Hyaluronidase and peribulbar block

G. A. DEMPSEY, P. J. BARRETT AND I. J. KIRBY

Summary

We have assessed the effect of two concentrations of hyaluronidase on the quality of peribulbar block, using a low volume, single injection technique. We studied 200 patients undergoing elective intraocular surgery, allocated randomly to one of three groups. Group 1 (n = 50) received peribulbar block with 5 ml of a 1:1 mixture of 0.5% plain bupivacaine and 2% plain lignocaine. Group 2 (n = 75) received this solution supplemented with hyaluronidase 50 iu ml⁻¹. Group 3 (n = 75) received the same solution supplemented with hyaluronidase 300 iu ml⁻¹. Lack of ocular motility was considered to be the only objective sign of successful block and movement of each rectus muscle was scored at 1-, 5- and 10-min intervals. If the block was successful at 5 min, the 10-min score was omitted. If the block was unsuccessful at 5 min, a second injection of 2% lignocaine 3 ml was given and additional assessments performed at 5-min intervals. At 1 min, ocular motility scores were significantly lower in group 3 compared with the control group (P < 0.05). The incidence of satisfactory block at 5 min was increased in both groups given hyaluronidase (group 2, P < 0.05; group 3, P < 0.001). There were no significant differences between groups 2 and 3 with respect to quality of block at 5 min. Hyaluronidase in both concentrations improved the quality of peribulbar block at 5 min, and when used in a concentration of 300 iu ml⁻¹, also improved the speed of onset of block. (Br. J. Anaesth. 1997; 78: 671–674).

Key words


Peribulbar block provides good quality local anaesthesia for intraocular surgery, combining low morbidity with high efficacy.¹ Hyaluronidase is thought to promote the spread of local anaesthetic solutions by hydrolysing glycosidic bonds within the hyaluronic acid which forms the interstitial barrier.² Its efficacy has been proved when used for retrobulbar block,³ However, its advantage in peribulbar block is less clear, with some studies claiming no beneficial effect⁴ and others reporting improved quality of block.⁵⁻⁷ Those studies claiming no beneficial effect have used varying concentrations of hyaluronidase, up to 150 iu ml⁻¹, and studied relatively few patients. More recently, pH-adjusted solutions containing hyaluronidase have been used to some effect.⁸

We postulated that the uncertainty relating to the effect of hyaluronidase on peribulbar block may result in part from insufficient numbers of patients studied and also from the use of inadequate concentrations. Therefore, we have performed a large, randomized, controlled study to assess the effect of two concentrations of hyaluronidase on the quality of peribulbar block.

Patients and methods

After approval from the local Ethics Committee and informed consent, we studied 200 unpremedicated patients, ASA I, II or III, undergoing elective intraocular surgery under local anaesthesia. Patients were allocated randomly to one of three groups: group 1 (n = 50) received peribulbar block with 5 ml of a 1:1 mixture of 0.5% plain bupivacaine and 2% plain lignocaine; this group served as a control. Group 2 (n = 75) received the same volume of solution supplemented with hyaluronidase 50 iu ml⁻¹. Group 3 (n = 75) received the same solution supplemented with hyaluronidase 300 iu ml⁻¹.

Before the block, a vein was cannulated and monitoring of heart rate, oxygen saturation and non-invasive arterial pressure was commenced in all patients. Topical anaesthesia to the infraorbital skin was provided by EMLA cream applied at least 1 h before surgery, and to the conjunctiva by 0.4% oxybuprocaine drops applied immediately before performing the block.

