Orbicular muscle akinesia in regional ophthalmic anaesthesia with pH-adjusted bupivacaine: effects of hyaluronidase and epinephrine

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The success rate and duration of lid akinesia after adding hyaluronidase and/or epinephrine to pH-adjusted bupivacaine was examined in a double-blind fashion in patients undergoing cataract surgery under local anaesthesia. A two-injection-site technique was used. For globe akinesia all patients (n = 120) received an inferolateral intraconal injection (3 ml) of pH-adjusted bupivacaine 0.75% and hyaluronidase. Lid akinesia was obtained with a medial extraconal injection (3.5 ml) of alkalized bupivacaine with or without an adjunct. The patients were randomized to four groups as follows: a medial injection of plain bupivacaine (n = 31), with added hyaluronidase (n = 30), with added epinephrine (n = 29) or with both epinephrine and hyaluronidase (n = 30). The final solutions had a pH of 6.7. Lid akinesia was supplemented with periosteal injections if needed. The degree of akinesia from clinical assessment was graded from 0–2 and also measured with electromyography at ten minute intervals for 30 min after surgery, and three hours after the block. The least satisfactory result ($P < 0.01$) and shortest duration of the lid block ($P < 0.05$) was obtained with plain pH-adjusted bupivacaine. No differences in the success rate or duration of the block among the other groups were seen. The duration of the block was longer in the epinephrine groups

than in the two other groups ($P < 0.01$) and longer in the epinephrine and hyaluronidase group than in the group receiving only hyaluronidase ($P < 0.05$). We conclude that the best initial results and longest duration of blocks were shown in the groups receiving epinephrine or epinephrine and hyaluronidase.

Cette étude à double insu évalue le taux de succès et la durée de l'akinésie de la paupière après l'ajout d'hyaluronidase et/ou d'épinéphrine à la bupivacaine à pH ajusté chez des patients soumis à une chirurgie de la cataracte sous anesthésie locale. Une technique à deux sites d'injections est préconisée. Pour l'anesthésie du globe oculaire, tous les patients (n = 120) reçoivent une injection inférolatérale dans le cône musculaire (3 ml) d'une solution à pH ajusté de bupivacaine 0,75% et d'hyaluronidase. L'akinésie palpébrale est obtenue par une injection médiane hors du cône (3,5 ml) de bupivacaine alcalinisée avec ou sans ajout. Les patients sont randomisés de la façon suivante en quatre groupes: injection médiane de bupivacaine simple (n = 31), avec hyaluronidase (n = 30), avec ajout d'épinéphrine (n = 29) ou épinéphrine associée à l'hyaluronidase (n = 30). Le pH final de chaque solution est ajusté à 6,7. L'akinésie palpébrale est complétée par des injections périostées au besoin. Le degré d'akinésie est coté de 0–2 et mesuré à l'électromyographie à des intervalles de dix minutes pour 30 minutes, après la chirurgie et trois heures après le bloc. Le résultat le moins satisfaisant ($P < 0,01$) et la durée la plus courte du bloc palpébral ($P < 0,05$) survient avec la bupivacaine simple à pH ajusté. Pour le taux de succès ou la durée du bloc, on ne trouve pas de différences entre les autres groupes. La durée du bloc est plus longue dans le groupe épinéphrine que dans les deux autres groupes ($P < 0,01$) et plus longue dans le groupe épinéphrine-hyaluronidase que dans le groupe ne recevant que de l'hyaluronidase ($P < 0,05$). Nous concluons que les meilleurs résultats initiaux et les plus longues durées d'action se retrouvent dans les groupes recevant de l'épinéphrine ou de l'épinéphrine associée à l'hyaluronidase.

Key words:

ANAESTHETIC TECHNIQUES: regional, peribulbar, retrobulbar;

ANAESTHETICS, LOCAL: bupivacaine;

SURGERY: ophthalmic.

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For adequate regional ophthalmic anaesthesia peroperative analgesia, akinesia of both the eye and the orbicular muscle are required. Poor lid akinesia can endanger surgery by increasing the pressure of the globe in an open eye.

