

Hyaluronidase in sub – Tenon’s anesthesia for phacoemulsification

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Abstract

• **AIM:** To investigate the effect of hyaluronidase use on the quality of sub-Tenon’s anesthesia for phacoemulsification.

• **METHODS:** This was a randomized, double – blind clinical trial which was conducted at Nikookari Eye Hospital for 5 months. Forty-two eyes of candidates for phacoemulsification under sub-Tenon’s anesthesia were randomly allocated to two equal groups and received either 2mL of lidocaine 2% solution with (LH), or without (L) addition of hyaluronidase (150U/mL). Akinesia was assessed 15 minutes after sub-Tenon’s injection. Patients and surgeon’s satisfaction, as well as the postoperative pain (the visual analogue scale, VAS) were investigated after operation. The contingency tables (including the Chi-square or Fisher’s exact tests, when appropriate) and parametric analysis (the independent samples *t* test) were used for statistical analysis.

• **RESULTS:** Complete akinesia (33.3% vs 4.8%, $P = 0.04$), as well as the patients (85.7% vs 57.1%, $P = 0.04$) and surgeon’s satisfaction (87.5% vs 52.4%, $P = 0.02$) were significantly more frequent in LH than in L group. The mean VAS was significantly lower in the same group (1.90 ± 1.45 vs 3.00 ± 1.55 , $P = 0.04$).

• **CONCLUSION:** Addition of hyaluronidase to lidocaine solution for sub – Tenon’s anesthesia significantly improves the ocular akinesia, enhances the intra – operative patients and surgeons’ satisfaction, and attenuates the postoperative pain.

• **KEYWORDS:** hyaluronidase; local block; sub-Tenon’s anesthesia

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INTRODUCTION

Sub-Tenon’s anesthesia is a safe and popular technique for ophthalmic local anesthesia. In this method the anesthetic drugs diffuse from the sub-Tenon’s space to the nerves and myoneural junctions of extraocular muscles. Any condition that facilitates this diffusion leads to a better ocular akinesia which is essential for operation^[1,2].

Hyaluronidase is an enzyme with known effects on the connective tissue. It is hypothesized that this enzyme enhances diffusion of local anesthetics through various tissues and thus, improves the regional blockade^[3,4].

There are conflicting data regarding the role of hyaluronidase when it is used as an adjuvant material along with anesthetic agents in cataract surgery. Some studies have shown that this material improves ocular akinesia and its time of onset in retrobulbar, peribulbar, or sub-Tenon’s anesthesia^[5-9]. In contrast, some other studies have failed to show such effects^[10-13].

There is limited number of studies which have addressed the role of hyaluronidase in sub – Tenon’s anesthesia with inconclusive results. This study aimed at examining the effect of hyaluronidase added to anesthetic solution in candidates of sub-Tenon’s anesthesia for elective cataract surgery.

MATERIALS AND METHODS

Subjects In this randomized, double-blind clinical trial, 44 consecutive candidates for elective cataract surgery (phacoemulsification) under sub – Tenon’s anesthesia were recruited from a referral eye centre (Nikookari Eye Hospital affiliated to Tabriz University of Medical Sciences, Tabriz, Iran) between February 2011 and July 2011. Patients with deafness or allergy to lidocaine or hyaluronidase were excluded. Two patients did not meet the criteria and were excluded, leaving 42 cases (42 eyes) in the study.

This study was performed according to the Declaration of Helsinki (revision 2008) and was approved by the ethics

Table 1 Outcomes of sub-Tenon's anesthesia in two groups

Variable	Hyaluronidase (n=21)	Control (n=21)	P	Odds ratio	¹ 95% CI
Postoperative pain (VAS)	1.90±1.45	3.00±1.55	0.02	-	
Akinesia					
Complete	7 (33.3)	1 (4.8)	0.04	10.00	1.10-90.59
Incomplete	14 (66.7)	20 (95.2)			
Surgeon's satisfaction					
Yes	18 (85.7)	11 (52.4)	0.02	5.46	1.22-24.39
No	3 (14.3)	10 (47.6)			
Patient's satisfaction					
Yes	18 (85.7)	12 (57.1)	0.04	4.50	1.00-50.00
No	3 (14.3)	9 (42.9)			

Data are presented as mean±standard deviation, or frequency (percentage). ¹For the odds ratio.

committee of Tabriz University of Medical Sciences. Informed consents were obtained from all participants.