All blocks were performed by the same investigator using a low volume (5 ml), single transcutaneous inferolateral injection technique, and a standard 25-mm, 23-gauge needle, as described by Apel and Woodward.¹⁰ With the gaze fixed straight ahead in the primary position, the injection site was identified at the junction of the lateral one-third and medial two-thirds of the inferior orbital rim. The direction of needle insertion was slightly medial and cephalad, with the tip of the needle being elevated towards the end of injection. Immediately after injection, a McIntyre weight (mercury-filled bag)
was applied to the closed eye to promote spread of local anaesthetic and softening of the globe. Reduction of ocular motility was considered to be the only reliably reproducible sign of successful block; movement of the superior, inferior, medial and lateral recti were scored by an observer blinded to the solution used, in a manner similar to that described by Nicoll and colleagues.4

Movements were scored as: normal = 2, reduced = 1 and akiniesia = 0, giving a maximum aggregate score for the four muscles of 8. Ocular motility was assessed at 1-, 5- and 10-min intervals and a score of 4 or less, from reduced movements in all directions, was taken to indicate successful block. If a successful block was achieved at 5 min, the 10-min score was omitted. If, however, the block was unsuccessful at 5 min, supplementary injection of 2% plain lignocaine 3 ml was administered, in the manner described earlier, with additional assessments performed at 5-min intervals. The total volume of local anaesthetic required to produce successful block was recorded. Increased intraocular pressure was assessed by experienced palpation only: it was noted whether or not the eye felt tense.

STATISTICAL ANALYSIS

Patient data were analysed using analysis of variance (ANOVA), while ocular motility scores and total volume of local anaesthetic required were compared using chi-square tests. Clinical detection of increased intraocular pressure in the three groups was compared using Fisher’s exact test.

Results

There were no significant differences between the three groups in age, sex or ASA status (table 1). Ocular motility scores at 1 min for group 3 were significantly lower than control values (group 1), with 39 (52%) patients achieving a score of ≤4. There were no significant differences at 1 min between groups 1 and 2 or groups 2 and 3 (table 2).

At 5 min, the incidence of successful blocks was significantly greater in both group 2 (P<0.05) and group 3 (P<0.001) compared with the control. There were no significant differences between groups 2 and 3 at this time for both achieving an ocular motility score of ≤4 (table 3) and achieving complete akinesia (table 4).

Four patients in group 1 had clinical evidence on palpation of a sustained increase in intraocular pressure (IOP). In one case this necessitated cancellation of surgery. In another patient, i.v. acetazolamide was required and in the two other patients, ocular compression for 20 min before surgery was necessary. None of the four patients noted to have a “tense” eye on palpation had received a volume of injectate greater than 5 ml, as all had achieved ocular motility scores of 4 or less by 5 min.

The two patients with the most marked increases

<table>
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<tr>
<th>Table 3</th>
<th>Numbers of patients achieving successful block at 5 min (%). *P&lt;0.05, **P&lt;0.001 compared with control (chi square). H=Hyaluronidase</th>
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<tbody>
<tr>
<td>Group 1</td>
<td>Successful block (%)</td>
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<tr>
<td>Control (n=50)</td>
<td>33 (66)</td>
</tr>
<tr>
<td>Group 2</td>
<td>H 50 iu ml⁻¹ (n=75)</td>
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<td>Group 3</td>
<td>H 300 iu ml⁻¹ (n=75)</td>
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<th>Table 4</th>
<th>Numbers of patients achieving complete akinesia by 10 min (%). *P&lt;0.05, **P&lt;0.001 compared with control (Chi squared). H=Hyaluronidase</th>
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<td>Complete akinesia (%)</td>
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<tr>
<td>Group 1</td>
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<th>Table 5</th>
<th>Numbers (%) of patients with clinical evidence of increased intraocular pressure (IOP). ***P&lt;0.001 compared with control (Fisher’s exact test). H=Hyaluronidase</th>
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<td>IOP satisfactory</td>
<td>“Tense” eye</td>
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<tr>
<td>Group 1</td>
<td>Control (n=50)</td>
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<tr>
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in IOP were brought to our attention by the ophthalmic surgeon who was unaware of the local anaesthetic solution used. The remaining two patients were noted to have “tense” eyes by one of the authors, who may have been aware of the solution used. Comparison of the number of patients in each group with a tense eye, using Fisher’s exact test, showed a highly significant difference ($P<0.001$) between the three groups (table 5).

