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Anesthetic effects from low concentrations of proparacaine and benoxinate

MICHAEL J. JAUREGUI, O.D., TIMOTHY L. SANDERS, O.D., KENNETH A. POLSE, O.D.

ABSTRACT — Using double masking procedures, the response to McKay-Marg and Goldmann tonometry of 361 randomly selected patients was determined following the installation of a single dose of either 0.125, 0.25 or 0.5% proparacaine or 0.1, 0.2 or 0.4% benoxinate. Examiners graded the adequacy, patient tolerance and conjunctival hyperemia induced by the drop, while the subjects reported on the sting of the drop, awareness of the tonometer and discomfort after the procedure. The results indicate that 0.25% proparacaine is an effective anesthetic dose on all patients and that 0.2% benoxinate and 0.125% proparacaine would be effective on patients over age 40. The implication of these results is that significantly lower doses of anesthetic can be used which will result in less stinging, reduced hyperemia and shorter duration of action.

KEY WORDS — topical anesthetic, benoxinate, proparacaine, corneal anesthesia, corneal sensitivity

Introduction

Currently, the most commonly used corneal surface anesthetics are benoxinate and proparacaine hydrochloride. They are commercially available in only one concentration: 0.4% for benoxinate and 0.5% for proparacaine. The recommended dosage for diagnostic procedures such as tonometry, gonioscopy and fundus contact lens examination is one drop (about 50ul) of either anesthetic.

It is of interest that benoxinate and proparacaine are only available in single concentrations, since early clinical reports on their anesthetic effects suggested that concentrations less than those presently available are clinically effective for some ophthalmic procedures. A study by Schlegel and Swan indicated that as little as a single drop of 0.1% benoxinate induces a clinically effective level of anesthesia for tonometry. Emmrich and his coworkers evaluated the anesthetic effect of smaller volumes of benoxinate by using a special eyedropper which reduced the amount applied to about one-third the regular amount (18ul). They found this reduced volume to be effective for routine tonometry. Boozan and Cohen tested proparacaine in 0.25% concentration, although their report did not include whether this dose was clinically effective. None of these reports gave any quantitative information on the dose-response effects of the anesthetics.

Apparenty, the concentrations of benoxinate and proparacaine which are now used were not determined by dose-response studies, but rather by arbitrary decision and empirical success.

The clinical use of lower doses of benoxinate and proparacaine might have some advantages, such as a shorter anesthetic duration, less local irritation and a reduced incidence of corneal epithelial toxicity.

Recently, two of us reported on the dose-response effects of 0.1, 0.2 and 0.4% benoxinate and 0.125, 0.25 and 0.5% proparacaine. Using a modified Cochet-Bonnet anesthesiometer, we determined that the corneal touch threshold (CTT) must be 75 mg/mm² or higher for applanation tonometry. The three concentrations of either anesthetic induced a CTT of 75 mg/mm² or greater and therefore we suggested that concentrations 1/4 to 1/2 of the commonly used anesthetic dose may be sufficient for routine applanation tonometry.

We report here on a double masked study in which one of three concentrations of either benoxinate or proparacaine were used for either Goldmann or McKay-Marg applanation tonometry. The results, using standard and lower doses of these anesthetics, are analyzed from both a subjective (patient) and an objective (examiner) perspective. The clinical implications of these results are discussed.

Methods

Three hundred sixty-one patients requiring routine eye examinations were selected randomly and given either Goldmann...
or McKay-Marg tonometry. Figure 1 illustrates the age distribution of the patients who participated. Patients were given a single drop (50μl) of one of the following six concentrations: 0.1, 0.2, 0.4% benoxinate, or 0.125, 0.25, 0.5% proparacaine.

The anesthetics were prepared so that the level of preservatives and diluents was unchanged from commercial preparations, but the amount of active ingredients was altered in order to provide the required concentration. All bottles were coded so that neither the drug nor its concentration were known to the examiner or patient (double masking).

Following the drop, either McKay-Marg or Goldmann applanation tonometry was done. McKay-Marg tonometry was done on 200 patients and Goldmann applanation tonometry on 161 patients.

The examiner made judgments related to the (a) adequacy of anesthesia, (b) patient tolerance to drop and (c) induced conjunctival hyperemia. Table I gives the criteria used by examiners for each judgment. Following tonometry, the patient was asked to grade the (a) stinging of the drop, (b) awareness of the tonometer during measurement and (c) discomfort following the procedure. The scale the patients used to grade these three parameters is given in Table II.

Results

Examiner judgment

Table III shows that for at least 70% of the patients, all six concentrations of anesthetics were judged by the examiner to provide satisfactory (grade 2) or better anesthesia to perform applanation tonometry. The 0.1% concentration of benoxinate did not provide a satisfactory level of anesthesia in 26.5% of the patients. The higher concentrations of proparacaine and benoxinate gave greater adequacy than the lower doses.

Figures 2 and 3 show the level of adequacy as a function of age. Using grade 2.5 as the acceptable level of anesthesia (between satisfactory and perfect) 0.125% proparacaine and 0.2% benoxinate provided satisfactory anesthesia for patients over age 40. In patients under 40, either 0.25% proparacaine or 0.4% benoxinate was required to provide a grade 2.5 of higher level of adequacy.

