Anesthesiology
72:230–232, 1990

pH-Adjusted Bupivacaine and Hyaluronidase for Peribulbar Block

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The onset of akinesia of the extraocular muscles was assessed after peribulbar block with a plain or pH-adjusted solution of 0.75% bupivacaine and hyaluronidase. Thirty-five patients were randomly assigned to receive either 0.75% bupivacaine with hyaluronidase 15 units/ml (pH 5.45 ± 0.12) or the same pH-adjusted solution (0.15 mEq sodium bicarbonate per 30 ml of 0.75% bupivacaine to give a final pH of 6.82 ± 0.09) in a double-blind, prospective manner. Onset of akinesia was determined to the nearest minute. Supplemental injections were given after 20 min in the event of incomplete akinesia. The group receiving pH-adjusted bupivacaine had a statistically faster onset time for complete akinesia than did the control group (5.3 ± 1.2 min *vs.* 14.3 ± 2.3 min, respectively; $P < 0.001$). Five of 17 patients in the control group required a supplemental injection, whereas only one of 17 patients in the treatment group had a supplemental block at 20 min ($P < 0.05$). Thus, pH adjustment of a solution of bupivacaine and hyaluronidase with sodium bicarbonate hastens the onset time and improves the initial success rate of peribulbar block. (Key words: Anesthesia: ophthalmic. Anesthetics, local: bupivacaine; lidocaine. Anesthetic techniques: peribulbar, retrobulbar. Surgery: ophthalmic.)

BUPIVACAINE, in a concentration of 0.75%, may be used as a sole agent for retrobulbar anesthesia.[1] Disadvantages of bupivacaine include a slow and variable onset of anesthesia and akinesia.[2,3] Hyaluronidase,[1,4] lidocaine,[1,5] or mepivacaine[1,6] are commonly added to improve the onset of retrobulbar anesthesia with bupivacaine. A mixture of bupivacaine and lidocaine with hyaluronidase is commonly used for retrobulbar anesthesia.

Peribulbar anesthesia has been advocated to decrease the complications associated with retrobulbar anesthesia.[7] In contrast to retrobulbar anesthesia, no attempt is made to redirect the needle behind the eye and enter the muscle cone. Thus, a retrobulbar block is an intraconal technique, whereas the peribulbar block is extraconal. Advantages include avoidance of retrobulbar hemorrhage, optic nerve trauma, and perhaps lack of brain stem anesthesia. Disadvantages of peribulbar anesthesia include delayed and inconsistent onset of anesthesia. In a previous study we demonstrated that pH adjustment of a mixture of lidocaine and bupivacaine with sodium bicarbonate improved onset time and spread of peribulbar anesthesia.[8]

Other studies have shown that pH adjustment of bupivacaine improves the onset of brachial plexus anesthesia.[9] To our knowledge, the use of bupivacaine for peribulbar anesthesia has not been reported. We undertook a double-blind, prospective, randomized study to determine if a pH-adjusted 0.75% bupivacaine–hyaluronidase solution compared with a non-pH-adjusted solution had a faster onset time and improved akinesia of the extraocular muscles when used for peribulbar anesthesia.

Materials and Methods

After approval of the Long Island College Hospital Institutional Review Board, 35 patients gave written informed consent for this study. All patients were scheduled for elective intraocular surgery with regional anesthesia and monitored anesthesia care. The only exclusion criterion was prior vitreoretinal surgery. Patients were randomly divided into two groups to receive a peribulbar injection from one of two solutions: B-P1 = 10 ml of 0.75% (plain) bupivacaine (Astra, Westborough, Massachusetts) or B-pH = 10 ml of 0.75% bupivacaine drawn from a 30 ml vial to which 0.15 mEq of bicarbonate was added. To each 10 ml syringe 150 units of hyaluronidase was added (Wyeth Labs, Philadelphia, Pennsylvania). Solutions were prepared by an operating room nurse no more than 3 h before use. Patients received 50–100 μg of fentanyl and 0.5 mg of droperidol iv 5–10 min prior to the peribulbar block.

Anesthetics (8–9 ml) were administered by the first author who was unaware of the mixture chosen. One injection was just above the inferior orbital rim in the inferotemporal quadrant and the second just lateral to the supratrochlear notch with a 25-G, 1.5-inch needle inserted past the equator of the globe. After the block each patient had digital massage of the eyelids with gauze for 2 min. Extraocular muscle movement was evaluated in each quadrant at 1-min intervals for the first 20 min. The block was considered satisfactory when akinesia occurred (defined as movement of less than 1 mm). In the event of incomplete akinesia at 20 min, a supplemental injection (with the same mixture) was given. Adequate analgesia

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Received from the Long Island College Hospital, Brooklyn, New York, Mount Sinai School of Medicine, New York, New York, and State University of New York Health Science Center, Brooklyn, New York. Accepted for publication August 31, 1989. Presented in part at the 63rd Annual Congress of the International Anesthesia Research Society, Orlando, Florida, March 1989.

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was determined by the lack of a patient response or complaint to incision of the conjuctiva. The adequacy of the lid block was assessed by the surgeon also unaware of the anesthetic used.

During the course of the study five vials representative of the lots of bupivacaine used were selected. Later the bupivacaine and hyaluronidase (with or without bicarbonate) were mixed together as described to simulate the clinical setting. The *p*H of the resulting mixtures was measured by a Beckman model 4500 *p*H meter.