As the risks involved in undertaking intraocular surgery in patients with a high IOP are significant, we felt that we were no longer justified in recruiting to group 1 and only 50 patients were studied.

Discussion

We have demonstrated a beneficial effect of hyaluronidase 300 iu ml$^{-1}$ combined with 0.5% bupivacaine and 2% lignocaine in improving the speed of onset of peribulbar block compared with local anaesthetic solutions alone. Hyaluronidase in concentrations of 300 iu ml$^{-1}$ and 50 iu ml$^{-1}$ also improved the quality of peribulbar block at 5 min compared with control, reducing the need for supplementary injection. We were unable to show any significant difference between the two concentrations of hyaluronidase with respect to quality of block at 5 min.

A study by Roberts, Macleod and Hollands suggested that the beneficial effects of hyaluronidase appeared only when local anaesthetic solutions were alkalinized to allow improved enzymatic action.9 Our findings do not concur with these results in that we found hyaluronidase to be effective in improving the quality of block without pH adjustment. This may partly result from the different concentrations of hyaluronidase used in the two studies (10 iu ml$^{-1}$ vs 50/300 iu ml$^{-1}$), differences in technique (two injection peribulbar technique vs single injection peribulbar block) and time of assessment (only at 30 min compared with 1, 5 and 10 min in our study). There were also differences in study design with the former using five different groups and studying only 100 patients.

In addition, our own observations showed that the use of hyaluronidase itself may alter the pH of a local anaesthetic because of the presence of phosphate buffers within the preparation, so that a 1:1 mixture of 0.5% plain bupivacaine and 2% plain lignocaine has a pH of 4.9, the same solution with hyaluronidase 50 iu ml$^{-1}$ has a pH of 5.0, while a solution with hyaluronidase 300 iu ml$^{-1}$ has a pH of 5.6. It is well recognized that local anaesthetics exist in both the uncharged and charged cationic forms within the body and that the ratio between the two varies with the pH of the surrounding tissues. It is believed that local anaesthetic molecules penetrate nerve membranes more rapidly in their uncharged form,11 with the ionized form being the active structure.12 For both lignocaine and bupivacaine, as pH decreases, there is an increase in the cationic form. Conversely, as pH increases, more of the drug exists in the free base form, allowing the drug to penetrate the nerve fibre more rapidly. Several authors have found alkalinizing local anaesthetic solutions to be effective for both peribulbar block13 and other blocks.14 It may be that the efficacy of hyaluronidase in improving onset of block is at least partly a result of its ability to increase the pH of local anaesthetic solutions.

It has also been postulated that because of its effects on absorption, hyaluronidase may lead to higher plasma concentrations of local anaesthetic and reduce the duration of action of block.15 A recent study showed that addition of hyaluronidase to local anaesthetic solutions hastened the absorption of both lignocaine and bupivacaine but did not increase the maximum plasma concentration achieved.16 Although we did not measure plasma concentrations of local anaesthetic, toxicity with this technique would not be expected because of the small amount of drug used. Duration of nerve block was sufficient to complete surgery in all patients.

Of additional interest in this study was the sustained increase in IOP in four patients in the control group, which occurred despite the use of a low volume of injectate (5 ml). We felt that this was so significant that we could no longer justify further recruitment to this group. There is only one previous report which suggested an association between peribulbar block without hyaluronidase and sustained increases in IOP.7 The underlying aetiology may be related to incomplete dispersal of local anaesthetic solution within the periocular compartment. However, all patients who had increases in IOP appeared clinically to have small orbits with short axial lengths (all $\leq 22$ mm). This observation may warrant further investigation.

Each time a needle is introduced into the orbit, there is a small but definite risk of complication. Successful block from a single injection is therefore desirable. Our study has shown that this is most likely to be achieved when hyaluronidase is added to the solution. Because of its beneficial effects on speed of onset, ease of administration and lack of significant toxicity or adverse effect on local anaesthetic absorption, we would advocate the use of hyaluronidase in a concentration of 300 iu ml$^{-1}$.

References


