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Comparison of plain with pH-adjusted bupivacaine with hyaluronidase for peribulbar block

Fifty patients scheduled for cataract surgery under peribulbar block were randomised to receive either plain (pH 5.4) or pH-adjusted (pH 6.8 range 6.7–6.9) 0.75% bupivacaine. Hyaluronidase was added to both solutions prior to peribulbar block. The time of onset of akinesia of the globe and the need for supplementary injections were recorded by an independent observer. Patients who returned for surgery to the second eye received the alternative local anaesthetic solution for the second peribulbar block. The relative efficacy of the different anaesthetic solutions was compared in patients who underwent unilateral surgery (Group A, n = 50). In 12 patients (Group B) who underwent bilateral surgery, direct comparisons between eyes in the same patient were possible. In both groups of patients, eyes receiving peribulbar block with the pH-adjusted solution showed a shorter time to partial akinesia of the globe ($P < 0.05$). However, there was no difference between the solutions in the time to complete akinesia of the globe, but the number of supplementary injections required for an effective block with the pH-adjusted solution was increased. Onset time to akinesia of the lateral and superior rectus muscles was shortened in patients receiving the pH-adjusted solution but there were minimal effects on the medial and inferior recti.

Cinquante patients devant subir une extraction de cataracte sous anesthésie régionale rétrobulbaire participent à cette étude. Le

choix de l'agent anesthésique utilisé se fait au hasard et comporte la bupivacaine 0,75% avec pH à 5,4 (formule commerciale) ou bupivacaine 0,75% avec pH corrigé à 6,8 (valeurs variant entre 6,7 et 6,9). Quand un patient revient pour une chirurgie de l'autre oeil, le choix de l'anesthésique local est alterné. Dans tous les cas, de l'hyaluronidase est ajoutée à l'anesthésique local. Un observateur non informé de l'agent utilisé note le temps nécessaire pour obtenir une akinésie de l'oeil, ainsi que le besoin d'injections supplémentaires. L'efficacité des deux solutions anesthésiques est comparée entre les patients soumis à une seule chirurgie (Groupe A, n = 50). Chez 12 patients subissant deux interventions (Groupe B), des comparaisons entre les yeux du même patient sont faites. Dans les deux groupes de comparaisons, la solution avec pH corrigé permet un début plus rapide d'akinésie partielle du globe oculaire ($P < 0,05$). Cependant, le temps nécessaire pour obtenir une akinésie complète est comparable avec une solution ou l'autre. L'utilisation de la solution à pH corrigé entraîne un plus grand nombre d'injections supplémentaires. Elle permet un début plus rapide d'akinésie des muscles droits supérieur et latéral, mais a peu d'effets sur les muscles droits interne et inférieur.

Key words

ANAESTHETICS, LOCAL: bupivacaine, hyaluronidase, pH-adjustment;
ANAESTHETIC TECHNIQUES: regional, peribulbar;
SURGERY: ophthalmological.

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Surgical anaesthesia with accompanying akinesia of the globe and eyelids (i.e., no detectable movement in response to stimulation) are the objectives when regional anaesthesia is performed for eye surgery. Globe akinesia may be achieved with small volumes of local anaesthetic using retrobulbar block with drug placement near the apex of the orbit. However, this technique carries a small but significant risk of major complications.^{1,2} More anterior placement of larger volumes of anaesthetic, by one or more injections, is the basis of peribulbar blocking which reduces the risk of brainstem anaesthesia or damage to the optic nerve.¹ Koornneef^{3,4} has stressed that orbital connective tissues are important in determining how local anaesthetics spread around the globe. Anatomical differences may account for the delayed or incomplete akinesia seen with peribulbar block in some patients perhaps due to

failure of anaesthetic spread to the orbital apex. Measures to improve spread and nerve penetration have included increasing the amount of drug in the non-cation form by alkalinisation,⁵ and adding hyaluronidase to the anaesthetic solution. Hyaluronidase improves onset time and enhances akinesia of extraocular muscles in retrobulbar block.⁶⁻⁸ Depolymerisation of hyaluronic acid by hyaluronidase leads to liquefaction of the gelatinous interstitial barrier,⁹ but there is no evidence for increased spread of solution across fascial planes.^{10,11} In addition, above an optimum dose of hyaluronidase, there is no increase in effect.¹¹

Local anaesthetic potency (degree of conduction block) depends on the concentration of charged ions at the sodium channel. This is determined by the quantity of drug, its volume of distribution within each compartment, drug kPa, local pH and lipid solubility of the free base which crosses the axonal membrane. Zahl *et al.*,⁵ in their study of regional anaesthesia for cataract extraction surgery, found highly significant differences in onset time and a reduced requirement for repeat injections when pH-adjusted bupivacaine with hyaluronidase was compared with plain bupivacaine with hyaluronidase for peribulbar blocks in different patients. However, this may reflect differences between patients, rather than the anaesthetic solutions used. Therefore, we have compared plain and pH-adjusted bupivacaine 0.75% solutions with hyaluronidase in different patients and in the same patient, using a similar design to that of Zahl *et al.* However, their patients were sedated with fentanyl and droperidol and their technique of peribulbar block was different in respect to placement of the second injection. Furthermore, we prepared our solutions in polypropylene syringes in contrast to Zahl *et al.* who appear to have used glass vials.