Methods Consecutive numbers were assigned to patients on admission. These numbers were previously randomized to the treatment groups by a staff member not involved in the study. Accordingly, the patients were allocated in two 21-eye groups: the 'L' group who received 2mL of lidocaine 2% solution; and the 'LH' group, who received 2mL of a solution contained a 50:50 mixture of lidocaine 2% plus hyaluronidase 150U/mL (Hyalase, CP Pharmaceuticals Ltd, UK). The ampoules were identical in appearance with a code (A or B) printed on them. They were previously prepared by a nurse with no role in the present study. These codes were disclosed for statistical analysis only at the end of the study. The nerve blockades and operations were performed by a single skilled ophthalmologist blind to the grouping and medications. Local anesthesia was achieved after sub-Tenon's injection through an incision at the inferonasal quadrant at a predefined point 5mm to the limbus by using a 19-gauge curved blunt cannula (Stevens®).

Variables Akinesia was assessed 15 minutes after injection and graded as complete immobilization of the operated eye; or incomplete akinesia (any degree of movement). The patients' postoperative pain was subjectively assessed by using a standard visual analogue scale (VAS) chart. This measurement instrument is similar to a ruler with 10 consecutive grades from 0 to 10 on a line. The patients were given appropriate and enough explanation in this regard prior to use. Based on this explanation, the patients were asked to choose a number between 0 and 10 which best described their pain intensity, emphasizing that the grade 0 represented "no pain" and the grade 10 "the most severe imaginable pain". The patients and surgeon's satisfaction was inquired with regard to intraoperative convenience and documented as 'yes=satisfied', or 'no=unsatisfied'. This investigator was also unaware of the grouping.

Statistical Analysis The SPSS software version 15.0 for the Windows (The SPSS Inc., Chicago, USA) was used for statistical comparisons. The contingency tables (including the Chi-square or Fisher's exact tests, when appropriate) and parametric analysis (the independent samples t test) were used for statistical analysis. $P \leq 0.05$ was considered statistically significant.

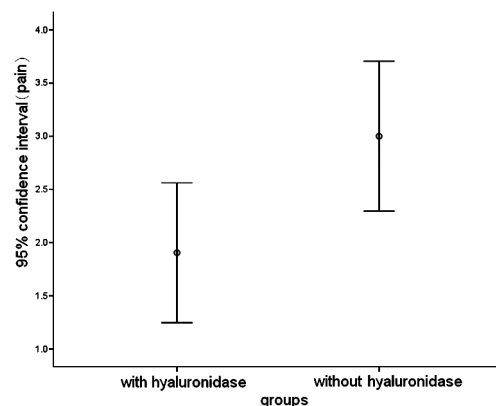


Figure 1 Error bars of the mean postoperative pain based on the visual analogue scale.

RESULTS

There were 13 males (61.9%) and 8 females (38.1%) with a mean age of (65.62±3.01) years (range: 60-72 years) in 'LH' group and 14 males (66.7%) and 7 females (33.3%) with a mean age of (67.00±4.40) years (range: 60-76 years) in 'L' group. The two groups were comparable for their members' gender ($P = 0.75$, odds ratio = 0.81 with 0.95 confidence interval of 0.23 to 2.88) and age ($P = 0.24$). One patient (4.8%) in the 'LH' group received one dose of intramuscular midazolam (4mg) prior to transferring to the operating room due to uncontrollable anxiety. Vitreous loss was encountered during intraocular lens implantation in another patient (4.8%) of the same group. In the 'L' group the anterior capsule rupture or partial Descemet's membrane detachment occurred in two patients (9.5%). The outcome variables are outlined and compared between the two groups in Table 1. Accordingly, mean VAS was significantly higher in 'L' than in 'LH' group; indicating more severe pain in the former (Figure 1). A 'complete' akinesia was reported significantly more frequent in 'LH' than in 'L' group (33.3% vs 4.8%, $P = 0.04$). The surgeon was satisfied with the intraoperative anesthesia in 85.7% of the cases in 'LH' group and in 52.5% of the cases in 'L' group ($P = 0.02$). After surgery was completed 85.7% of the patients in 'LH' group were satisfied with their operation, while this rate was 57.1% in 'L' group ($P = 0.04$, Table 1).

DISCUSSION

In the present study the outcome of adding hyaluronidase to local anesthetic was investigated for sub-Tenon's anesthesia in phacoemulsification. For the first time to our knowledge, the intraoperative akinesia and surgeon's satisfaction, as well as the postoperative pain and patient's satisfaction were assessed in a simple way.

Our results are in line with previous findings that indicate the quality of a regional block can be assessed by patient's comfort on administration, depth and duration of anesthesia, and the onset of akinesia. The latter, in particular, is desirable in anesthesia for intraocular surgery^[3,14].

We showed that all outcome variables were significantly in better condition in the cases who underwent anesthesia with a mixed local anesthetic solution containing hyaluronidase and lidocaine. A number of studies have attempted to address this issue with varying outcomes.