Table IV shows the examiner’s judgment as to the patient’s tolerance of the anesthetic. All concentrations of proparacaine had a rating between “slight” and “no reaction” for at least 80% of the patients. The 0.1 and 0.4% concentrations of benoxinate had a

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**Table I**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Adequacy</th>
<th>Tolerance</th>
<th>Conjunctival Hyperemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>inadequate</td>
<td>no reaction</td>
<td>no change</td>
</tr>
<tr>
<td>1</td>
<td>borderline</td>
<td>slight reaction</td>
<td>slight injection</td>
</tr>
<tr>
<td>2</td>
<td>satisfactory</td>
<td>moderate reaction</td>
<td>moderate injection</td>
</tr>
<tr>
<td>3</td>
<td>perfect</td>
<td>marked reaction</td>
<td>marked injection</td>
</tr>
</tbody>
</table>

**Table II**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Sting</th>
<th>Awareness</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>none</td>
<td>no</td>
</tr>
<tr>
<td>1</td>
<td>slight</td>
<td>slightly</td>
</tr>
<tr>
<td>2</td>
<td>moderate</td>
<td>moderately</td>
</tr>
<tr>
<td>3</td>
<td>marked</td>
<td>markedly</td>
</tr>
</tbody>
</table>
"moderate reaction" or more in 41% and 35.1% of the patients, respectively. Of those patients receiving the 0.2% dose of benoxinate, 9% showed a "moderate reaction" or more.

Results from the examination of the bulbar conjunctiva are shown in Figure 4. Ten percent of the 361 patients showed some hyperemic reaction to the topical anesthetics. Benoxinate produced conjunctival hyperemia in 23 of 133 patients (17%); 12 of the 228 patients who received proparacaine (5.3%) showed some reaction.

**Patient judgment**

Table V shows the patient's rating of the "sting" of the drop. Benoxinate caused a significantly greater amount of stinging than did proparacaine (aligned ranks method: p = 0.14 × 10^19). All three concentrations of proparacaine caused stinging that ranged from "none" to "slight" in at least 75% of the subjects; 0.125% proparacaine caused slight or no stinging in approximately 82% of the patients. All concentrations of benoxinate produced moderate to marked stinging in at least one third of the patients. The 0.1% benoxinate produced moderate to marked stinging in 47% of the patients, while 0.2% and 0.4% preparations caused this level of stinging in 33% and 45% of the patients, respectively.

Figure 5 shows how the patients rated the "feeling" (awareness) of the tonometric procedure. As the concentration of the anesthetic increased, fewer subjects were aware of the tonometer. Thirty

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**TABLE III**

<table>
<thead>
<tr>
<th>Drug Concentration (%)</th>
<th>Adequacy Values (percentage of patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benoxinate</td>
<td>0</td>
</tr>
<tr>
<td>0.1</td>
<td>8.8</td>
</tr>
<tr>
<td>0.2</td>
<td>15.2</td>
</tr>
<tr>
<td>0.4</td>
<td>1.3</td>
</tr>
<tr>
<td>Proparacaine</td>
<td>0.125</td>
</tr>
<tr>
<td>0.25</td>
<td>1.2</td>
</tr>
<tr>
<td>0.5</td>
<td>0</td>
</tr>
</tbody>
</table>

Percentage of patients with adequacy values for various concentrations of benoxinate and proparacaine.

**TABLE IV**

<table>
<thead>
<tr>
<th>Drug Concentration (%)</th>
<th>Tolerance Values (grade)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benoxinate</td>
<td>0</td>
</tr>
<tr>
<td>0.1</td>
<td>17.6%</td>
</tr>
<tr>
<td>0.2</td>
<td>45.5%</td>
</tr>
<tr>
<td>0.4</td>
<td>24.6%</td>
</tr>
<tr>
<td>Proparacaine</td>
<td>0.125</td>
</tr>
<tr>
<td>0.25</td>
<td>70.4%</td>
</tr>
<tr>
<td>0.5</td>
<td>51.4%</td>
</tr>
</tbody>
</table>

Percentage of patients with tolerance values for various concentrations of benoxinate and proparacaine.
percent of the patients felt the tonometer with the 0.125% proparacaine, while approximately 11% felt the tonometer with the 0.25% concentration. There was almost no difference between the 0.25 and 0.5% proparacaine in the number of patients feeling the tonometer. With benoxinate, approximately 66%, 50% and 22% of the patients reported feeling the tonometer with the 0.1, 0.2 and 0.4% concentrations, respectively.

Conclusions

The results of this study suggest that lower concentrations of proparacaine and benoxinate than presently available can be effectively used for appplanation tonometry. A concentration of 0.25% proparacaine (0.5 the present dosage available) would provide an adequate level of anesthesia for almost all patients, and in patients over the age of 40, one drop of either 0.125% proparacaine or 0.2% benoxinate would provide effective anesthesia.

The anesthetic effect of lower concentrations was much greater for the older than the younger patients. The increased effect might be explained either by a decrease in corneal sensitivity or a reduction in tear flow which would result in less dilution of the anesthetic. Corneal sensitivity and tear flow both decrease during the aging process. Advantages to using lower doses would include a shorter duration of effect, thus reducing the time possible to abrade the cornea by rubbing the anesthetized cornea, reduced stinging and less conjunctival injection. Occasionally, hypersensitive reactions to 0.5% proparacaine and 0.4% benoxinate have been observed.

Use of a lower dose might reduce or eliminate such reactions.

It is interesting that all three dose levels of benoxinate caused significantly greater stinging than any of the proparacaine dosages. This is in agreement with many clinicians' impressions but differs from what has been reported previously. We feel that in patients who are apprehensive about the drops (e.g., young children, mental retardation, overly anxious patients) the 0.25% proparacaine would be the anesthetic of choice, since there would be little if any stinging expected from the lower dose of the anesthetic.

Based on the study results, we recommend that lower doses of both benoxinate and proparacaine be available for clinical use. The advantages of using 0.25% proparacaine would be sufficient to warrant making this the first drug of choice where corneal anesthesia is required for routine procedures such as tonometry, gonioscopy and contact lens examination of the retina. On patients over age 40, either 0.125% proparacaine or 0.2% benoxinate would provide satisfactory anesthesia.

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REFERENCES


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