Injection of Bupivacaine & Botulinum Type A Toxin to Treat Strabismus

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ABSTRACT:

Seventy-four adult patients given injection treatments for horizontal strabismus participated in a prospective observational clinical series. Doses per injection averaged 58mg of Bupivacaine and 2.3u of Botulinum type A toxin. Two or more treatments were given in 39% of cases. On average, misalignment of 24.6∆ was reduced by 17.5∆. Sixty-nine percent of our patients had successful outcomes (residual deviation ≤10∆) at average followup of 31mo. Injection treatment for horizontal strabismus achieves stable corrections lasting up to 10 yrs.

KEY WORDS: Botox injection, Bupivacaine injection, Strabismus treatment

1. INTRODUCTION

Bupivacaine (BUP) injection in muscle elicits a type of damage similar to weight-bearing exercise, the physiologic repair of which can correct strabismus by strengthening and shortening injected muscles. Botulinum type A toxin (BTX) in the antagonist allows the BUP-injected muscle to rebuild at reduced length [1,2,3].

This study was a prospective observational clinical series, which included patients with varying diagnoses and treatment histories in which treatment parameters were continually refined as we learned to best suit different cases.

We here report alignment outcomes with up 10-year followups in 74 cases of horizontal strabismus. We describe the use of BUP and BTX, and discuss indications for injection treatment.

2. METHODS

All experimental procedures were approved by IRBs of California Pacific Medical Center or the Smith-Kettlewell Eye Research Institute, and followed regulations of the US Health Insurance Portability and Accountability Act (HIPAA) of 1996. We offered injection treatment as an alternative to all adult patients requesting correction of horizontal strabismus. Those who understood the experimental nature of the treatment and wished to participate gave written consent. Patients were excluded from the study if there was evidence of paresis, muscle atrophy, mechanical restriction, or systemic disease that might impact extraocular muscle physiology. We did not otherwise exclude patients who had previous strabismus or other orbital surgery.

Of our 74 strabismus patients, 69 (93%) were comitant, five (7%) were non-comitant, and 28 (38%) had significant vertical components, including 4 (5%) with DVD. Forty-one (55%) had 1 or more prior unsuccessful surgical attempts to correct their strabismus, a total of more than 55 surgeries, and 5 had had other prior orbital surgeries.

Prior to injection, we instilled several drops of proparacaine 0.5% to reduce discomfort, and a drop of vasoconstrictor (e.g., brimonidine tartrate 0.1%). We optimized needle placement in the
target muscle using the electromyogram (EMG) recorded at the tip of the injection needle as the awake patient made voluntary gaze shifts.

Patients received BUP injections in one horizontal muscle, some with BTX injections in the antagonist. A second treatment was given to 29 (39%) patients who had residual strabismus after the first: either BUP (5), BTX (2), or both (22). Nine (12%) patients required further treatments. In 6 (8%) patients, BTX was injected in the muscle previously treated with BUP to redress an overcorrection.

Decisions concerning BUP dose and use of adjuvants were made clinically, using higher concentrations and greater volumes for larger deviations. BUP doses averaged 58 mg per injection. For larger deviations we used BTX in the antagonist muscle, an average 2.3u per injection. These modest BTX doses resulted in mild paresis lasting about a month.

Eye alignment was measured using prism-cover tests with a viewing distance of 3 m, and estimated by prism and corneal reflex for patients without steady central fixation. Alignment was measured before injection and as close as possible to predetermined 6 mo, 1 yr, 2 yr, 3 yr, 4 yr, 5 yr, 6 yr, 7yr and 10 yr followup times.

3. RESULTS

There were no statistically significant differences on any outcome measure for esodeviations (34 or 46% of patients) compared to exodeviations (40 or 54% of patients).