In clinical practice, lid paralysis seems to wear off considerably faster than globe akinesia. Supplementation is needed if surgery is delayed or if the function of the orbicular muscle recovers during prolonged and complicated surgery. There are few studies on the duration of orbicular muscle akinesia.¹⁻³ The evaluation of the block is often poorly separated from that of globe akinesia.^{4,5} Only three reports were found which examined the effect of hyaluronidase or epinephrine on lid block.⁶⁻⁸

The aim of this study was to investigate the effect of hyaluronidase and epinephrine on (1) the success rate and (2) the duration of lid akinesia produced by pH-adjusted bupivacaine 0.75%.

Methods

With the approval of the Ethics Committee and the informed consent of the patients, 120 patients scheduled for elective cataract surgery under local anaesthesia were enrolled randomly into four groups. The allocation to treatment groups was stratified by sex with the same female/male ratio in each group.

The patients received oral diazepam 0–10 mg (depending on age) as premedication followed by fentanyl 50 µg *iv* two to three minutes before the peribulbar block. A two-injection-site technique was used. After topical anaesthesia with oxybuprocaine, the first inferolateral intracanal injection of 3 ml pH-adjusted bupivacaine 0.75% with hyaluronidase (Table I, mixture #2) was administered through the conjunctiva to all patients with a 31 mm 27-G sharp needle (Visitec Company, FL, U.S.).⁹ The patients were in the primary gaze position. Gentle digital massage was applied for one minute after the injection.

The second transconjunctival injection (3.5 ml) was made from the nasal corner of the caruncle with a 12 mm 30-G needle (Microlance®, Becton Dickinson, Ireland). This injection was directed medially to the medial rectus muscle. One of the four local anaesthetic mixtures (Table I) was prepared immediately before the injection by an operating room nurse and was given at room temperature. The anaesthetist (JS) was unaware of the mixture chosen. Ocular compression (Autopressor®, Storz, Germany) was applied for ten minutes at a pressure of 25 mmHg.

Patients were asked by a nursing assistant who was unaware of the local anaesthetic used to move their eyes, using maximal effort in each of the four directions (superior, inferior, medial and lateral), and then to open their eyelids and to squeeze them together. She measured the

TABLE I Anaesthetic mixtures used in the study

1 (Group B) pH-adjusted bupivacaine (n = 30)			
Bupivacaine 0.75%	20	ml	
Sodium bicarbonate 14 mg · ml ⁻¹	0.22	ml	
Sterile water	1	ml	to 21.22 ml pH 6.7
2 (Group BH) pH-adjusted bupivacaine with hyaluronidase (n = 30)			
Bupivacaine 0.75%	20	ml	
Sodium bicarbonate 14 mg · ml ⁻¹	0.2	ml	
Hyaluronidase 150 IU · ml ⁻¹	1	ml	to 21.2 ml pH 6.7
3 (Group BE) pH-adjusted bupivacaine with epinephrine (n = 29)			
Bupivacaine 0.75%	20	ml	
Sodium bicarbonate 14 mg · ml ⁻¹	0.25	ml	
Epinephrine 1 mg · ml ⁻¹	0.1	ml	
Sterile water	0.9	ml	to 21.25 ml pH 6.7
4 (Group BHE) pH-adjusted bupivacaine with hyaluronidase and epinephrine (n = 31)			
Bupivacaine 0.75%	20	ml	
Sodium bicarbonate 14 mg · ml ⁻¹	0.22	ml	
Hyaluronidase 150 IU · ml ⁻¹	1	ml	
Epinephrine 1 mg · ml ⁻¹	0.1	ml	to 21.32 ml pH 6.7

TABLE II Scoring system

Akinesia of extraocular muscles including the levator muscle

- 0 = 0–1 mm movement in one or two main directions or 0–4 mm movement in levator muscle.
 1 = 2 mm movement in any main direction or 1 mm movement in more than 2 directions or >4 mm movement in levator muscle.
 2 = >2 mm movement in any main direction or 2 mm movement in 2 or more main directions.

