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Original research article

"Comparative outcome in Tonsillectomy by using Hydrogen Peroxide and Adrenaline as haemostatic agent: A Randomized Controlled Study"

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Abstract: This study aimed to further evaluate the benefit of topical hemostasis agents in tonsillectomy. We compared the clinical effects of topical application between hydrogen peroxide and adrenaline in tonsillectomy. Overall, 120 patients (240 tonsils) were prospectively enrolled for tonsillectomy between September 2019 and Septemberr 2022. The patients were randomly assigned to either the hydrogen peroxide or adrenaline group. Then, tonsillectomy was performed using hydrogen peroxide as a hemostatic agent on the assigned side, while adrenaline was applied to the other side. All procedures were performed by a surgeon who was blinded to the randomization. The outcome measurements of operation time, intraoperative blood loss, postoperative pain, and hemorrhage events were analyzed. The intraoperative blood loss was significantly lower in the hydrogen peroxide group than in the adrenaline group (9.99 ± 4.51 mL

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vs. 13.87 ± 6.32 mL; p = 0.0). The median operation time was also significantly lower in the hydrogen peroxide group (8.02 ± 3.59 min vs. 9.22 ± 3.88 min; p = 0.019). Meanwhile, the visual analogue scale (VAS) scores were significantly higher in the hydrogen peroxide group (4.98 ± 1.94 vs. 4.27 ± 1.97; p = 0.001). **Conclusion-** The topical application of hydrogen peroxide as a hemostatic agent effectively decreases the operation time and intraoperative blood loss. Thus, hydrogen peroxide can be used as a routine hemostatic agent for bleeding control in tonsillectomy.

Keywords: hydrogen peroxide; adrenaline; blood loss; tonsillectomy

Introduction

Tonsillectomy is one of the most common surgical procedures in otolaryngology. Despite improvements in anesthesia and surgical techniques, intraoperative and postoperative hemorrhage remains major concerns in tonsillectomy [1], with primary (<24 hr) postoperative bleeding occurring in 0.3-5.4 % of patients. [2, 3]

Tonsillectomy is still the treatment of choice in the management of Recurrent and Chronic Tonsillitis. [4] Despite being the commonest and simplest. Surgery the surgeon is always keen about the high risk of complications in Tonsillectomy i.e. intra and post-operative hemorrhage which may even lead to shock and death [5].

Traditional electrocauterization for hemostasis may create thermal injury and result in explosive vaporization, which would lead to severe damage to the surrounding tissue. Topical hemostatic agents help the surgeon to target bleeding sources and reduce tissue damage in non-bleeding regions. In this regard, several topical agents, such as hydrogen peroxide, adrenaline, saline solution, and lidocaine [5–7], have been introduced to minimize blood loss. However, there is still no gold standard for topical hemostasis in tonsillectomy.

Post-tonsillectomy pain is another major problem, as it might lead to poor oral intake, dehydration, sleep disturbance, and prolonged hospitalization. Thus, the effect of pain control should be considered when a hemostasis agent is applied. Many local applications, such as bismuth sulfate, oral rinse, lidocaine spray, fibrin glue, and betadine silver nitrate, have been investigated to control postoperative pain [8].

Hydrogen peroxide is an oxidizing agent that is easily degraded by tissue catalase to form oxygen and water. It is a widely available topical antiseptic and nontoxic hemostasis agent that produces oxidative burst and local oxygen production [9]. In the early stages, the “bubble effect” may provide some chemical burn and mechanical debridement in areas of the wound that are not easily accessible to the surgeon. In addition, the bubble effect caused by erythrocyte catalase degradation of hydrogen peroxide can help the surgeon to localize areas that require cauterization and rapidly reduce hemorrhage [10]. In the late stages, delivering hydrogen peroxide into wounds can kill fibroblasts and promote re-epithelialization [11]. A previous report showed that the topical application of hydrogen peroxide could control hemostasis and greatly reduce operation time in tonsillectomy [6]. Adrenaline has also been demonstrated to be a reasonable hemostatic agent because of its low cost, low risk, powerful vasoconstrictor, and

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platelet aggregation. Topical use of adrenaline is an effective and reasonable hemostatic agent in tonsillectomy [12].

Side effects to high doses of adrenaline such as sinus tachycardia have been reported but its use in diluted concentrations such as 1:200,000 is quite beneficial as a hemostatic agent during tonsillectomy. [13, 14]

The advantages of both hydrogen peroxide and adrenaline include rapid onset, acceptable duration, easy accessibility, and cost effectiveness. However, to date, there has been no direct, comparative, randomized controlled trial to achieve consensus on the optimal topical hemostasis agent in tonsillectomy.

