Reducing intraocular-pressure spike after intravitreal-bevacizumab injection with ocular decompression using a sterile cotton swab soaked in proparacaine 0.5%: A quasi-experimental study

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Article history:
Received 21 June 2015
Received in revised form 13 December 2015
Accepted 29 December 2015
Available online 19 April 2016

Keywords:
bevacizumab
decompression
intraocular pressure

A B S T R A C T
Background/Purpose: The study was conducted to determine the effect of preinjection ocular decompression by a cotton swab soaked in local anesthetic on the immediate postinjection rise in intraocular pressure (IOP) after intravitreal bevacizumab (IVB).

Methods: A nonrandomized, quasi-experimental interventional study was conducted at Al-Shifa Trust Eye Hospital, Pakistan, from August 1, 2013 to July 31, 2014. One hundred (n = 100) patients receiving 0.05-mL IVB injection for the first time were assigned to two preinjection anesthetic methods: one with ocular decompression using a sterile cotton swab soaked in proparacaine 0.5%, and the other without ocular decompression using proparacaine 0.5% eyedrops. The IOP was recorded in the eye receiving IVB at three time intervals: Time 1 (preinjection), Time 2 (immediately after injection), and Time 3 (30 minutes after injection).

Results: There was a significant difference in the mean IOP change (between Time 1 and Time 2) for the group injected with ocular decompression (M = 1.00, standard deviation (SD) = 1.47) and the group injected without ocular decompression (M = 5.00, SD = 2.38; t (68) = 9.761, p < 0.001). There was also a significant difference in the mean IOP change (between Time 1 and Time 3) for the group injected with ocular decompression (M = 0.428, SD = 1.58) and the group injected without ocular decompression (M = 4.318, SD = 3.34; t (58) = 7.111, p < 0.001).

Conclusion: Patients receiving IVB injections with ocular-decompression soaking in proparacaine 0.5% experience significantly lower postinjection IOP spike, and that too for a considerably shorter duration as compared to those receiving IVB without ocular decompression.

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1. Introduction

The use of repeated intravitreal injections has become a familiar treatment modality for a wide range of retinal diseases. Current practices include the use of intravitreal bevacizumab (IVB), dexamethasone, and triamcinolone for problems ranging from diabetic macular edema to vitreous hemorrhage.¹ The patients may receive intravitreal injections at regular intervals, and the periodicity may be as frequent as every 2 weeks.²

Injecting an additional volume of an intravitreal agent may result in an acute short-term rise of intraocular pressure (IOP), which can ultimately occlude the central retinal artery momentarily. This phenomenon can be attributed to the noncompliant nature of the spherical globe, and can pose a serious threat to the vision.² This can be explained as elevated IOP impairs the retinal and optic-nerve-head blood flow, it results in mechanical damage of the optic-nerve axons.³

A review of international literature shows that transient, yet extreme, elevation of IOP, after IVB injection, at times, takes about 30 minutes to return to baseline levels.³ Contrary to this, there are
reported incidences, in which the elevated IOP persisted for about 2 hours after IVB injection. Hollands et al reported the use of topical antiglaucoma medication for a period of 1 week to control the IOP after an IVB injection.

Patients who have a prior history of glaucoma have a propensity to sustain elevated IOP after IVB injections for longer durations. The elevated IOP in these patients usually takes longer to return to baseline. It is therefore imaginable that these elevated IOP spikes after IVB injections, repeated almost every month for years as long as the treatment continues, may consequently damage the optic nerve axons permanently in normotensive patients in general and in patients with preexisting glaucoma in particular.^

Keeping in view the grave consequences of sustained IOP elevation after IVB injections, efforts should be done to minimize the increase in IOP after IVB injections. Moreover, the international literature proposes lowering of preinjection IOP by ocular decompression and/or with medication.^

In our attempt to minimize the postinjection spike in IOP after IVB injection, this study was conducted to determine the rise in IOP after 0.05 mL of intravitreal anti–vascular endothelial growth factor (VEGF) (IVB) injection using two preinjection anesthetic methods.

