



A comparative study between haemocoagulase and adrenaline in type 1 tympanoplasty

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ABSTRACT

Introduction: Haemostasis is a critical component of ear surgeries, which can be achieved by topical methods including simple manual pressure with gauze or cotton balls soaked with adrenaline, administration of haemostatic agents or vasoconstrictive materials.

Objective: To compare efficacy of haemocoagulase and adrenaline in attaining middle ear haemostasis in type - 1 tympanoplasty with or without cortical mastoidectomy. To study the effect of haemocoagulase in middle ear.

Materials and method: This is a prospective comparative study conducted in a tertiary care hospital from January 2013 to June 2014. Patients undergoing type 1 tympanoplasty with or without cortical mastoidectomy were divided into two groups. In group A (50 cases), cotton balls soaked in 2 ml Haemocoagulase was used and in group B (50 cases) cotton balls soaked in 2 ml Adrenaline (1:1000 dilution) was used for middle ear haemostasis. The efficacy of haemocoagulase and adrenaline was compared.

Results: The mean number of cotton balls used in haemocoagulase group in cases with congested middle ear mucosa was more than those used in the adrenaline group. Duration of surgery was more in haemocoagulase group (65 min) with congested mucosa, compared to adrenaline group (50 min). The mean blood pressure was significantly higher in adrenaline group compared to haemocoagulase group. Post-operative hearing improvement in both groups showed no significant difference with p value 0.694.

Conclusions: Adrenaline is a better middle ear haemostatic than haemocoagulase. However, haemocoagulase can safely be used in patients with hypertension.

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1. Introduction

Ever since the first surgery was conducted, intraoperative bleeding has always lingered in the minds of surgeons. The pursuit for a bloodless field has been a never ending one for surgeons. Even a small amount of bleeding can obscure the surgical field resulting in poor visualization of critical structures.

Use of adrenaline soaked cotton balls is the gold standard in middle ear haemostasis. Haemocoagulase topical solution is an

enzyme complex isolated from the poison of snake *Bothrops jararaca* or *bothrops atrox*, which has coagulative and antihaemorrhagic properties. It acts by accelerating the conversion of fibrinogen to fibrin polymer and promotes the interaction of platelets with fibrin clot to coagulate the blood (Ramesh et al., 1990).

Previous studies have used haemocoagulase for the treatment of sudden sensorineural hearing loss (Thelwell et al., 2016). But there are no reports of haemocoagulase being used in middle ear surgeries for achieving haemostasis. Thus, we have done a novel study comparing adrenaline and haemocoagulase for attaining haemostasis.

2. Materials and methods

This was a prospective, double blinded comparative study conducted in tertiary care hospital in Mangalore, Southern India

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from January 2013 to June 2014. Hundred patients between the age groups of 15 and 50 undergoing type I tympanoplasty with or without cortical mastoidectomy were included in the study. The patients selected were normotensive with normal coagulation profile. Patients with aditus block were excluded from the study. Patients with clotting disorders and systemic illnesses, including blood pressure of >150/99 mmHg were excluded. Patients were randomized into 2 groups. Randomization and preparation of drug was done by a trained assistant not involved in data collection and surgery. The patients and investigators were unaware of which solution would be injected. Informed consent was taken from all the patients. In group A (50 cases), cotton balls soaked in 2 ml Haemocoagulase (0.2 Coagulation Units per ml of Bortoclot; Juggat Pharma, Bangalore, India) were used for middle ear haemostasis. In Group B (50 cases), cotton balls soaked in 2 ml Adrenaline (1:1000 dilution of Adrenaline, Dheer Healthcare Private Limited, Mumbai, India) were used for middle ear haemostasis. Ten cotton balls of equal size were dipped in 2 ml of either of the solutions. Ethical clearance was obtained from the institutional ethical committee prior to the study. Although multiple surgeons were involved in the study, the average time taken by the surgeons was similar.