Therefore, this study aimed to compare the clinical effects on operating time, blood loss, no of ties use and postoperative pain on topical application of hydrogen peroxide, adrenaline and saline solution in tonsillectomy.

Method and material-

A total of 120 patients (240 tonsils) aged 6–60 years were enrolled for tonsillectomy in the Otorhinolaryngology department, Bundelkhand Medical College Sagar (M.P) September 2019 between September 2022.

Pre-operative Assessment all the 120 patients (240 tonsil) underwent detailed evaluation and history taking with examination of Ear, Nose, Throat, Head and Neck. If the patient was found to have Chronic Tonsillitis, he/she was asked for consent to be part of study and General Anaesthesia. All patients with consent were then included in the study.

Preoperatively, patients had routine blood investigations which include Full Blood Count (FBC), Prothrombin/Partial Thromboplastin Time (PT/PTT).

Inclusion Criteria-

- Age between 6 and 30 years.
- Haemoglobin of more than 10 gm%.
- Clinically diagnosed Chronic Tonsillitis by the Paradise Criteria [12].
- Chronic or recurrent tonsillitis, recurrent tonsil hemorrhage, peritonsillar abscess, or tonsillar hypertrophy with obstructive symptoms.

Exclusion Criteria

- Bleeding and clotting disorders.
- Enlarged tonsils which is not Chronic Tonsillitis e.g. Neoplasm, Abscess.
- Pregnancy and lactation.
- Chronic systemic illnesses.
- Unilateral tonsillar growth.

All the patients underwent Tonsillectomy under General Anaesthesia. To avoid surgeon bias, all the surgeries were performed by the same surgeon with the same set of instruments.

Patients were randomized into two groups, each of group consisting of 60 patients (120 tonsils). All patients had cold dissection tonsillectomy. The first group A had 3% hydrogen peroxide soaked gauze, second group B had adrenaline (1:200,000 dilutions) soaked gauze to compress the tonsils fossa. Patients were monitored intraoperatively for the side effects of adrenaline use.

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Bipolar electrocauterization was used for hemostasis if persistent active bleeding was not controlled.

The intraoperative blood loss on each side was measured by weighing the cotton balls and suction bottle before and after the operation. The operation time was calculated as the period between the first incision and the time all bleeding or oozing was secured entirely on the single side, encompassing the time of dissection and hemostasis.

The cotton ball was left for 30 s after which it was removed and fossa was inspected for any bleed. On the confirmation of a clear field by the Surgeon and the Assistant Surgeon, the timer was stopped. A microscope was used to look into the fossa for any bleed, venous or mucosal. Care was taken not to use more than 10 ml of solution in both groups. Count of the number of cotton balls were also kept at par for each side.

The second parameter was the amount of blood loss on each side. The operative blood loss was calculated by weighing the blood impregnated gauze packs against an equal number of unused packs as well by measuring the volume of blood for each side separately. The volume of NS/H2O2 was subtracted. The volume of blood in the packs was calculated by dividing the weight of blood on the pack by the specific gravity of blood, i.e. 1.055 [15].

Postoperative pain in the first 24 h and 48 h after tonsillectomy was recorded. Postoperative pain was assessed by determining the more painful side during follow-up. Pain intensity was evaluated by a blinded physician using a visual analogue scale, with a score of 0 indicating no pain and 10 indicating maximum pain. All patients were blinded to which technique was applied. Postoperative data about pain score, fever, time to oral intake, and bleeding events were collected. All patients received the same dose of acetaminophen four times daily. In general, the patients were discharged 2 days postoperatively after examination of the uneventful surgical wound without oozing.

Data on operation time, intraoperative blood loss, postoperative pain, and hemorrhage events were collected and analyzed. Descriptive statistics were presented as the means and standard deviations, and categorical variables were presented as counts and percentages. The 95% confidence intervals (CIs) were determined for the strength of association and intergroup correlation. For the main analysis, the differences in operation time, blood loss and postoperative pain between groups are expressed as means (95% CI). The paired t test was used to analyze postoperative pain score, intraoperative blood loss, and operation time. All statistical analyses were performed using SPSS 20.0 statistical software. $p < 0.05$ was considered statistically significant.

Results

In total, 120 subjects were enrolled. None of the patients had any hypersensitivity response to the ingredients of the locally applied hydrogen peroxide and adrenaline. No complications or postoperative secondary bleeding were noted after tonsillectomy. The operation time, hemostasis time and intraoperative blood loss for each side are shown in Table 1. The postoperative pain scores in the first 24 h and 48 h after tonsillectomy are shown in Table 2. A comparison of the operation time, hemostasis time and blood loss on each side is shown in Table 3

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Table-1 Between-group comparison of operation time, hemostasis time and blood loss.

