Effect of hyaluronidase on ocular motility and eyelid function in sub-Tenon's anaesthesia: randomised controlled trial

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Abstract

Purpose To assess the effect of hyaluronidase on eye and eyelid movements when used as an adjunct in sub-Tenon's anaesthesia.

Methods A total of 60 patients who had sub-Tenon's anaesthesia prior to phacoemulsification surgery were divided into two equal groups in a double-masked randomised controlled fashion. Of these, Group A had 4 ml lignocaine 2%, while Group B had 4 ml lignocaine 2% with the addition of sodium hyaluronidase 75 IU/ml. Ocular motility, levator, and orbicularis oculi function were measured in all patients at 5 and 8 min. Levator function was scored from 0 (no function) to 3 (complete function) while orbicularis function was scored from 0 to 2. The score for ocular motility was the sum in four positions of gaze, each position scoring from 0 to 2. Results were compared using a nonparametric test.

Results Group B achieved significantly better ocular and lid akinesia than Group A both at 5 and 8 min with $P < 0.01$. The median scores for levator function at 5 and 8 min were 2 for Group A and 0 for Group B. For orbicularis function, the median scores at both time intervals were 2 for Group A and 1 for Group B. For ocular motility, the median score for Group A at 5 min was 3 and at 8 min was 2.5; for Group B at 5 min was 0.5 and at 8 min was 0.

Conclusions The addition of hyaluronidase in sub-Tenon's anaesthesia has a significant effect in improving ocular and lid (levator and orbicularis) akinesia.

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Introduction

The sub-Tenon's block (STB) has become increasingly popular since its reintroduction as an anaesthetic technique for intraocular surgery.¹ It is relatively quick and effective, and allows the use of a blunt cannula thereby avoiding the risk of a needle near the globe.

The role of hyaluronidase as an adjunct in local anaesthesia was first described by Atkinson² in 1949, where he concluded that its use in retrobulbar anaesthesia produced a more effective akinesia of orbicularis and extraocular muscles.

Hyaluronidase is an enzyme that depolymerises hyaluronic acid, thereby aiding the spread of the local anaesthetic through the extracellular matrix.³ Its use in retrobulbar and peribulbar blocks has been open to question, especially with the improved spreading of newer local anaesthetic agents.⁴

The effect of hyaluronidase on ocular akinesia in sub-Tenon's anaesthesia has been reported in previous studies. Their results are conflicting, one such study showing it to facilitate the onset of ocular akinesia⁵ whereas another reports no difference.⁶ However, there is scant literature on its effect on levator and orbicularis function in sub-Tenon's anaesthesia.

Our study involved a randomised double-masked trial to assess the effect of the addition

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of hyaluronidase on ocular motility, orbicularis and levator function in sub-Tenon's anaesthesia.

Materials and methods

After receiving informed consent, 60 patients were chosen, all of whom were to undergo phacoemulsification and intraocular lens implantation. Ethical approval was not required as all methods used were well established in routine ophthalmic practice. Patients with eyelid pathology or a known allergy to lignocaine or hyaluronidase were not used. Also, those patients who had retinal detachment surgery with an explant or those with a conjunctival lesion, which would preclude the administration of a sub-Tenon's injection, were excluded.

Subjects were divided into two equal groups in a double-masked randomised controlled fashion. Patients were randomly allocated to either group by corresponding each of them to the letter A or B picked from a brown envelope. Group A received 4 ml lignocaine 2% only, while Group B received 4 ml lignocaine 2% with the addition of sodium hyaluronidase at a concentration of 75 IU/ml.

There was no statistically significant difference between the two groups in terms of age or gender (unpaired *t*-test). The patient demographics are shown in Table 1.

The blocks were performed by one of the three operators (SAA, MTD, and LY) either with or without the addition of hyaluronidase (see Table 1). Topical benoxinate 0.4% was applied before a wire eye speculum was used to hold the eyelids open. The conjunctiva was grasped in the inferonasal quadrant using Moorfields forceps and the conjunctiva and Tenon's capsule were cut and bluntly dissected using curved spring scissors. A 19-gauge sub-Tenon's cannula was introduced and the anaesthetic agent was slowly injected. A single ophthalmologist (TRGP), who was unaware of patient group allocation, assessed all of the blocks at 5 and 8 min

Table 1 Patient demographics and blocks by group

Characteristic	Group A (n = 30)	Group B (n = 30)
Age (years)		
Mean $\pm$ s.d.	75.80 $\pm$ 9.40	76.83 $\pm$ 9.73
Range	55–92	56–95
Men: Women	10:20	12:18
Blocks given by each operator		
SAA	15	15
MTD	6	7
LY	9	8

Table 2 Scoring system for eyelid function and ocular motility

Movements	Degree of function	Score
Levator function	Full function/no block	3
	Moderate function/mild block	2
	Mild function/moderate block	1
	Nil function/complete block	0
Orbicularis function	Full function/no block	2
	Reduced function/partial block	1
	Nil function/complete block	0
Ocular motility (each position of gaze)	Full function	2
	Reduced function	1
	Nil function	0

post administration. The following movements were assessed: levator function, orbicularis oculi function, and ocular motility.