Table 1 gives mean presenting deviations, number of treatments, and corrections at the most recent examinations for all 74 patients, and for the subgroups with “small” (<25°) presenting deviations receiving BUP-only and BUP-BTX treatments, and large (>25°) presenting deviations, all of whom received BUP-BTX treatment. Overall, 69% of patients had successful outcomes, with average corrections of 17.5° overall. Patients with large deviations had corrections (24.4°) almost twice that of patients with small deviations (12.8°; p < 0.0003). A success rate of 85% was achieved with the smallest misalignments (mean 12.8°) using BUP only.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Presenting Misalignment (°)</th>
<th>Number of Patients</th>
<th>Presenting Misalignment (mean, °)</th>
<th>Number of Treatments (mean)</th>
<th>Absolute Correction (mean, °)</th>
<th>“Success” – Residual Misalignment ≤ 10° (% of patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small - BUP-Only</td>
<td>13</td>
<td>12.8</td>
<td>1.4</td>
<td>11.4</td>
<td>85</td>
<td></td>
</tr>
<tr>
<td>Small - BUP-BTX</td>
<td>31</td>
<td>18.9</td>
<td>1.7</td>
<td>13.3</td>
<td>77</td>
<td></td>
</tr>
<tr>
<td>All Small (&lt; 25)</td>
<td>44</td>
<td>17.1</td>
<td>1.6</td>
<td>12.8</td>
<td>80</td>
<td></td>
</tr>
<tr>
<td>All Large (&gt; 25)</td>
<td>30</td>
<td>35.8</td>
<td>1.7</td>
<td>24.4</td>
<td>53</td>
<td></td>
</tr>
<tr>
<td>All Patients</td>
<td>74</td>
<td>24.6</td>
<td>1.6</td>
<td>17.5</td>
<td>69</td>
<td></td>
</tr>
</tbody>
</table>

Table 1: Most Recent Measures Following All treatments

Figure 1 shows the stability of alignment correction by separating patients into cohorts according to length of followup. Alignment corrections were impressively stable over followups as long as 10 years.

4. DISCUSSION

Most of our patients – 69% overall, and 80% presenting with small deviations – enjoyed successful outcomes. In the present study we achieved overall absolute corrections of 17.5°, which
is 9% larger than previously reported by Debert et al [4] in patients with similar initial misalignments. Our absolute corrections were 67% larger than those of Miller, Scott et al [5]. The improved outcome is most remarkable for patients with large initial misalignments, where corrections averaged 24.4Δ. We believe that more confident dosing is responsible for the improved outcomes. We obtained clinically significant improvements with misalignments up to 50Δ, and demonstrated stability for as long as 10 years.

BUP and BTX in coordination are powerfully synergistic. Injection treatment has been shown to yield stable, apparently permanent corrections of large misalignments [4], comparable to those of traditional incisional surgery, at lower cost [6].

Injection treatment has several intrinsic benefits not shared by surgery [4]. First, injection treatment can increase contractility, stiffness, and shorten a muscle, whereas surgery is generally limited to compensatory impairment; second, it does not damage extraocular biomechanics by excising tissue or causing scarring [7]; and third, surgery requires significant general anesthesia, whereas injection can be performed under local anesthesia in cooperative adults.

Given an upper limit of about 90 mg of BUP in a single injection, large misalignments will often require 2 treatments. Forty-one of our study patients had prior failed strabismus surgeries, and five more presented with strabismus secondary to retinal or glaucoma surgery. The outcomes from injection in these cases were no less successful than cases without prior surgery. BUP treatment may be particularly useful where previous procedures have left adhesions and fibroses that complicate surgical approach. BUP should be also be considered to correct postoperative deviations in patients with good potential for binocularity who wish to avoid reoperation.

REFERENCES


6- Mathias SA, Josephson M. Treatment of intermittent exotropia of the convergence insufficiency type with bupicacaine 0.75%: 5 year experience and outcomes. Journal of American Association for Pediatric Ophthalmology and Strabismus 2017;21(7):e11