Variables	Hydrogen Peroxide Group (n = 120)	Adrenaline Group (n = 120)	Median Difference Mean (95% CI)	p-Value *
Operation time (min)	8.02 ± 3.59	9.22 ± 3.88	−71.62 (−127.70,−15.53)	0.019
Hemostasis time (min)	3.43 ± 2.75	4.49 ± 3.35	−63.83 (−110.91,−16.76)	0.007
Blood loss (mL)	9.99 ± 4.51	13.87 ± 6.32	−3.88 (−5.76, −2.00)	0

Data are presented as the median values and 95% confidence intervals. The paired t test is used for continuous variables. * $p < 0.05$

Table-2 Between-group comparison of postoperative pain score.

Variables	Hydrogen Peroxide (n = 120)	Adrenaline (n = 120)	Median Difference Mean (95% CI)	p-Value *
VAS, 24 hr	4.98 ± 1.94	4.27 ± 1.97	0.72 (0.32, 1.12)	0.001
VAS, 48 hr	3.47 ± 1.58	3.23 ± 1.52	0.23 (−0.83, 0.55)	0.147

Data are presented as the median values and 95% confidence intervals. The paired t test is used for continuous variables. * $p < 0.05$.

Table-3 Comparison of operation time, hemostasis time and blood loss by side of application.

Variables p	Left (n = 60) Value *	Right (n = 60)	P Value *
Operation time (min)	8.85 ± 4.04	8.39 ± 3.49	0.458
Hemostasis time (min)	4.04 ± 3.23	3.88 ± 2.99	0.504
Blood loss (mL)	12.55 ± 6.28	11.30 ± 5.26	0.239

The paired t test is used for continuous variables. * $p < 0.05$

Outcomes

1. Intraoperative Blood Loss- The average intraoperative blood loss was significantly lower in the hydrogen peroxide group than in the adrenaline group (9.99 ± 4.51 mL vs. 13.87 ± 6.32 mL, p = 0; Table 1). The ratio of patients with <10cc blood loss was also significantly higher in hydrogren peroxide group. (61.6% vs 36.6%)
2. Operation Time- The median operation time was 8.02 ± 3.59 min in the hydrogen peroxide group and 9.22 ± 3.88 min in the adrenaline group (Table 1). Apparently, surgery was significantly faster in the hydrogen peroxide group than in the adrenaline

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group ($p = 0.019$; Table 1). The hemostasis time was also significantly shorter in the hydrogen peroxide group (3.43 ± 2.75 min vs. 4.49 ± 3.35 min, $p = 0.07$; Table 1).

3. Postoperative Pain- The mean 24 h postoperative VAS score was significantly higher in the hydrogen peroxide group than in the adrenaline group (4.98 ± 1.94 vs. 4.27 ± 1.97, $p = 0.001$; Table 2). However, there was no significant difference in the mean 48 h postoperative VAS score between the two groups (3.47 ± 1.58 vs. 3.23 ± 1.52, $p = 0.147$; Table 2).
4. Left versus Right Side Outcomes- The median operation time was 8.85 ± 4.04 min in the left group and 8.39 ± 3.49 min in the right group, with no significant difference ($p = 0.458$; Table 3). The median hemostasis time was 4.04 ± 3.23 min in the left group and 3.88 ± 2.99 min in the right group. The intraoperative blood loss in the left and right groups were 12.55 ± 6.28 and 11.30 ± 5.26, respectively, with no significant difference ($p = 0.239$).

Discussion

Post-tonsillectomy hemorrhage and pain are the major complications of tonsillectomy; the optimal modality for achieving hemostasis remains unclear. According to our results, both hydrogen peroxide and adrenaline can help to reduce intraoperative blood loss; moreover, the intraoperative blood loss and the median operation time were significantly lower in the hydrogen peroxide group than in the adrenaline group. To the best of our knowledge, this is the first study to compare hydrogen peroxide and adrenaline as hemostatic agents for tonsillectomy.

Previous studies showed that the general operation time by blunt dissection in tonsillectomy was 24.6–29.1 min [16, 17].

Adopting the above-mentioned strategies, including preoperative local anesthetic injection and postoperative topical application of hemostatic agents, reduced the mean operation time to 9.99–13.87 min in our study.