Akinesia of orbicular muscle

- 0 = Complete akinesia.
 1 = Partial movement in either or both eyelid margins.
 2 = Pronounced movement in either or both eyelid margins.

opening capacity of the eye (indicating levator muscle force) and the movements of the extraocular muscles in all four main directions (rectus muscle movements) in mm at 15 and 30 min after the initial injections unless complete akinesia had been achieved earlier. The force used to squeeze the eyelids together was graded at 10, 20 and 30 min by the same study nurse and postoperatively by the ophthalmologist. The lids were held apart with fingers and the patient was asked to squeeze the eyelids together maximally. The estimation was made from both eyelid margins. The results were scored as shown in Table II. If globe akinesia was incomplete (Score 1 or 2) at 15 and 30 min, a supplemental injection (2 ml) was administered inferolaterally. If lid akinesia was inadequate, supplemental injections were given to the pe-

TABLE III Patient characteristics

	<i>B</i> (<i>n</i> = 31)	<i>BH</i> (<i>n</i> = 30)	<i>BE</i> (<i>n</i> = 29)	<i>BHE</i> (<i>n</i> = 30)
Age, yr	74 ± 8	74 ± 9	74 ± 9	73 ± 12
Sex (female/male)	18/13	18/12	18/11	18/12
BMI	25.9 ± 4.0	26.2 ± 4.2	26.1 ± 3.7	26.4 ± 4.3
Axial length, mm	24 ± 1	23.2 ± 1.2	23.3 ± 0.9	23.3 ± 1.1
Time 1, min	80 ± 24	65 ± 24	69 ± 22	77 ± 27
Time 2, min	116 ± 27	102 ± 24	105 ± 26	117 ± 34

Expressed as mean ± SD.

BMI = body mass index.

Axial length = axial length of the eye.

Time 1 = time from administration of anaesthesia to beginning of surgery.

Time 2 = time from administration of anaesthesia to end of surgery.

riosteum on the zygomatic bone (1.5 ml superotemporally and 1 ml inferolaterally) at 20 and/or 30 min and/or later.

In addition, orbicular muscle activity was examined electromyographically (EMG) immediately before and at 10, 20 and 30 min after block of both eyelids. Because of the cataract wound the postoperative and three hour measurements after the block were made only from the lower eyelid. A paediatric ECG surface electrode was attached first to the upper and then to the lower eyelid. The reference electrode was on the patient's nose, the ground electrode on the cheek. During the measurements, the patient was told to squeeze his or her eyelids as forcefully as possible.

Motor-unit action potentials were measured with a modified differential preamplifier (Anaesthesia and Brain Activity Monitor, Datex-Instrumentarium, Helsinki, Finland) and recorded on a strip recorder (paper speed 5 cm · sec⁻¹). The total number of both positive and negative spikes exceeding 10 mm during two seconds of maximal muscle activity were counted.

All patients were observed after the block and during surgery by an anaesthetist and monitored continuously with ECG and pulse oximetry and intermittently by non-invasive measurements of blood pressure. Two preblock and four postblock blood pressures and respective heart rates every five minutes after the block were recorded for each patient. Peroperatively, inspiratory (FI) and end-tidal (ET) concentrations of O₂ and CO₂ were also observed through an adaptor placed in the nostril. Intraoperatively an oxygen-enriched air flow (2 L : 8 L · min⁻¹, FI O₂ 0.25–0.35) was directed at the face of the patient to prevent rebreathing. For nervous and hypertensive patients, additional fentanyl, 25–50 µg, *iv* was given at the start of surgery.

The descriptive data are expressed as mean ± SD. Differences among the four groups were analyzed by Kruskal-Wallis one-way analysis of variance, while those within groups were studied by means of Friedman's two-

FIGURE 1 Mean of two systolic BP measurements preblock (pre), immediately after administration of the block (post), 5 min postblock (5'), 10 min postblock (10') and 15 min postblock (15') in each of the four study groups (B = bupivacaine, BH = bupivacaine hyaluronidase, BE = bupivacaine epinephrine and BHE = bupivacaine hyaluronidase epinephrine) ± 95% confidence limits of the mean.

way analysis of variance. For qualitative differences, the groups were compared using the chi-square test (differences among proportions). A *P* value of <0.05 was considered significant.