Differences between the onset times of akinesia between groups were evaluated by a Student's *t* test. The need for supplemental injections was compared among groups by the Fisher exact test. A *P* of less than 0.05 was used to reject the null hypothesis.

Results

Seventeen patients received B-P1 and 18 patients received B-*p*H. Both groups had similar demographic characteristics in terms of age and sex. Mean *p*H values (±SEM) and volume of initial injectate used are shown in table 1. The number of patients needing supplemental blocks at 20 min are also shown in table 1. Patients receiving plain bupivacaine had a higher need for supplementation, which was statistically significant ($P < 0.05$).

The mean time to akinesia in all quadrants (±SEM) is presented in figure 1. The B-*p*H group had a faster onset time to complete extraocular muscle akinesia than the B-P1 group (5.3 ± 1.2 *vs.* 14.3 ± 2.3 min, respectively; $P < 0.001$). All patients had adequate analgesia and lid akinesia for surgery. No patient required further supplemental local anesthetic injections once surgery started.

Discussion

The results of our study demonstrate that *p*H adjustment of a 0.75% bupivacaine–hyaluronidase solution results in a more rapid onset of block when used for peribulbar anesthesia. This is in agreement with the results of our previous study.[8] The onset time of the *p*H-adjusted bupivacaine under investigation was comparable to the onset of akinesia with the *p*H-adjusted lidocaine–bupivacaine mixture used in that study. Because we did not randomly compare *p*H-adjusted bupivacaine to *p*H-adjusted lidocaine–bupivacaine in this study, no claims are made to the superiority of either solution.

TABLE 1. Final *p*H and Need for a Supplemental Injection

	B-P1	B-*p*H
*p*H	5.45 ± 0.12	6.82 ± 0.09
Volume of injectate (ml)	8.4 ± 0.12	8.6 ± 0.21
Supplemental block	5/17	1/18*

* $P < 0.001$, compared with patients receiving plain bupivacaine.

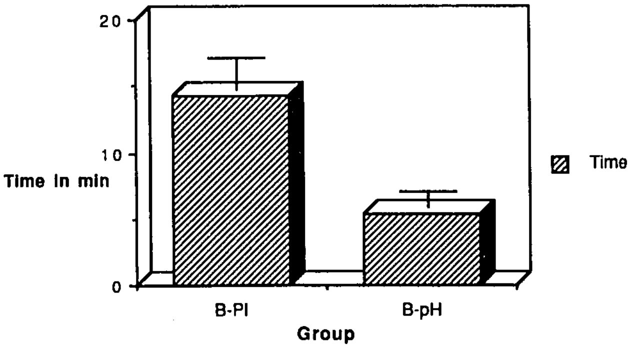

FIG. 1. Onset times for complete akinesia (mean ± SEM) in minutes for both groups. The *p*H-adjusted bupivacaine (B-*p*H) had a statistically faster onset time to complete akinesia when compared with the plain bupivacaine (B-P1).

Depending on the *p*H, local anesthetic drugs exist in various ratios of cation to noncation concentrations. The cation form is thought to be the active structure of the local anesthetic.[10] However, it is believed that local anesthetic molecules, in their noncation form, penetrate nerve membranes more quickly.[11] Hence, *p*H adjustment of a local anesthetic solution should increase the concentration of the noncation form of the drug. This in turn is thought to promote quicker neural membrane penetrance.

A variable that deserves discussion relates to our methodology. Between 8 and 9 ml of anesthetic was given initially. This may account for a 12.5% difference in local anesthetics given. The volume was adjusted in each patient, based upon the size of the orbit, to avoid significant proptosis of the eye. The mean volumes of local anesthetic used were statistically equivalent in each group. Because the identity of the solution was unknown, no bias should have been introduced to either group by this variation.

Hilgier reported faster onset of brachial plexus block with a *p*H-adjusted 0.5% bupivacaine–epinephrine solution.[9] In contrast, Bedder *et al.* reported conflicting results.[12] This may be due to the fact that the first study involved a more acidic bupivacaine solution with epinephrine.[13] Hyaluronidase has been shown to be highly efficacious in terms of improved onset of retrobulbar anesthesia.[14] Consequently, it is our customary practice to use it as an adjuvant to peribulbar anesthesia. Hyaluronidase has not been shown to be of benefit in epidural[15] or other regional blocks.[16] Hyaluronidase depolymerizes hyaluronidic acid and theoretically promotes spread of local anesthetic. Therefore, another possible reason for our favorable results is that *p*H adjustment may improve the activity of the hyaluronidase enzyme.

Reduction of the onset time for extraocular muscle blockade resulted in a decreased need for supplemental peribulbar injections at 20 min. This has three practical clinical implications. First, avoidance of secondary injections reduces the likelihood of complications related to needle trauma of the globe or hemorrhage. Second, supplemental injections increase the volume of local anesthetic in the orbit. This ultimately increases overall forward pressure on the eye, which makes surgery difficult. Finally, improved success with the primary injections should make the peribulbar technique more popular as an alternative to retrobulbar anesthesia. In conclusion, *p*H adjustment of a 0.75% solution of bupivacaine and hyaluronidase with sodium bicarbonate dramatically shortens the onset of peribulbar anesthesia.

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