2. Methods

A nonrandomized, quasi-experimental interventional study was conducted at the Department of Retina of Al-Shifa Trust Eye Hospital, Rawalpindi, Pakistan, from August 1, 2013 to July 31, 2014. The study was approved by the Institutional Ethical and Research Committee. A written informed consent was taken from all the participants of the study.

A total of 100 (n = 100) patients were included in the current study. Only those patients who were receiving intravitreal anti–VEGF (IVB) injection for the first time were included in the current study. All those patients who had already received any kind of intravitreal injection or had previously raised IOP due to any cause were excluded from the study.

In our attempt to minimize the postinjection spike in IOP after IVB injection, this study was conducted to determine the rise in IOP after 0.05 mL of IVB injection using two preinjection anesthetic methods: one with ocular decompression using a sterile cotton swab soaked in proparacaine 0.5%, pressed for 30 seconds, at 3.5 mm inferotemporally from the limbus measured by a sterile caliper (injection site) before IVB injection; and the other without ocular decompression, using proparacaine 0.5% eyedrops, one drop repeated three times at 1-minute intervals.

The IOP was recorded by Goldmann applanation tonometer in a sitting position using slit-lamp biomicroscopy, in the eye receiving IVB at three time intervals: Time 1 (preinjection and before ocular decompression/ocular manipulation), Time 2 (immediately after injection), and Time 3 (30 minutes after injection). The ocular decompression and IVB injection were administered to all the studied patients by the same treating ophthalmologist (Naveed A. Qureshi). Similarly, the IOP measurements at Time 1, Time 2, and Time 3 were recorded by the same ophthalmologist (H.M.). None of the patients received pressure-lowering drugs or underwent anterior-chamber paracentesis before or after the IVB injection.

After the IOP recording at Time 1, the lids and lashes were cleaned by 10% povidone-iodine swab. A standard sterile lid speculum was used in both anesthetic techniques, which was removed before the first postinjection IOP recording (Time 2), and 5% liquid povidone-iodine solution was applied on the ocular surface and conjunctival fornices for 60 seconds. The ocular decompression using a cotton swab soaked in proparacaine 0.5% at the injection site in the inferotemporal quadrant was gauged by applying moderate pressure to cause visible circular indentation of the globe. As the cotton swab was removed, an additional drop of 5% liquid povidone-iodine solution was applied at the injection site. A sterile 30-gauge needle attached to a 1-mL syringe was used for the IVB injection at the designated injection site, which was followed by a cotton swab covering the injection site momentarily (without application of pressure) to avoid egress of vitreous as the needle was withdrawn from the cavity. The IOP was then recorded by Goldmann applanation tonometer in a sitting position using slit-lamp biomicroscopy in the eye receiving IVB at Time 2 and Time 3.

Statistical analysis was performed by using SPSS version 17.0 (SPSS Inc., Chicago, IL, USA). A value of p < 0.05 was taken to indicate statistical significance.

A one-way repeated measures analysis of variance (ANOVA) was conducted to evaluate the mean IOP change following intravitreal anti–VEGF injection (IVB) with ocular decompression at Time 1, Time 2, and Time 3. A one-way repeated measures ANOVA was also conducted to evaluate the mean IOP change following intravitreal anti–VEGF (IVB) injection without ocular decompression at Time 1, Time 2, and Time 3.

An independent-sample t test was conducted to compare the mean IOP change before the injection (Time 1) and immediately after the injection (Time 2) between the two groups (i.e., with ocular decompression and without ocular decompression). A one-sample independent-sample t test was also conducted to compare the mean IOP change before the injection (Time 1) and 30 minutes after the injection (Time 3) between the two groups (i.e., with ocular decompression and without ocular decompression).