Methods

Approval for this study was obtained from the Gimbel Eye Centre Ethics Committee and patients gave written informed consent. The only exclusion criterion was previous vitreoretinal surgery. No patient received sedation before or during the procedure. Fifty patients (Group A) were randomised to receive either the pH-adjusted (24 patients) or plain solution (26 patients). Twelve of the Group A patients returning for surgery to the opposite eye received the alternative anaesthetic mixture and their second block was compared with their first in a separate analysis (Group B).

The local anaesthetic solutions were prepared as either plain bupivacaine 0.75% (60 ml plus 0.3 ml sterile water – resultant pH 5.4) or pH-adjusted bupivacaine 0.75% (60 ml plus 0.3 mmol (mEq) of 8.4% sodium bicarbonate – resultant pH 6.8, range 6.8–6.9). To ensure stability of PCO₂ and pH,¹² the solutions were prepared in polypropylene syringes not more than five hours before

TABLE 1 Incidence of failed block (score <8) at 20 min. Initial eye blocks all patients *n* = 50

	Rectus activity		Total
	Present	Absent	
Plain	9	17	26
pH-adjusted	6	18	24
Total	15	35	50

use. The pH of each solution was measured immediately after preparation using a Corning 106 pH meter, and then the solution was left capped at room temperature. During the five-hour period there were no changes in pH or PCO₂. Immediately before peribulbar block, 1 ml of hyaluronidase (150 units) was added to 10 ml of local anaesthetic solution.

All peribulbar blocks were performed by the same anaesthetist who was unaware of the choice of anaesthetic solution as was the observer. After prior topical anaesthesia of the conjunctiva with proparacaine 0.5 %, a 5 ml injection of the local anaesthetic solution was made through the inferotemporal conjunctival fornix. The needle tip was advanced in a curvilinear fashion to reach but not pass the sagittal plane of the lateral limbus at a depth of 1" from the inferior orbital rim. A second medial compartment injection of 5 ml of the same anaesthetic solution was made at the medial canthus, medial to the caruncle. With needle and syringe perpendicular to the frontal plane of the face, the needle tip was advanced to a depth of 1" from the surface entry point. To ensure that the initial volume of injectate had time to pass posteriorly, the second injection was performed four minutes after the first. Time to complete akinesia of the four recti was recorded by the observer every minute from the initial inferotemporal injection. Continuous digital pressure was applied over the closed eyelids after each injection except when observations were being made. Movements of the globe were scored according to the method described by Nicoll *et al.*⁷ where 0 represents full movement of the associated rectus muscle, 1 partial movement of the associated rectus muscle and 2 complete paralysis of the associated rectus muscle. Scoring continued until complete akinesia was present (a total of 8) or until 20 min had elapsed. A total score of 4 was designated as partial akinesia. All combinations of scores for muscle weakness were included from complete paralysis of any two rectus muscles to partial paralysis of all four recti. Supplemental injections were given to patients who failed to develop extraocular muscle akinesia (total score <8) after 20 min and to patients (total score 8), who retained sufficient orbicularis oculi muscle function to hinder surgery. Time to complete akinesia was recorded separately by muscle

TABLE II Requirement for anaesthetic supplement at 20 min. Initial eye blocks all patients $n = 50$

	Supplement		Totals
	Yes	No	
Plain	9	17	26
pH-adjusted	13	11	24
Total	22	28	50

TABLE III Time to complete rectus muscle akinesia (score 8). Initial eye blocks all patients $n = 35^*$

	Number	Minutes	SD
Plain	17	10.7	4.8
pH-adjusted	18	8.5	2.7

Differences not significant.

*Total number of patients = 50, but 15 patients had a score < eight.

for each of the patients. Group A comprises data from initial eye blocks in all patients. Group B were patients who returned for surgery to the opposite eye. No evidence of order-treatment interaction was found in this group, with respect to their first injection, so they were analysed as a completely randomised design. Differences between the onset times for akinesia were evaluated by Student's *t* test.