Results

The groups were similar in their demographic characteristics, and in the time of anaesthesia and surgery (Table III). After administration of local anaesthesia, the pH values of four samples of each bupivacaine mixture ranged from 6.7 to 6.8 (NS).

The mean systolic blood pressures were lower (*P* < 0.05) in all groups after the block, but there were no differences among the groups (Figure 1). Heart rates also decreased (*P* < 0.01) in all the groups except BHE (Figure 2).

No differences in globe akinesia were recorded between the study groups (Table IV).

TABLE IV Globe and orbicular muscle akinesia and pH of the final solutions

	B (n = 31)	BH (n = 30)	BE (n = 29)	BEH (n = 30)
<i>Globe akinesia</i>				
Initial success rate, at 15 min	84%	77%	66%	83%
Supplementation required, 15 min	5/31	7/30	10/29	5/30
Success rate at 30 min	97%	100%	100%	97%
Supplementation required, 30 min	1/31	-	-	1/30
<i>Lid akinesia</i>				
Initial success rate, at 10 min	39%	67%	65%	73%*
Initial success rate, at 20 min	35%	67%	72%	83%*
Supplementation required, 20 min	20/31	10/30	8/29	5/30*
Success rate at 30 min	81%	93%	97%	97%*
Supplementation required, 30 min or later	8/31	2/30	1/29	1/30*
Postoperative akinesia	26%	33%	55%	60%*
<i>pH</i>				
mean + SD	6.77 ± 0.03	6.72 ± 0.07	6.79 ± 0.02	6.78 ± 0.03

**P* < 0.05.

FIGURE 2 Mean of two heart rate measurements preblock (pre), immediately after administration of the block (post), 5 min postblock (5'), 10 min postblock (10') and 15 min postblock (15') in each of the four study groups. Abbreviations as in Figure 1.

Orbicular muscle akinesia was least satisfactory in the group receiving plain pH-adjusted bupivacaine at 10 ($P < 0.05$), 20 min ($P < 0.005$) and at 30 min ($P < 0.01$) after the initial block (this group also required supplementation more often at 20 and 30 min or later before surgery). The difference remained after surgery ($P < 0.05$), although the patients with lower initial success rates had been given additional periosteal injections more often. Immediately postoperatively, both lids showed full lid paralysis in 26% of the patients in Group B compared with 33% in Group BH and 55% and 60% in Groups BE and BHE, respectively. The duration of lid block lasted longer in the epinephrine groups than in the two other

FIGURE 3 EMG activity of the upper and lower eyelids in the four study groups in patients who did not require additional periosteal injections. B = bupivacaine group ($n = 10$), BH = bupivacaine hyaluronidase group ($n = 19$), BE = bupivacaine epinephrine group ($n = 20$) and BHE = bupivacaine hyaluronidase epinephrine group ($n = 24$). The total number of spikes ($\pm 95\%$ confidence limits of the mean) during a period of two seconds of maximal muscle activity before, 10 min, 20 min, 30 min, immediately postoperatively, and three hours after regional anaesthesia.

groups ($P < 0.001$) and in the BHE group than in the BH group ($P < 0.05$) (Table IV).

Figure 3 shows the electromyographic measurements recorded for all patients with adequate lid akinesia not requiring additional periosteal injections. In the upper lid, no differences were seen among the groups at any time although EMG activity was numerically highest in Group B. In the lower eyelid, EMG activity decreased more slowly in the Groups BE and BHE and remained low-

est in them postoperatively. The only difference among the four groups was recorded at 30 min in the lower eyelid, which in Group BE showed the most marked reduction in EMG activity ($P < 0.05$). When each group was compared for its preoperative, 10 min, 20 min and 30 min values (%) the only decrease in EMG activity was recorded in the lower lid in Group BE ($P < 0.05$). No increase was found in any group between the 30 min and three hour measurements.