All the patients underwent tympanoplasty through post aural approach. Time duration for tympanoplasty was considered from placing the canal incision till replacement of tympanomeatal flap after the placement of graft. In patients who underwent cortical mastoidectomy, the mastoidectomy was performed initially and tympanoplasty was performed later so that the time calculation was more satisfactory. Mean blood pressure during the procedure was noted. The number of cotton balls required for middle ear haemostasis was also noted. According to the surgeons comfort levels, scores were given as score 3 (Excellent response), score 2 (Good response), score 1 (Average response), and score 0 (Poor response). Post operative hearing level was assessed after 3 months and was compared with preoperative hearing levels.

Statistical analysis was done using IBM SPSS statistics for windows, version 20.0 Armok, NY: IBM corp. t- Test, Chi- Squire Tests and P value of <0.05 was considered to be statistically significant.

3. Results

Hundred patients who were undergoing type 1 tympanoplasty with or without cortical mastoidectomy were included in the study. In group A, 16% underwent cortical mastoidectomy while 84% underwent only tympanoplasty. In group B, 20% underwent cortical mastoidectomy along with type 1 tympanoplasty while 80% underwent only type 1 tympanoplasty.

There was no difference in gender distribution between the groups. The highest number of patients in this study belonged to age group of 21–30 years (36 cases). In group A (haemocoagulase) 19 cases (38%) belonged to age group of 21–30 years, and in group B (adrenaline) 17 cases (34%) were between 21 and 30 years.

It was noted that in group A (haemocoagulase), 16 cases had congested middle ear mucosa and 34 cases had normal middle ear mucosa, out of a total of 50 cases. In group B (adrenaline), 22 cases had congested middle ear mucosa while 28 cases had normal middle ear mucosa, out of a total of 50 cases.

The average number of cotton balls used in group A was 4 and in

group B was 3, with a P value of 0.008 (Table 1). Thus, adrenaline proved to be better at haemostasis compared to haemocoagulase. Comparison was also made between numbers of cotton balls used in middle ear for attaining haemostasis in cases with congested middle ear mucosa in both the groups. It was noted that in cases where haemocoagulase was used, the mean of number of cotton balls used was 6, while in cases where adrenaline was used, the mean was 4. P value obtained was <0.001 which is statistically significant. It is thus clearly seen that the number of cotton balls used was significantly more in case of haemocoagulase group than adrenaline group in cases with congested middle ear mucosa.

The mean blood pressure in group A was 78 mmHg, while in group B it was 94 mmHg. The p value obtained was <0.001 which was statistically significant. While analysing the subjects with congested mucosa, the mean blood pressure in group A was 78 mm Hg while that in group B was 93 mm Hg. P value was <0.001 which was statistically significant (Fig. 1).

It was noted that mean time taken from the step of placing canal incision till the placement of graft in group A was 46 min, compared to 44 min in group B (Fig. 2). Thus, there was no significant difference in duration of the procedure in both groups. However, among the cases with congested mucosa, the mean time duration was 65 min in group A and 50 min in group B (Fig. 3). P value was <0.001, which is statistically significant.

Analyzing the comfort level of the operating surgeons, a poor score (Score 0) was given to 5 cases in group A while no case in

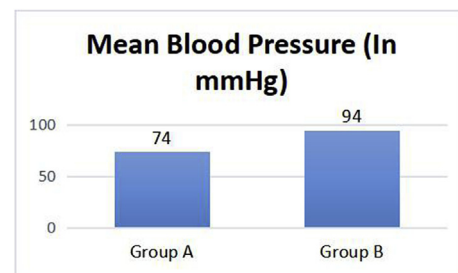


Fig. 1. Mean blood pressure of both groups.

