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THE USE OF HYALURONIDASES IN OPHTHALMIC SURGERIES

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INTRODUCTION

Sub-Tenon's block is one of the common technique used in local anesthesia in ophthalmic surgery that provides a good quality of analgesia and ocular akinesia.[1] It methods was the use of a blunt needle rather than sharp one, so the risks of perforation of the eye globe and anesthesia of brainstem are reduced but not entirely prevented.[2,3] These procedures had some complications; these include conjunctival hemorrhage and chemosis.[3,4] which can make surgical access more difficult than usual and may interfere with formation of the scleral flap in glaucoma surgery.[5] this can be minimized by decreasing local anesthetic volume that was injected.[6]

But when reductions in the volume of local anaesthetic was done it was associated with decreasing in analgesia and extra-ocular muscle akinesia, which may make surgery more difficult so hyaluronidase addition was beneficial, which hydrolyses some parts of the intracellular matrix that maintains tissue integrity, that in turn allowing the local anesthetic to spread more extensively around the orbit and it allow smaller volumes to be given. This could lead to a reduction in complications without loss of efficacy.[6]

Some studies that using fixed volumes of local anesthetic solution have a failure in confirming the hyaluronidase benefits and this was due to uncertainty about the optimum concentration of hyaluronidase, pH variability of local anaesthetic solutions, effect of added vasoconstrictors, and differing properties of individual local anaesthetics.[7,8,9]

Guise and Laurent evaluated 30 IU per mL hyaluronidase added to a 5 mL sub tenon block and showed improvement in akinesia after 3 minutes.[10] while Rowley et al performed a randomized control trial of 30 IU per mL.

Hyaluronidase that was added to Sub tenon block for patients with cataract extraction surgery and showed an improvement in akinesia after 10 minutes, but failure in demonstration of any significant difference in pain scores.[11,12]

In this study we added 7.5 IU of hyaluronidase to each ml of the subtenon mixture.

Hyaluronidases are enzymes that degrade hyaluronic acid which is a fundamental component of the extracellular which can be injected subcutaneously for several medical purposes. Hyaluronidases role was to prevent complications from inappropriate injection of hyaluronic acid, eliminating hyaluronic acid nodules, or correcting unsightly hyaluronic acid overfilling. Hyaluronidases have been employed for several years as a spreading agent to promote the diffusion of several substances injected subcutaneously, that had several application such as removal of the cumulus-corona-oocyte complex formed during intracytoplasmic sperm injection, prevention the tissue damage afterextravasation of many substances, to decrease the edema size and in the treatment of vitreous hemorrhage.[13]

Hyaluronidases was derived from crude extracts of ovine or bovine testicular tissue. The enzyme obtained with this procedure is impure and immunogenic, containing several contaminating substances such as proteases, immunoglobulin, and vasoactive factors. An alternative, hyaluronate lyase from Streptococcus agalactiae, may be employed. This formulation is purer than BTH and has a higher specificity. Moreover, BTH produces several oligosaccharide fragments of hyaluronan that could have a role in allergic reactions and act as growth factors, promoting possible metastasis.[14]

The another formulation called Hylenex, a human recombinant hyaluronidase that is considered less immunogenic and safer.[15]

After intravenous administration, hyaluronidases

undergo elimination through the kidneys with a known clearance (t1/2 = 2.1 + 0.2 min), where t1/2 is half-time. Nevertheless, the mechanism of inactivation inside the dermis and other tissues is still unknown, mainly depending on Hyaluronic Acid (HA) synthesis. The hyaluronidase effects in this context persist for approximately 48 hours.[16]

The Aim of this study To demonstrate the hyaluronidase effect to local anesthetic action in ophthalmic surgeries.

PATIENTS AND METHODS: written informed consent was obtained from the patients to participate in this randomized prospective double blinded study in Ibn El Haitham specialized ophthalmology hospital from the period of September 2018 till January 2019 scheduled for retrobulbar / peribulbar block for elective cataract, glaucoma, or eye muscle surgery.

Patients refusal, patients with emergency eye surgery, corneal transplantation, retinal ablation, only eye patient, any patient with known sensitivity to any drugs given during the study or vitreous operations were excluded from the study.

All patients eye were blocked by a trained skilled anesthesiologist. The block done by local anesthetic with a 1:1 mixture of bupivacaine 0.50% and lidocaine 2%, with epinephrine 5 mg/mL added to the injection at the medial canthus. The volume of the initial block was adjusted according to the lean body weight:70 kg and below given 6 mL of the mixture, patients between 70 and 80 kg was given 7 mL of the mixture, and 8 mL of the mixture for those with 80 kg and above.

The patients were randomly allocated to two groups; group C: control group; that given only the lidocaine, bupivacaine and adrenaline mixture.