Discussion

The pH-adjusted bupivacaine 0.75% was selected as the local anaesthetic agent because addition of bicarbonate has been shown to improve globe akinesia and to hasten the onset of the block.¹⁰ Bupivacaine also provides a better block at a concentration of 0.75% than at 0.5% or than etidocaine at 1–1.5%.⁹ Because epinephrine is deactivated in alkaline solution all the solutions in the study were prepared immediately before use.

The two-injection-site technique was chosen after a study by Ropo in which a nasal extraconal injection (4 ml etidocaine 1.5%) was shown to produce additional globe akinesia and also lid akinesia.¹¹ At the medial canthus, immediately above and below the medial ligament, there are "hernial orifices" of weak connective tissue leading to the upper and lower eyelids¹² through which anaesthetic solution is able to diffuse to the eyelid margins.

In regional ophthalmic anaesthesia, hyaluronidase has been shown to improve the quality of globe akinesia,^{13,14} both globe and orbicular muscle akinesia,⁸ and to accelerate the onset,^{6,15} but also to decrease the duration of globe akinesia.¹⁶ Epinephrine in contrast has been shown to prolong the duration of infiltration anaesthesia with bupivacaine.¹⁷

In the present study, both hyaluronidase and epinephrine increased the initial success rate of lid akinesia. The duration of the orbicular muscle block was not reduced by addition of hyaluronidase compared with plain pH-adjusted bupivacaine, although in both epinephrine groups the duration was longer. In globe akinesia, however, Chin and Almquist found the addition of hyaluronidase with or without epinephrine to bupivacaine 0.75% to provide a better and faster globe akinesia when compared with the addition of epinephrine. In that study the duration of globe akinesia was not longer when epinephrine was added to bupivacaine hyaluronidase solution.¹⁵ In the present study, several patients in the epinephrine group required additional inferolateral injections to complete the globe block. This may have increased the initial success rate and postoperative lid akinesia in Group BE, because the use of larger intraorbital volumes causes retrograde diffusion of a part of the local anaesthetic into the lids.¹⁸ No additive effects on the success

rate or duration of anaesthesia were found when hyaluronidase was added to epinephrine.

Attempts were made to estimate the orbicular muscle function quantitatively using the EMG. The same method had been used by Ropo,¹¹ who compared several techniques of orbicular muscle block. They observed differences among techniques but, in our study, the method was not able to differentiate lid paralysis. The EMG measurements during maximal activity seemed to be confused with upper and lower facial and more peripheral ocular muscle activity. Although a decrease in EMG activity was seen in all groups, the range of variation within each group was too broad to present any reliable differences. A similar result with EMG has been reported by Schimek *et al.* in a study in which different techniques of lid akinesia were compared.¹⁹ In that study, EMG activity was abolished only with the modified O'Brien block,²⁰ whereas with the Atkinson²¹ and van Lint techniques,²² the activity was diminished by about 20% and a wide variation of EMG activity was recorded in each group. It seems that in the two-site-injection technique, the anaesthetic spreads mainly to the thin portion of the orbicular muscle, leaving the more peripheral circular muscle fibres intact and so allowing muscle activity when the patient is urged to squeeze the eyelids maximally.

The addition of epinephrine to the local anaesthetic did affect heart rate or systolic blood pressure. The blood pressures in all groups and heart rates in all but the BHE group decreased after administration of the block. This seems to reflect the relief from anxiety experienced by the patients after administration of the block.

In conclusion, orbicular muscle block can be improved by adding either hyaluronidase and/or epinephrine to pH-adjusted bupivacaine 0.75%. The block lasts longer after addition of epinephrine or of both epinephrine and hyaluronidase. When a two-injection-site technique is used in which the medial injection partially blocks also the extraocular muscles, we recommend the addition of epinephrine and hyaluronidase to pH-adjusted bupivacaine to provide good quality of lid block and to accomplish adequate globe akinesia with low intraorbital volumes.

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