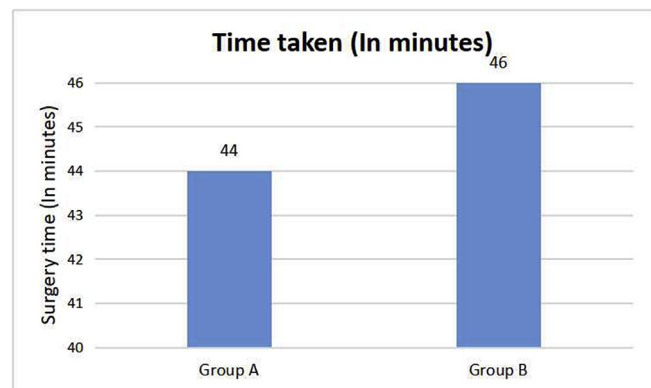


Fig. 2. Operative time in both groups.

Table 1
Number of cotton balls used in both groups.

Group	Number of cotton balls used	Mean	Std. Deviation	t	Degree of freedom	P Value
A	50	4	1.877	2.727	83.455	0.008
B	50	3	1.204			

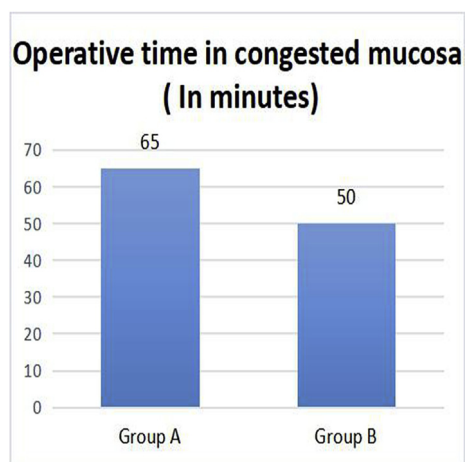


Fig. 3. Operative time in subjects with congested middle ear mucosa.

group B obtained score 0. Score 1 was given to 13 cases in group A while 8 cases in group B obtained score 1. Twenty six cases in group A got score 2 while 28 cases in group B got score 2. Only 6 cases in group A got an excellent score (score 3) while 14 cases in group B got a score of 3. A significant p value of 0.005 showed that surgeons were more comfortable with adrenaline compared to haemocoagulase in middle ear haemostasis.

There was no statistical difference between the post-operative hearing levels between the two groups. The mean post-operative hearing improvement in cases where haemocoagulase was used was 11.64 dB while, the mean hearing improvement in cases with adrenaline was 12.12 dB.

The graft uptake in both the groups was also studied. In group A, graft was taken up in 47 cases (94%) while graft failure was noted in 3 cases (6%). In group B, graft uptake was seen in 49 cases (98%) while failure was noted in 1 case (2%). The p value was 0.307 which is not significant.

4. Discussion

Chronic otitis media is a long standing infection of the middle ear space characterized by ear discharge and permanent changes in tympanic membrane. It can be treated by ear toileting, topical and systemic antibiotics and surgical treatment to eradicate the disease and to close the perforation (Gopen, 2010). Bleeding is a major drawback in all ear surgeries. A bloodless field reduces the risk of intraoperative complications.

Haemostasis in middle ear surgeries can be achieved by means of adrenaline, bone wax, gelatin based haemostats, collagen based haemostats, fibrin based haemostats, hydrogen peroxide and cautery (Acar et al., 2010; Anschuetz et al., 2017).

Adrenaline is a sympathomimetic hormone and a neurotransmitter, with both alpha and beta adrenergic receptors. Vasoconstriction of arterioles in mucosa is seen due to alpha receptor predominant stimulation. Haemocoagulase is an enzyme complex present in south American snakes species “Bothrops Jarararca” and “Bothrops Atrax” [2]. This enzyme complex has extensive clinical application in arresting the capillary bleeding and promoting wound healing. Haemocoagulase solution reduces blood clotting time significantly (Joshi et al., 2014), enhances capillary network formation and hastens wound healing. It is known that haemocoagulase is devoid of antigenic capacity and does not cause the appearance of immunologic phenomenon (Windholz et al., 1983).