Guise and Laurent compared efficacies of four anesthetic solutions used for sub-Tenon's anesthesia; (1) 2% plain lidocaine (3mL) plus 0.5% plain bupivacaine (2mL); (2) 2% lidocaine (1mL) plus 150U/mL of hyaluronidase; (3) 2% plain lidocaine (2mL); and (4) 0.5% plain bupivacaine (2mL). They reported significantly better akinesia after 9 minutes in hyaluronidase receivers comparing in other groups. When they considered the quality of block at 13 minutes, however, no significant difference was found between the groups^[15].

In another series by Alwitary *et al*^[14], patients received either plain lidocaine or lidocaine plus sodium hyaluronidase (150U/mL). They reported that the hyaluronidase improved only the speed of onset of ocular akinesia with sub-Tenon's anesthesia with no beneficial effects in terms of final ocular akinesia.

These reports are in contrast with our finding which indicated the quality of blockade at 15 minutes was significantly better in hyaluronidase receivers. On the other hand, however, our result was confirmed by some other series^[16,17].

During a busy cataract list with average operating time of 10–20 minutes, this improvement in rate of onset of akinesia is clearly advantageous in terms of list efficiency^[16].

In addition, it is previously shown that adding hyaluronidase to an anesthetic solution for sub-Tenon's anesthesia may lead to no significant effect on the sensory blockade, in despite of significant improvements in the quality of the motor blockade^[16,18].

In contrast, the postoperative VAS was significantly lower in our 'LH' group. The failure in sensory blockade may be due to low dose of administered hyaluronidase in the mentioned studies (15–30U/mL).

Radhakrishna *et al*^[19] assessed the effect of hyaluronidase 15U/mL added to a mixture of 2% lidocaine and 0.75% bupivacaine made to a total of 10mL in elective cataract surgery patients. They concluded that the hyaluronidase facilitates early onset of block and gives marginally better conditions for surgery, though the surgical conditions in both

groups were adequate for phacoemulsification to be carried without any patient discomfort or surgical dissatisfaction. We showed superior satisfaction by both the surgeon and patients in the 'LH' than in the plain lidocaine group.

Low dose of hyaluronidase is again a major limitation of the mentioned study. However, to the best of our knowledge, there is not any similar report in the literature on these two parameters as outcome variables.

Available heterogeneity in the results of studies may be justified by presence of a large degree of variability in methodology, particularly in respect to used concentration of hyaluronidase, anesthetic technique, and constituents of the local anesthetic solution^[14,20].

The most common complications associated with sub-Tenon's block have been reported to be conjunctival haemorrhage and chemosis^[21,22].

We did not encounter any similar complication. It is thought that the risk of these complications can be attenuated by reducing the volume of used local anesthetics. It is previously reported that hyaluronidase permits a significant 2.4-fold reduction in the minimum local anesthetic volume for sub-Tenon's anesthesia.^[18] There are some concerns about the cost-effectiveness of adding hyaluronidase to the anesthetics in patients undergoing cataract surgery, albeit in a setting with incomplete agreement on the beneficial effects of the drug^[19]. Nonetheless, this is another issue which should be addressed in further studies.

In conclusion, we showed that the addition of hyaluronidase at a concentration of 150U/mL to anesthetic solution is accompanied with higher satisfaction of surgeon and patient, mainly by providing a better blockade and lower pain, respectively.

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超声乳化术中透明质酸酶在筋膜下麻醉中的应用

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摘要

目的:探讨超声乳化术中透明质酸酶对筋膜下麻醉的疗效。

方法:该研究是一项双盲随机临床试验,在 Nikookari 眼科医院进行了长达 5mo。行超声乳化术的候选患者中接受筋膜下麻醉的 42 眼随机分为均等的两组,分别应用 20g/L 的利多卡因溶液 2mL+150U/mL 透明质酸酶(LH),和单纯 20g/L 的利多卡因溶液 2mL(L)。筋膜下注射 15min 后活动受抑制。患者和医生都非常满意,对于术后疼痛的抑制(视觉模拟评分,the visual analogue scale, VAS)也同样满意。统计学分析采用列联表(包括卡方检验或 Fisher's 精确检验)和参数分析(独立样本 t 检验)。

结果:活动抑制(33.3% vs 4.8%, $P=0.04$)、患者满意度(85.7% vs 57.1%, $P=0.04$)和医生满意度(87.5% vs 52.4%, $P=0.02$),LH 组明显高于 L 组。VAS 在相同组内明显较低(1.90 ± 1.45 vs 3.00 ± 1.55 , $P=0.04$)。

结论:利多卡因溶液+透明质酸酶的筋膜下麻醉明显使得眼部活动受限,提高了患者和医生的满意度,并减轻了术后疼痛。

关键词:透明质酸酶;局部阻塞;筋膜下麻醉