In our study, the intraoperative blood loss was small (median volume < 15 mL) in both the hydrogen peroxide and adrenaline groups. Topical hemostatic agents that have the benefit of rapid onset, easy accessibility, cost effectiveness and analgesic effect are highly beneficial. We performed blunt dissection and applied topical hemostatic agents. Topical application of a hemostatic agent can treat all potential bleeding sites, not only focusing on an active bleeding area, but also on hard-to-access bleeding areas, such as the low pole of the tonsil. Thus, a topical hemostatic agent may be a feasible method to control hemorrhage. Hemostasis with the compression of a cotton ball may also cause lower postoperative pain than bipolar cauterization and ligation [18]. Topical hemostatic agents can also prevent sloughing of the eschar and help control mucosal bleeding across surface areas. No secondary bleeding after tonsillectomy occurred in the present study.

Hydrogen peroxide is widely used for wound irrigation, owing to its hemostatic and antimicrobial effects. Chang et al. and Al-Abbasi et al. reported that the use of hydrogen peroxide significantly reduced the operation time in tonsillectomy by 35% and 31%, respectively [6,19]. In our study, hydrogen peroxide better reduced the operation time by 14.9% and achieved

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a better hemostatic effect than adrenaline. The decreased operation time in the hydrogen peroxide group could be due to the relatively short hemostasis time, in line with previous findings [6, 19].

For intraoperative blood loss, the median volume was significantly lower in the hydrogen peroxide group than in the adrenaline group. We found that both hydrogen peroxide and adrenaline could decrease intraoperative hemorrhage. However, although the effect size of 3.88 mL of intraoperative blood loss may be significantly different, this little change may not have clinical significance. In addition, we also found that the mucosa and soft tissue turned white after hydrogen peroxide was pressed tightly. The chemical burns and bitter taste of hydrogen peroxide might explain the higher 24 h postoperative pain score in the hydrogen peroxide group (4.98 ± 1.94) than in the adrenaline group (4.27 ± 1.97).

There are numerous theories regarding the hemostatic effects of hydrogen peroxide, including thermal injury of the vascular ends, oxygen embolization of vessels, and reactive vascular spasms [21]. More recently, it has been suggested that thrombolytic hyperactivity and thrombus formation can trigger hemostatic effects [21]. In addition, when catalase in red blood cells reacts with hydrogen peroxide, the chemical reaction induces the release of oxygen and heat, helping the surgeon to localize the bleeding site. Currently, hydrogen peroxide is used clinically not only as a hemostatic and antiseptic agent, but also as a wound-healing agent [20]. Hydrogen peroxide may help to clear pathogen debris and promote cytokine secretion, helping tissue regeneration [22].

In our study, 3% hydrogen peroxide appeared to have no negative effect on wound healing. It should be noted that highly concentrated hydrogen peroxide (30%) carries a risk of cardiac arrest and stroke, due to oxygen embolism formation [23]. However, the use of a low concentration of hydrogen peroxide (3%) does not induce serious systemic side effects [10, 21, and 24]. The application time should be limited to prevent tissue damage and limit pain. Collectively, these findings support the fact that 3% hydrogen peroxide is a safe and effective agent for intraoperative hemostasis and wound cleaning.

Hatton et al. reported that topical adrenaline is an effective hemostatic agent in tonsillectomy [12]. The application of bismuth subgallate and adrenaline paste to the tonsillar fossae reduced the operating time by 23% and blood loss by 21% [25]. Epinephrine, a platelet-stimulating agent, can cause aggregation of human platelets through alphaadrenergic mechanisms [26]. In this study, we found that the topical use of adrenaline is mildly inferior to hydrogen peroxide, with respect to hemostatic function. The vasoconstriction effect of adrenaline on arterioles, capillaries and venules helps to delay intraoperative bleeding initially. However, post-tonsillectomy bleeding may result from a blood vessel that initially spasms and later resumes bleeding if hemostasis is not complete. Importantly, adrenaline takes longer to work in these cases. In the current study, the operation time and intraoperative blood loss were lower, at 14.9% and 38.8% (3.88 cc), respectively, in the hydrogen peroxide group than in the adrenaline group. However, in comparison with hydrogen peroxide, adrenaline was more effective in controlling postoperative pain in the first 24 h, but the pain scores were similar at 48 h postoperatively.

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Conclusion

3% Hydrogen Peroxide is a potent agent for antimicrobial activity and haemostasis when placed in the tonsillar fossa post tonsillectomy. The topical application of 3% hydrogen peroxide is beneficial for reducing the operation time and intraoperative blood loss, with minor complications, in tonsillectomy. Thus, hydrogen peroxide can be used as a routine topical hemostatic agent in tonsillectomy. Meanwhile, the topical application of adrenaline provides significant pain relief on the first day compared to hydrogen peroxide.

Conflict of interest- Nil

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