Abstract

Recurrent tonsillitis is one of the most common ORL diseases. Tonsillectomy, as a method of surgical treatment associated with blood loss, is accompanied by frequent perioperative bleeding. For the control of bleeding, it is advisable to use fibrinolysis inhibitors, one of which is tranexamic acid (TA). The study aimed to optimize the approach to performing tonsillectomy by preoperative application of a TA solution to reduce the volume of perioperative blood loss. Clinical studies were performed in 107 patients with recurrent tonsillitis who underwent bilateral tonsillectomy. The patients were divided into two groups. In the 1st (main) group of 54 patients in the preoperative period was administered a 10% solution of TA at the rate of 10 mg/kg body weight. The 2nd (control) group consisted of 53 patients without the use of TA. The efficacy of using tranexamic acid was evaluated by clinical (surgery time, the volume of blood loss intraoperatively, accounting for postoperative events, evaluation of the incidence of postoperative bleeding), and laboratory data (baseline and postoperative levels of D-dimer, level of soluble fibrin complexes. In group 1, a statistically significant decrease in the volume of blood loss, a decrease in the frequency of occurrence of intraoperative complications, postoperative bleeding, and a reduction in the triviality of the operation were determined. According to laboratory data, in patients of this group, the increase in the content of fibrin lysis products, the extension of thrombin time was significantly less pronounced than in the 2nd comparison group. The use of 10% TA solution before performing bilateral tonsillectomy leads to a decrease in blood loss, frequency, and the degree of occurrence of perioperative complications. Due to this, the duration of the operation of bilateral tonsillectomy is reduced.

Key words: recurrent tonsillitis, tonsillectomy, bleeding, tranexamic acid, D-dimer,

Introduction

The problem of recurrent tonsillitis (RT) remains relevant today, due to the frequency of pathology and its relationship with diseases of other organs and body systems (1). RT occupies a central place among diseases of the pharynx, being the most common pathology in the practice of an otorhinolaryngologist. The frequency of this disease is continuously growing and does not tend to decrease (2). According to recent studies, RT affects 15 - 20% of the adult population (3, 4). One of the treatment methods for RT is a tonsillectomy, one of the most common operations in otorhinolaryngology. In specialized departments of hospitals, the proportion of tonsillectomy reaches 20% of all surgical interventions (4). The main criteria for the safety of tonsillectomy are the frequency of intraoperative, early and late postoperative complications, long-term results of treatment. Among all perioperative complications, tonsillectomy is most often accompanied by postoperative primary and secondary bleeding; their frequency varies from 0.1 to 8-10% (5). The best preventive measure to prevent postoperative bleeding is a reliable primary surgical hemostasis. However, especially in the event of secondary bleeding, it is advisable to use drug hemostatic therapy, which is an inhibitor of fibrinolysis, which includes tranexamic acid (6, 7, 8). TA is a synthetic derivative of the amino acid lysine, belongs to the group of antifibrinolytics, and is used as a hemostatic drug. The antifibrinolytic effect of tranexamic acid is to block the lysine binding sites in the plasminogen molecule.
This block, in turn, prevents the conversion of plasminogen to plasmin and prevents the connection of plasmin and tissue plasminogen activator with fibrin. As a result, fibrin degradation is suppressed. TA has a local and systemic hemostatic effect in bleeding associated with increased fibrinolysis activity. In addition to antifibrinolytic action, TA normalizes platelet function and capillary permeability.

TA is widely used to reduce blood loss during operations in cardiac surgery, orthopedics and traumatology, urological operations, and during cesarean section (9, 10, 11, 12, 13). The authors present clinical data that indicate a decrease in the volume of blood loss and the frequency of blood transfusion during surgical intervention with the use of a TA solution (14). At the same time, in some of the studies, there was no significant efficacy of using a solution of TA in tonsillectomy (15). In contrast, others confirmed a significant decrease in blood loss (16, 17). A systematic review and meta-analysis of the use of TA in tonsillectomy showed that most studies were conducted before 1980. Therefore, to study the risks and benefits of using a TA solution, it is necessary to perform a new, extensive, and well-planned randomized controlled trial (18).

The study aimed to optimize tonsillectomy surgery to reduce the volume of intraoperative blood loss, the frequency of intraoperative and postoperative complications, and to improve the course of the postoperative period in patients by preoperative use of a tranexamic acid solution.

Material and methods.