Results

All study patients (Group A) developed a satisfactory block for cataract surgery either before or after supplementation. Twenty-six patients received the plain, and 24 the pH-adjusted solution. Analysis of the first block compared with the second in Group B patients showed no significant difference in any of the measured variables as compared with Group A. Therefore, only their first block is included for further analysis.

Twenty-two patients were supplemented after the 20 min point, 15 patients because of failure to develop akinesia of the extraocular muscles and seven because of persisting orbicularis oculi muscle activity as judged by the observer. These seven patients all received the pH-adjusted solution (Tables I, II). Patients who failed to achieve complete extraocular muscle akinesia by 20 min (score of 8) were recorded as failed blocks. The incidence of a failed block at 20 min between treatments was not different for the group overall nor for any individual muscle.

Onset time to complete globe akinesia in those with successful blocks was reduced in the pH-adjusted group ($P < 0.05$), but only attained significance at the point of partial akinesia – Tables III, IV. The analysis of individual recti for Group A is shown in Table V. The medial rectus

TABLE IV Time to partial rectus akinesia (Score 4). Initial eye blocks in all patients $n = 47^*$

	Number	Minutes	SD
Plain Bp	24	6.9	1.98†
pH-adjusted	23	5.7	1.76†

*Total number of patients = 50, but three patients had a score < four.

†Student's *t* test ($P < 0.05$).

TABLE V Time in min (SD) to akinesia by anaesthetic for the individual rectus muscles

	Rectus muscle			
	Medial	Lateral	Superior	Inferior
Plain	$n = 25$ 6.3 (2.5)	$n = 21$ 9.2 (4.1)*	$n = 20$ 9.8 (4.4)*	$n = 24$ 8.9 (4.0)
pH-adjusted	$n = 24$ 5.9 (2.0)	$n = 22$ 6.5 (2.7)*	$n = 18$ 6.6 (1.9)*	$n = 21$ 8.3 (3.4)

*Student's *t* test ($P < 0.05$).

muscle was most rapidly blocked for the group as a whole. Onset time to akinesia was reduced in the pH-adjusted group for the superior and lateral rectus muscles ($P < 0.05$).

When all injections were complete there was adequate analgesia and lid akinesia in all patients. No supplementary injections were required once surgery had commenced and all patients were comfortable and had no complaints on follow up.

Discussion

In this study pH-adjusted bupivacaine shortened the onset time of peribulbar block but was associated with excessive orbicularis muscle activity and a requirement for increased supplementation compared with the plain solution. In contrast, Zahl *et al.*⁵ observed both a shortened onset time and a reduced need for supplementary injections in patients who received pH-adjusted bupivacaine compared with plain bupivacaine for peribulbar block. Although there were differences in anaesthetic technique between the two studies, for example no patients received any sedatives in this study, this does not explain the similar incidence of failed block in the patients receiving plain bupivacaine, 9 out of 26 in our study compared with 5 out of 17 in Zahl *et al.*'s study. Interpatient variation does not seem a likely explanation, since we observed no difference in those patients who received two blocks compared with the randomised patients receiving a single block. We speculate that a more likely cause for the inconsistency relates to the stability of the pH-adjusted solution. Although no macroscopic precipitation in this solution

occurred after storage for up to five hours in the polypropylene syringes, microscopic precipitation or binding of bupivacaine to polypropylene leading to injection of a reduced concentration of drug could account for the different failure rates: 13 of 24 compared with 1 in 18 of Zahl *et al.* after three hours storage of pH-adjusted solution in glass. Investigations of the efficacy of pH-adjusted local anaesthetics for epidural anaesthesia have also yielded conflicting results.¹³⁻¹⁵ Ackerman and Juneja¹⁶ maintain that the PCO₂ of a freshly buffered local anaesthetic solution is the critical factor determining onset time. However, we observed no change in PCO₂ of our solutions.

The pattern of blocking of individual recti suggests that the spread of anaesthetic from the initial inferotemporal peribulbar injection is in a horizontal plane, since the medial and lateral rectus muscles were the most rapidly blocked of all the recti. The pH-adjustment of local anaesthetic shortened the time to akinesia of the lateral and superior recti but not the medial or inferior recti. This may reflect differences in the diffusion barrier to the nerve supply in these muscles.

The similar variation in onset times of peribulbar block between eyes in the same patient and between eyes in different patients was unexpected but explicable if the pH-adjusted bupivacaine was of variable concentration. The anatomy and diffusion characteristics of connective tissue from different orbits in the same patient is likely to be similar. A view consistent with the predictions made by Koornneef.⁴ We conclude that pH-adjustment of bupivacaine 0.75%, while shortening onset time, may be associated with loss of bupivacaine from solution and an increased failure rate in peribulbar block.

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