Grading for levator and orbicularis function was scored as shown in Table 2. The score for ocular motility was the sum of each movement measured in upgaze, downgaze, left gaze, and right gaze. Therefore, complete ocular akinesia would give a score of 0, whereas normal ocular motility would give a score of 8. The reduction of average score of at least 2, with the addition of hyaluronidase, was considered clinically important.

The observed scores did not follow a normal distribution and thus the nonparametric Mann–Whitney U test was used to assess the findings with a two-sided test at the 5% level of significance.

Results

All patients had normal levator function (score of 3), orbicularis function (score of 2), and ocular motility (score of 8) before injection. Table 3 presents the median lid and ocular motility scores at each time point with Mann–Whitney U test results for Groups A and B. The test results show that there is a significant difference ($P < 0.01$) between Group A and Group B in levator function, orbicularis function, and ocular motility both at 5 and 8 min. Further tests with male and female specific data confirm this significant result except in the case of orbicularis function. Although orbicularis function shows a significant difference between the two groups for males (at 5 min: $P = 0.002$ and at 8 min: $P = 0.008$), there is no significant difference between the two groups for females (at 5 min: $P = 0.285$ and at 8 min: $P = 0.228$).

Percentage distribution of blocks for levator function, orbicularis function, and ocular motility are shown in Figures 1–3, respectively. It is clear from these figures that there is a higher percentage of complete or partial blocks in Group B compared to those in Group A. Moreover,

Table 3 Median eyelid and ocular motility scores

	Time interval (min.)	Score (interquartile range)		P value
		Group A (control)	Group B (hyalase)	
Levator function	5	2 (1–3)	0 (0–1.25)	<0.0001
	8	2 (1–2.25)	0 (0–1)	<0.0001
Orbicularis function	5	2 (1–2)	1 (1–1.25)	0.006
	8	2 (1–2)	1 (1–1.25)	0.008
Ocular motility	5	3 (2–6)	0.5 (0–1.25)	<0.0001
	8	2.5 (1–4)	0 (0–1)	<0.0001

Figure 1 Levator function by group and time. Y-axis = %. **Figure 3** Ocular motility by group and time. Y-axis = %. **Figure 2** Orbicularis function by group and time. Y-axis = %.

these percentages increase over time in both groups for levator function and ocular motility.

Discussion

The use of hyaluronidase as an adjunct in sub-Tenon's anaesthesia has been reported in previous studies with conflicting results in terms of final ocular akinesia. The results of these studies are summarised in Table 4. The purpose of our study was to assess its effect on ocular and lid function.

Two previous studies were performed using differing concentrations of hyaluronidase, one showing it to speed up its onset (with 150 IU/ml hyaluronidase)⁷ and the other showing it to be of no benefit (when 15 IU/ml).⁶ Rowley *et al*⁸ showed that the addition of only 30 IU/ml hyaluronidase to the STB significantly improved ocular akinesia.

Our study shows that the addition of hyaluronidase at a concentration of 75 IU/ml—this dose having been selected as an approximate average of previous studies—to 4 ml lignocaine 2% facilitates development of ocular akinesia, which may be desirable during cataract surgery so as to provide control of the eye for the surgeon and especially for the trainee. It is also shown to facilitate the development of lid paralysis, which carries several advantages. It provides good control of the lids so as to allow for a more effective draping technique. It also prevents any eye movements from involuntary blinking or voluntary squeezing of the eyelids.

Overall, our study showed there to be a statistically significant difference in orbicularis function with the addition of hyaluronidase (see Table 3). However, the greatest benefit of hyaluronidase in terms of total orbicularis akinesia (complete block 6.7%) was achieved only after 8 min of the injection but not after 5 min (see Figure 2). On the other hand, a stratified analysis of the data according to gender showed no significant

Table 4 Results of previous studies of STB with hyaluronidase (H^*)

Study reference	H^* conc. (IU/ml)	Anaesthetic mixture	Time to measurement (min)	Effect on ocular function	Effect on lid function
6	15	2.5 ml lignocaine 2% + 2.5 ml bupivacaine 0.5%	Every 30 s	Non significant	—
7	150	3 ml lignocaine 2% + 2 ml bupivacaine 0.5%	0–9	Significant	—
8	30	3 ml lignocaine 2% + adrenaline 1:200000	10	Significant	Significant
9	150	5 ml lignocaine 2% + 5 ml bupivacaine 0.75%	5 and 8	—	Significant with 7 ml of solution
Present study	75	4 ml lignocaine 2%	5 and 8	Significant	Significant

difference for females ($P > 0.05$). There is no obvious explanation for this result and a larger trial would underline the significance of this finding. Rowley *et al* showed that the reduction of eyelid movement was significantly better with the addition of 30 IU/ml hyaluronidase to the STB. However, lid movement was not assessed according to levator and orbicularis action separately, nor were the groups divided according to gender. Another study (see Table 4) showed that the addition of hyaluronidase to the anaesthetic solution resulted in effective akinesia of orbicularis oculi.⁹

There were no adverse effects during our study. However, recent cases of orbital swelling and acute orbital cellulitis following sub-Tenon's anaesthesia have been reported.^{10,11} In future studies, exclusion criteria may be broadened to increase safety, thereby excluding any previous eye surgery or injury and any process which may occlude the sub-Tenon's space, such as scleritis. In conclusion, this study shows that hyaluronidase has a significant effect in improving ocular and lid akinesia when used as an adjunct in sub-Tenon's anaesthesia.

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