3. Results

A total of one hundred (n = 100) patients were included in the current study with 60 (n = 60) males (60%) and 40 (n = 40) females (40%). The right eye (OD) received intravitreal anti–VEGF (IVB) injection in 55% (n = 55) of the cases, whereas the left eye (OS) received the same injection in 45% (n = 45) of the cases. Fifty-six patients (n = 56) received intravitreal anti–VEGF (IVB) injection following ocular decompression, and 44 (n = 44) patients received intravitreal anti–VEGF (IVB) injection without ocular decompression, accounting for 56% and 44%, respectively, of the study population.

The one-way repeated measures ANOVA conducted to evaluate the mean IOP change following intravitreal anti–VEGF injection (IVB) with ocular decompression at Time 1, Time 2, and Time 3 showed significant effect for time, Wilk’s lambda = 0.682, F (2, 52) = 11.197, p < 0.005, and multivariate partial η² = 0.318. The post hoc Bonferroni test revealed that there was a significant difference between the mean IOP before the injection and the mean IOP immediately after the injection, with a mean difference = 1.00 and p < 0.001. There was also a significant difference between the mean IOP immediately after injection and 30 minutes after injection, with a mean difference = 0.571 and p = 0.043. However, no significant difference was observed between the mean IOP before the injection and the mean IOP 30 minutes after the injection, with a mean difference = 0.429 and p = 0.143 (Table 1).

The one-way repeated measures ANOVA conducted to evaluate the mean IOP change following intravitreal anti–VEGF (IVB) injection without ocular decompression at Time 1, Time 2, and Time 3 showed a significant effect for time, Wilk’s lambda = 0.176, F (2, 42) = 72.504, p < 0.005, and multivariate partial η² = 0.824. The post hoc Bonferroni test revealed that there was a significant difference between the mean IOP before the injection and the mean IOP immediately after the injection, with a mean difference = 5.024 and p < 0.001. There was also a significant difference between the mean IOP before the injection and the mean IOP 30 minutes after the injection, with a mean difference = 4.238 and p < 0.001.
However, no significant difference was observed between the mean IOP immediately after the injection and after 30 minutes of injection, with a mean difference of 0.786 and \( p = 0.352 \) (Table 1).

The independent-sample \( t \) test conducted to compare the mean IOP change before the injection and immediately after the injection between the two groups (i.e., with ocular decompression and without ocular decompression) revealed a significant difference in the mean IOP change for the group injected with ocular decompression [\( M = 1.00 \), standard deviation (SD) = 1.47] and the group injected without ocular decompression [\( M = 5.00 \), SD = 2.38; \( t \) (68) = 9.761, \( p < 0.001 \), two tailed]. The magnitude of the differences in the means of these two groups was 4.00 (mean difference = 4.00, 95% confidence interval 3.182–4.817) (Table 2).

The independent-sample \( t \) test conducted to compare the mean IOP change before the injection and 30 minutes after the injection between the two groups (i.e., with ocular decompression and without ocular decompression) showed a significant difference in the mean IOP change for the group injected with ocular decompression [\( M = 0.428 \), SD = 1.58] and the group injected without ocular decompression [\( M = 4.318 \), SD = 3.34; \( t \) (58) = 7.111, \( p < 0.001 \), two tailed]. The magnitude of the differences in the means of these two groups was 3.89 (mean difference = 3.89, 95% confidence interval 2.794–4.984; Table 2).

4. Discussion

It has been well expressed in the international literature that intravitreal anti-VEGF agents, with introduction of additional fluid in the vitreous cavity, can lead to a momentary elevation in the IOP.\(^5\) This phenomenon has also been seen after intravitreal antibiotic and steroid injections. Moreover, the transient elevation of IOP normalizes within 30 minutes in majority of the eyes.\(^6\) Contrary to this claim, long-term sustained elevation of IOP has also been reported in some eyes receiving anti-VEGF therapy.\(^11,12\)

The long-term effects of repeated IOP elevation in patients receiving several intravitreal anti-VEGF agents are not known. Whether such transient elevation in IOP warrants the need for antiglaucoma therapy is still debatable. Eyes with preexisting glaucoma are more susceptible to damage. Also, glaucomatous eyes take longer to return to preinjection pressure levels.\(^7\) In our attempt to minimize the postinjection spike in IOP after IVB injection, the current study was conducted to determine the elevation in IOP after 0.05 mL of IVB (anti-VEGF) injection using two preinjection anesthetic methods.