Haemocoagulase has been used in surgical procedures like

adenotonsillectomy, ophthalmic surgeries (Lee et al., 1989), dental extraction (Gupta et al., 2018), cosmetic surgeries, to prevent pulmonary hemorrhage (Shi et al., 2005), in treating sudden deafness (Thelwell et al., 2016) and in bleeding disorders (Wang et al., 2012). Haemocoagulase is devoid of antigenic capacity and does not cause the appearance of immunologic phenomenon (Windholz et al., 1983).

There are no previous studies with the use of haemocoagulase in middle ear surgeries. In this study, a comparison was made between the action of Haemocoagulase and Adrenaline in attaining haemostasis in type 1 tympanoplasty (with or without cortical mastoidectomy). A total number of 100 subjects were included in this study and were divided into two groups.

We found that adrenaline was better at achieving haemostasis compared to haemocoagulase. However, the intraoperative rise in blood pressure was more in adrenaline compared to haemocoagulase. The mean number of cotton balls used in haemocoagulase group in cases with congested middle ear mucosa was more than those used in the adrenaline group. The duration of surgery was more in haemocoagulase group (65 min) with congested mucosa, compared to adrenaline group (50 min). Poor scores (score 0) were given by surgeons in haemocoagulase group in cases with congested middle ear mucosa. The mean blood pressure was significantly higher in adrenaline group (94 mmHg) compared to haemocoagulase group (78 mmHg). Post operative hearing improvement was similar in both groups with improvement of 11–12 dB. No patient developed sensorineural hearing loss or any other complications after surgery. There was no significant difference in post operative graft uptake in both the groups with 98% uptake in adrenaline group and 94% in haemocoagulase group. The cost of haemocoagulase however, is double that of adrenaline.

Haemocoagulase has been extensively studied in dental surgeries. Majumder et al. (2014) evaluated the efficacy of topical hemocoagulase on 50 surgical sites in 25 patients who underwent simple dental extractions. Parameters such as bleeding stoppage time, pain, and swelling were measured. A significant difference was found in bleeding stoppage time, postoperative pain, and swelling between the test (hemocoagulase) and control (no drug) group. They concluded that the use of hemocoagulase solution after extractions not only provides faster haemostasis but also enhances healing by rapid formation of healthy tissue with less chance of infection.

A study conducted by Conrado et al. (2007) on cardiovascular effects of local anaesthesia with epinephrine in periodontal treatment revealed an increase in systolic and diastolic blood pressure post local anaesthetic administration. According to Saarnivaara et al. (Saarnivaara L; Leander P, 1977) use of adrenaline for middle ear haemostasis was found to increase blood pressure both under general and local anaesthesia. Similar results were also found in our study. Our study shows that haemocoagulase can be used safely in middle ear in patients with hypertensive diseases. The mean blood pressure was significantly less in haemocoagulase group.

Haemocoagulase is known to increase the blood flow in the inner ear and it has been used in sudden sensory neural hearing loss (Kwakami et al., 1992; Thelwell et al., 2016). In our study, when preoperative hearing level of the patient was compared with postoperative hearing level, it showed a mean improvement of 11.64 dB in haemocoagulase group and a mean improvement of 12.12 dB in adrenaline group. P value of 0.694 was obtained which suggested no significant difference in hearing between the two groups. Out of 100 patients, one patient had no improvement in hearing and none of our patients had developed sensorineural hearing loss after the surgery. This clearly indicates that both adrenaline and haemocoagulase can be used safely in middle ear haemostasis without causing any inner ear damage. The limitation

of our study is the subjective assessment of congestion and edematous middle ear mucosa. There were no other confounding factors in our study. Further studies with bigger sample size need to be done to study the role of haemocoagulase in middle ear surgeries.

5. Conclusion

Achieving middle ear haemostasis is vital to the outcome of tympanoplasty. In our study we found that adrenaline was a better haemostatic agent than haemocoagulase. However, haemocoagulase may be the preferred agent in hypertensives.

Declarations of interest

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.joto.2019.02.002>.

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