The group H (hyaluronidase); given the mixture in addition to hyaluronidase 7.5 IU/mL.

Patient data were collected on sex, age, initial local anesthetic volume (mL), and the need for a supplementary block, The eye movements were checked after 10 min post injecting the local anesthetic solution. The patients were asked to move their eye and any Movements of the six extraocular muscles were recorded (superior/ inferior/lateral/medial rectus and superior/ inferior oblique) and scored 0–2 as the score 0 means no movement, score 1means partial movement, and score 2 when performing full movement of any of these six muscles.

Levator palpebrae and orbicularis oculi muscle movements (0-2). Consequently, were also recorded and noted, the maximum score of all eye movements was six and the minimum zero.

Statistical analysis: done by IBM SPSS program version 20 and Microsoft excel version 2010, the means were compared by t test methods significance between the two groups (C group and H group) were recorded when p value was less than 0.05.

RESULTS

The mean age of the C group was 60.5 ± 6 years, group H was 61.4± 5.9 years, and there was no significant differences between the groups as p value was 0.748.

There was 22 male and 28 female in group C and 23 male, 27 female in group H, there was no significant differences between the groups as p value was 0.697.

The initial volume of the block given in group C was 7.3±0.82 ml, while of group H 7.68 ± 0.71 ml, and there was no significant differences between the groups as p value was 0.125.

The patients that need supplementary top up during the operation was 9 patients in group C while 4 patients in group H, there was a significant differences between the C and H groups regarding the needs of supplementary top up as p value was 0.003 as shown in table 1.

Table 1: the comparison of the demographic data between the groups.

Group		N	Mean	Std. Deviation	Std. Error	P value
Age	C	50	60.560	6.055	0.856	0.748
	H	50	61.400	5.969	0.844	
Sex	C	50	M22 /F 28			0.697
	H	50	M23 / F27			
Initial Volume	C	50	7.360	0.827	0.117	0.125
	H	50	7.680	0.713	0.101	
Supplementary top up	C	50	Y9 / N41	0.388	0.055	0.003
	H	50	Y4 / N46	0.274	0.039	

T test was significant when p value was < 0.05.

The mean extraocular muscle movement score was 0.54 + 0.73 in group C while in group H the mean extraocular muscle movement score was 0.28±.

0.6, there was a significant differences between the two groups as p value was 0.008 as shown in table 2.

The mean score of Levator palpebrae in group C was 0.32 = 0.55 and for group H was 0.22 = 0.418, there was a significant differences between the two groups as p value was 0.03 as shown in table 2.

The mean score of orbicularis oculi was 0.34± 0.62 in C group while 0.16 ± 0.468 in group H, there was a significant differences between the groups as p value was 0.003 as shown in table 2.

Table 2: comparison of the eye muscle movement between the group.

Group		N	Mean	Std. Deviation	Std. Error	P value
Extraocular muscle	C	50	0.540	0.734	0.104	0.008
	H	50	0.280	0.607	0.086	
Levator palpebrae	C	50	0.320	0.551	0.078	0.030
	H	50	0.220	0.418	0.059	
Orbicularis oculi	C	50	0.340	0.626	0.089	0.003
	H	50	0.160	0.468	0.066	

T test was significant when p value was < 0.05

DISCUSSION

The resulting data obtained from our study shows that the hyaluronidase addition to the mixture made a significant difference between the control and hyaluronidase group in regard to the needs of supplemental top up during the operation, as the number of patients needed in control group was 9 (18 %) as compared with hyaluronidase group (4 patient 8%) and this was statistically significant as p value was 0.003.

These results were similar to results seen in the Kallio et al (2001 Finland) as they showed that the hyaluronidase free group had a significant more patient need the top up then the hyaluronidase group.[8]

The akinesia performed after the block was noted in the patient and was recorded according to a score; the extra ocular muscle score was significantly lower in the hyaluronidase group as compared with control group as the p value was 0.008, the same was applicable to the Levator palpebrae muscle (p value 0.03) and Orbicularis oculi muscle (p value was 0.003) and this means that the hyaluronidase increase the severity of akinesia when added to the local anesthetic mixture.

This was seen in other studies ; as Kallio et al 18, Dempsey et al (Liverpool 1997),[18] as they show that the addition of the hyaluronidase to the local anesthetic mixture will make the akinesia and successful blockage faster and more successful as compare to hyaluronidase free solution.[8,18]

But Crawford et al,[17] shows that there was no benefit in making akinesia to the muscle movement of the eye from adding the hyaluronidase to the local anesthetic mixture.

We conclude that Adding the hyaluronidase to the local anesthetic mixture will cause less patient need for top up to achieve the anesthesia and akinesia.

Hyaluronidase addition will make the akinesia to the eye muscle more successful than does hyaluronidase free mixture.

There should more future study with more patients sample to ensure the result seen in this study.

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