A comparative study was conducted at the Department of Otorhinolaryngology of Odessa National Medical University in Odessa City Clinical Hospital No. 11. Under the supervision were 107 patients with recurrent tonsillitis. Among the patients were men - 51 (48%) and women - 56 (52%). The average age of patients was 24.6 years. All patients underwent surgical treatment in the volume of bilateral tonsillectomy.

The conditions for inclusion in the study were: voluntary consent to participate in the study, the presence of recurrent tonsillitis, confirmed by the history and objective examination, the presence of indications for surgical intervention. The exclusion criteria were: age up to 18 years, pregnancy and lactation, acute infectious diseases, chronic concomitant diseases in the stage of exacerbation or decompensation.

All patients were divided into two groups. The first group consisted of 54 patients operated on in the volume of bilateral tonsillectomy using endotracheal anesthesia. In the preoperative period, 30 minutes before the start of surgery, the patients were injected with 10% TA solution at a rate of 10 mg/kg body weight. The second control group consisted of 53 patients operated on with the use of endotracheal anesthesia, who were not given TA in the preoperative period. The groups were homogeneous by age, gender, and clinical course of the disease ($P > 0.05$). In the first group, there were 31 men (57%) and 23 women (43%), the median age was 24.5 years. In the second group, there were 28 men (53%) and 25 women (47%), the median age was 24.7 years.

The disease in most patients has been observed for more than five years: 39 (72%) in the first group and 41 (77%) in the second. According to the doctor's appointment, 30% and 36% of patients in groups 1st and 2nd were treated, respectively. 39% and 26% of patients preferred self-medication, respectively. The groups also did not differ significantly in the average number of exacerbations of recurrent tonsillitis in the anamnesis (Table 1). All patients underwent a comprehensive general clinical examination: a collection of complaints, and clarification of the medical history, standard examination of ORL organs. Laboratory and instrumental studies included a general analysis of blood and urine, a coagulogram, a blood test for sugar, a biochemical blood test, a blood group, a Rh-factor, a blood coagulation time, a D-dimer, a soluble fibrin-monomer complex (SFMC), and thrombin time. Additionally, an ECG, chest x-ray, and a blood test for syphilis were performed.

In the postoperative period, a daily medical examination of patients was performed. We took into account the presence of reactive phenomena in the oropharynx, such as edema, hyperemia, fibrinous deposits, the reaction of regional lymph nodes, and signs of ongoing bleeding. When evaluating the performed surgical intervention, the following indicators were taken into account: the volume of blood loss during the operation, the presence of episodes of bleeding during the operation that required coagulation or ligation of the vessels, flashing with a tampon, the presence of primary and secondary bleeding in the postoperative period, and the duration of the operation.
The effectiveness of TA use was evaluated according to clinical data (time of surgical intervention, intraoperative blood loss, assessment of the incidence of postoperative bleeding), and laboratory parameters (initial and postoperative level of D-dimer, SFMC level, thrombin time). The activation of fibrinolysis is accompanied by the cleavage of fibrin under the influence of the proteolytic action of plasmin, and the formation of degradation products of fibrin and fibrinogen, which interact with fibrin monomers, increasing the amount of SFMC. The specific product of the degradation of fibrin under the action of plasmin and other fibrinolytic is the D-dimer. Its concentration in the blood is proportional to the activity of fibrinolysis and the amount of fibrin subjected to lysis. The degradation products of fibrin and fibrinogen compete with thrombin and, thus, slow down the formation of clots, preventing the conversion of fibrinogen to fibrin. This process contributes to the extension of thrombin time, an indicator that marks the interval necessary for the conversion of fibrinogen to fibrin. We determined the level of D-dimer, the amount of SFMC, and the thrombin time in patients immediately before surgery and in the postoperative period.

Statistical data processing was performed using the programs for biomedical research, Microsoft Excel 2010, and Statistica 6.0 (StatSoft, 2006). The average values are given in the form (M ± m), where M is the average value of the indicator, m is the standard error of the mean. The reliability of the differences was evaluated using Student's t-test. Statistical processing of data that did not correspond to the normal distribution was performed using non-parametric methods of statistical analysis according to the Mann-Whitney U test.

**Results.**

To assess the surgical intervention and the effectiveness of the use of TA, we conducted a comparative analysis of the duration of the operation in different groups of patients. The average time of tonsillectomy in patients of group 2 was 43 min (from 32 to 50 min), and in group 1 - 37 min (from 30 to 48 min). The intergroup difference is statistically significant (p <0.01), which confirms the shorter duration of the operation using a 10% solution of TA. The average volume of blood loss during tonsillectomy in group 1 was 82 ml (from 45 to 112 ml), and in group 2 it was 101 ml (from 53 to 147 ml). Thus, the volume of blood loss in 1st group of patients was significantly lower (p <0.01) compared with 2nd group.

