc/kg of diluted TA before surgery and the other group was injected with the same amount of normal saline. According to the results, there was no significant difference between the two groups in terms of BL during surgery, but there was a significant difference between the TA-receiving group and the control group regarding the amount of BL over 24 h after surgery, both results inconsistent with the results of the present study.\[^11\]

Thakur *et al.* conducted a study in 2019 to investigate the effect of TA on the amount of BL during and after head and neck surgeries. Ninety-two patients were admitted to the study and divided into Group 1 and Group 2 based on the type of surgical procedure. Fifty patients that had undergone total thyroidectomy, total parotidectomy, and various neck dissections were placed in Group 1, and 42 patients that

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**Table 1:** Mean and standard deviation of post-surgery BL in the two evaluated groups based on pathology type

<table>
<thead>
<tr>
<th>Number</th>
<th>Studied groups</th>
<th>Variable</th>
<th>MNG</th>
<th>PTC</th>
<th>( P )-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>TXA receiving</td>
<td>BL after surgery</td>
<td>23.8±4.2</td>
<td>38.4±5.68</td>
<td>0.019</td>
</tr>
<tr>
<td></td>
<td></td>
<td>BL during surgery</td>
<td>26.47±4.14</td>
<td>24.46±4.12</td>
<td>0.748</td>
</tr>
<tr>
<td>2</td>
<td>Control</td>
<td>BL after surgery</td>
<td>36.02±4.03</td>
<td>35.04±7.95</td>
<td>0.088</td>
</tr>
<tr>
<td></td>
<td></td>
<td>BL during surgery</td>
<td>35.01±4.95</td>
<td>34.16±3.49</td>
<td>0.854</td>
</tr>
</tbody>
</table>

*Independent Sample \( t \)-test, BL: Blood loss, TXA: Tranexamic acid, MNG: Multinodular goiter, PTC: Papillary thyroid carcinoma

**Table 2:** Mean and standard deviation of pre- and post-surgery hemoglobin levels in the two evaluated groups

<table>
<thead>
<tr>
<th>Number</th>
<th>Variable</th>
<th>TXA receiving</th>
<th>Control</th>
<th>( P )-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Pre-surgery hemoglobin level</td>
<td>13.08±1.53</td>
<td>13.53±1.44</td>
<td>0.156</td>
</tr>
<tr>
<td>2</td>
<td>Post-surgery hemoglobin level</td>
<td>12.22±1.42</td>
<td>12.52±2/36</td>
<td>0.492</td>
</tr>
</tbody>
</table>

TXA: Tranexamic acid, *Independent sample \( t \)-test
had undergone subtotal thyroidectomy, lobectomy, and superficial parotidectomy were placed in Group 2. In each group, patients were divided into two groups of TA-receiving and control. According to the results, there was no statistically significant relationship between the control and experimental groups of Group 1 and Group 2 regarding BL during and after surgery, which was consistent with the results of the present study in terms of BL after surgery but inconsistent with the present results in terms of BL during surgery.\(^{[12]}\)

**CONCLUSION**

According to the results of the present study, the amount of BL during surgery significantly reduced in the group that received 20 mg/kg of TA before surgery, compared to the control group, and although post-surgery BL in the TA-receiving group also decreased in comparison to the control group, the difference was not statistically significant. Moreover, based on the results of the present study, injecting this amount of TA had no significant effect on post-surgery hemoglobin levels. In the TA-receiving group, post-surgery BL of MNG was significantly lower than PTC, whereas this difference was not significant in the control group. Furthermore, BL during surgery in the TA-receiving group was not significant for the two evaluated pathologies, which was also true for the control group. Considering the insufficient studies regarding TA effectiveness on controlling BL during and after thyroid surgeries based on the pathology type and with reference to the results of the present study, it appears that TA results in a higher reduction of post-surgery BL in benign diseases of the thyroid than in the malignant kinds, which requires further research. According to the results of the present study, prescribing TA before thyroid surgeries with the dose applied in the present study is recommended to reduce BL during surgery and thus provide a cleaner operating field to reduce the complications of surgical procedures.

**REFERENCES**


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