The physiological response of the eye to elevated IOP leads to increased aqueous-humor drainage through the trabecular meshwork and uveoscleral routes.\(^13\) Primarily, aqueous humor drains through the trabecular meshwork, a pressure-dependent gradient into the canal of Schlemm, which communicates directly with the episcleral veins. Goldmann\(^14\) analyzed the aqueous–humor flow and stated that, as the globe is indented, the volume of fluid exiting the eye exceeds the volume of fluid flowing in by aqueous–humor production. He also opined that a reduction in the intraocular volume is manifested as lowered IOP, thus permitting the additional fluid to be injected in the form of intravitreal injections.\(^14\) This phenomenon lowers the risk of experiencing abnormally high IOP after intravitreal anti-VEGF injections.

Kim and Jee\(^10\) used the tunneled scleral technique to study the effect of Honan intracameral pressure reducer (HIPR) on IOP rise after an intravitreal injection. They showed that the use of HIPR resulted in significantly lowering the preinjection, immediate postinjection, as well as 10-minute postinjection IOP levels as compared to the non-HIPR group. Since the use of HIPR was cumbersome, other methods of decompressing the eye had to be considered.\(^10\)

Gregori et al\(^5\) showed that preinjection decompression of the eye with cotton swabs using 4% liquid lidocaine preparation during an anesthetic preparation led to a significantly lowered post-injection IOP spike. The current study used a different anesthetic agent, and showed that ocular decompression using cotton swabs soaked in proparacaine 0.5% also resulted in significantly lowered postinjection IOP spike as compared to topical anesthesia without ocular decompression. Davis et al\(^15\) showed that topical proparacaine 0.5% compared to 4% lidocaine preparation is inexpensive and provides a very effective anesthesia during office-based intravitreal injections. It also has minimum side effects and is easily administered.\(^16\) Kozak et al\(^17\) compared different anesthetic methods used for intravitreal injections, and concluded that topical proparacaine eyedrops had the lowest average combined pain score. However, Andrade and Carvalho\(^18\) recommended that topical proparacaine may be coupled with subconjunctival lidocaine to avoid pain and eye movements during intravitreal injections.

The current study shows that irrespective of whether ocular decompression was done or not, a significant raise in IOP was seen immediately after intravitreal anti-VEGF (IVB) injection. Moreover,

### Table 1

Comparison of means within the groups.

<table>
<thead>
<tr>
<th>Group according to intervention technique</th>
<th>N</th>
<th>Mean ± SD</th>
<th>CI</th>
<th>df 1</th>
<th>df 2</th>
<th>( p )</th>
</tr>
</thead>
<tbody>
<tr>
<td>With ocular decompression</td>
<td>56</td>
<td>14.611 ± 3.531</td>
<td>14.018 − 15.910</td>
<td>2</td>
<td>54</td>
<td>11.197 &lt;0.001</td>
</tr>
<tr>
<td>IOP immediately after injection</td>
<td>56</td>
<td>15.532 ± 3.903</td>
<td>14.919 − 17.010</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Without ocular decompression</td>
<td>44</td>
<td>12.476 ± 2.830</td>
<td>11.642 − 13.406</td>
<td>2</td>
<td>42</td>
<td>72.504 &lt;0.001</td>
</tr>
<tr>
<td>IOP immediately after injection</td>
<td>44</td>
<td>17.497 ± 3.086</td>
<td>16.586 − 18.509</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IOP after 30 minutes of injection</td>
<td>44</td>
<td>16.523 ± 4.487</td>
<td>15.363 − 18.160</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CI – confidence interval; df – degree of freedom; IOP – intraocular pressure; SD – standard deviation.

### Table 2

Comparison of mean differences between the two groups.