Intraoperative events were distributed as follows (Table 2). The need for vascular stitching arose in 13 patients: in 5 patients from the main group and in 8 patients from the control group. The need for stitching brackets with a cotton-gauze ball arose in 8 patients, three patients of the main group, and five patients from the control group. The need for additional administration of procoagulants was in 16 patients, among them six patients from the main group and ten patients from the control group. Primary bleeding was recorded in five patients of the 1st group and eight patients of the 2nd group. Secondary bleeding was observed in four patients, three patients from the control group, and one of the main.

Eleven hemorrhages of degree A1-A2 were recorded. In this case, there are no signs of ongoing bleeding, normal laboratory parameters are noted, and bloody saliva is anamnestically noted. During the examination, a fibrin film or a blood clot is observed after the removal of which there is no bleeding. Such bleeding occurred in 4 patients from group 1 and in 7 patients from group 2. Four episodes of bleeding related to type B1, in which minimal bleeding is visualized, which stops after the use of an adrenaline-treated swab. Of these, there were two patients from group 1 and two patients from group 2. Two cases of grade B2 bleeding were also noted when hemostasis using local anesthesia was necessary. Both of these cases occurred in patients from group 2. Bleeding related to class C and D was not recorded.

In the postoperative period, a statistically significant increase in the parameters of SFMC, D-dimer, and thrombin time occurred in patients of both groups. However, in group 1, the increase in the content of fibrin lysis products and lengthening of thrombin time was significantly less pronounced than in group 2 (Table 3).

Based on the results obtained, it was found that the proposed method with the introduction of a 10% tranexamic acid solution in the preoperative period allows optimizing the operation of bilateral tonsillectomy.
Conclusions
1. The use of TA significantly reduces the duration of surgery for bilateral tonsillectomy. The average time to perform surgery in group 1 is 37 min versus 43 min in the control group, which is 6 min.
2. The use of TA significantly reduces the amount of blood loss during surgery. The average volume of blood loss in group 1 is 82 ml versus 101 ml in the control.
3. The use of TA helps to reduce the incidence of intraoperative complications.
4. The use of TA minimizes the incidence and degree of postoperative bleeding.

The authors declare no conflict of interest.

Informed consent was obtained from all patients included in this study.

Table 1 - The frequency of exacerbations of recurrent tonsillitis

<table>
<thead>
<tr>
<th>Frequency of exacerbations</th>
<th>1st group</th>
<th>2nd group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than once a year</td>
<td>6 (11%)</td>
<td>7 (13%)</td>
</tr>
<tr>
<td>1-2 times a year</td>
<td>8 (15%)</td>
<td>6 (11%)</td>
</tr>
<tr>
<td>3-4 times a year</td>
<td>28 (52%)</td>
<td>31 (59%)</td>
</tr>
<tr>
<td>More than 4 times a year</td>
<td>12 (22%)</td>
<td>9 (17%)</td>
</tr>
</tbody>
</table>

Table 2 - Recording perioperative events

<table>
<thead>
<tr>
<th>Indicators</th>
<th>1st group</th>
<th>2nd group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Need for flashing vessels</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td>Need for firmware brackets with a cotton-gauze ball</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>The need for additional administration of procoagulants</td>
<td>6</td>
<td>10</td>
</tr>
<tr>
<td>Episodes of primary bleeding</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td>Episodes of secondary bleeding</td>
<td>1</td>
<td>3</td>
</tr>
</tbody>
</table>

Table 3 - Laboratory parameters in groups of patients undergoing tonsillectomy surgery with and without the use of preoperative administration of 10% TA solution

<table>
<thead>
<tr>
<th>Indicators</th>
<th>1st group</th>
<th>2nd group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before surgery</td>
<td>After surgery</td>
</tr>
<tr>
<td>D-dimer, mkg/ml</td>
<td>0.35± 0,13</td>
<td>0.70± 0,09</td>
</tr>
<tr>
<td>SFMC, mg/100 ml</td>
<td>4.2± 0,35</td>
<td>5.5± 0,27</td>
</tr>
<tr>
<td>Thrombin time, s</td>
<td>11,1± 0,27</td>
<td>12,1± 0,18</td>
</tr>
</tbody>
</table>
References