<table>
<thead>
<tr>
<th>Group according to intervention technique</th>
<th>N</th>
<th>Mean ± SD</th>
<th>Mean difference</th>
<th>( t )</th>
<th>df</th>
<th>( p )</th>
</tr>
</thead>
<tbody>
<tr>
<td>IOP change between, before, &amp; immediately after injection</td>
<td>56</td>
<td>1.00 ± 1.47</td>
<td>4.00</td>
<td>9.761</td>
<td>68</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>With ocular decompression</td>
<td>56</td>
<td>0.429 ± 1.58</td>
<td>3.89</td>
<td>7.111</td>
<td>58</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Without ocular decompression</td>
<td>44</td>
<td>4.318 ± 3.34</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Without ocular decompression</td>
<td>44</td>
<td>5.000 ± 2.38</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

df – degree of freedom; IOP – intraocular pressure; SD – standard deviation.
the significantly raised IOP persisted in patients receiving intravitreal anti-VEGF (IVB) agent without ocular decompression even 30 minutes after the injection. This was not seen in patients receiving intravitreal anti-VEGF (IVB) agents with ocular decompression. Therefore, in patients who receive intravitreal injections with ocular decompression, IOP returns to near normal levels sooner as compared to those who receive intravitreal injections without ocular decompressing, thus posing a serious risk to adversely affect the eye due to raised IOP.

The current study also shows that, although the mean change in IOP before and immediately after the injection was statistically significant ($p \leq 0.001$) in both groups, the mean change in IOP in the group without ocular decompression ($5.00 \pm 2.38$) was more compared to the mean change in IOP in the group with ocular decompression ($1.00 \pm 1.47$). Likewise, the mean change in IOP before the injection and 30 minutes after the injection between the two groups (i.e., with ocular decompression and without ocular decompression) was also statistically significant ($p \leq 0.001$). Also, the mean change in IOP in the group without ocular decompression ($4.32 \pm 3.34$) was more compared to the mean change in IOP in the group with ocular decompression ($0.43 \pm 1.58$) even 30 minutes after the injection.

Furthermore, the current study lays emphasis the fact that patients receiving intravitreal anti-VEGF (IVB) injections without ocular decompression experience significantly higher postinjection IOP, and for a considerably longer duration compared to those receiving intravitreal injections with ocular decompression. It is therefore advisable to use ocular decompression during intravitreal injections to avert grave visual consequences.

The critics of the proposed method of reducing the post-injection (IVB) IOP spike in the current study may raise the question of raised IOP during cotton-swab application. In fact, Gregori et al. came across one patient, in which the IOP rose to 68 mmHg during preinjection anesthetic preparation using cotton swabs. In their study, despite experiencing short-term preinjection raised IOP, anesthetic preparation using a cotton swab resulted in shorter as well as significantly lowered IOP spike postinjection (IVB). We did not come across any patient who showed a bizarre raise in IOP during anesthetic preparation using ocular decompression.

Another advantage of using the proposed technique by the authors as compared to the HIPR is that cotton swabs soaked in local anesthetic provide anesthesia and ocular decompression at the same time, making it a time-efficient tool to reduce alarming postinjection (IVB) spike.

Kim et al. stated that a smaller needle size and a larger volume of intravitreal injection have a role to play in sustained high IOP postinjection. They were of the opinion that smaller needle bore size reduces the pain and vitreous reflux simultaneously, and hence, used in clinical practice frequently. They also showed that 30- or 32-gauge needles used for injecting 0.05 mL of intravitreal injections caused higher postinjection IOP compared to a 27-gauge needle injection (0.1 mL). In the current study, the authors used 30-gauge needle for 0.05 mL of intravitreal anti-VEGF (IVB) agent, further compelling the need for ocular decompression.

In conclusion, the current study shows that ocular decompression with cotton swabs soaked in proparacaine 0.5% produces a significantly lowered postinjection (IVB) spike compared to other topical anaesthesia without ocular decompression. As patients around the world continue to receive frequent intravitreal injections, efforts should be done to minimize the rise in IOP after intravitreal injections to avoid severe visual morbidities.

References