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Comparison of topical and subconjunctival anesthesia in intravitreal injection administrations

B. KADERLI, R. AVCI

Department of Ophthalmology, Uludag University Hospital, Bursa - Turkey

PURPOSE. *To compare the effectiveness of topical and subconjunctival anesthesia in intravitreal injection administrations.*

METHODS. *Twenty-eight patients from a university clinic with bilateral diabetic macular edema were prospectively randomized to receive intravitreal injection of 4 mg triamcinolone under topical anesthesia for one eye and subconjunctival anesthesia for the other eye by using lidocaine 4%. Patients were asked to grade the pain they experienced during administration of both anesthesia and intravitreal injection by using a 4-point pain scale: from 0=no pain to 3=severe pain. Complications that developed during both procedures were recorded.*

RESULTS. *The mean pain score experienced during subconjunctival injections was 0.78 ± 0.62, whereas no anesthesia-related pain was reported in the topical group. The mean pain score experienced during intravitreal injection was 1.64±0.67 in the topical and 0.85±0.52 in the subconjunctival group ($p<0.001$). The mean total pain scores of both procedures were 0.82±0.34 in the topical and 0.82±0.51 in the subconjunctival group ($p>0.05$). Nine eyes (32%) developed subconjunctival haemorrhage after subconjunctival injection, whereas no anesthesia-related complication developed in the topical group. Subconjunctival haemorrhage was also observed in 5 eyes (18%) in the topical group and in 11 eyes (40%) in the subconjunctival group ($p>0.05$) after intravitreal injection.*

CONCLUSIONS. *Although subconjunctival anesthesia provides better pain control during intravitreal injections, its application is more painful and leads to subconjunctival haemorrhage. Moreover, the mean total pain scores are similar in both methods. Therefore, topical anesthesia may be more suitable for daily practice. (Eur J Ophthalmol 2006; 16: 718-21)*

KEY WORDS. *Intravitreal injection, Subconjunctival anesthesia, Topical anesthesia*

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INTRODUCTION

In the past, intravitreal injections only used to be performed for administration of antibiotics, antiviral agents, and gas in rare conditions such as endophthalmitis (1), cytomegalovirus retinitis (2, 3), retinal detachment (4), and submacular haemorrhage (5-7). Today, intravitreal injections are applied to much healthier eyes and the medicine of current interest is triamcinolone acetonide, which is being tested especially in macular diseases related with different etiologies (8-11). Several vision-threatening complications like traumatic cataract, retinal detachment, and vitreous haemorrhage can develop due to the anatomic site of the injections (12, 13). The pain associated with injection can lead to eye movement and blepharospasm, which may result in injection related complications or in the patient's refusal of further injections. Therefore, the application of an effective anesthesia must be comfortable for both physician and patient. The present study aims to compare the effectiveness of topical and subconjunctival anesthesia in intravitreal injection administrations.

METHODS

The study overseen and approved by the local ethical committee of our university was designed and performed

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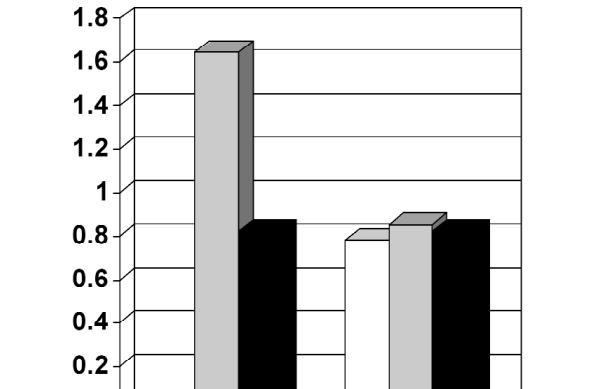

	Topical anesthesia group	Subconjunctival anesthesia group	P
Anesthesia application	0	0.78 ± 0.62	-
Intravitreal injection	1.64 ± 0.67	0.85 ± 0.52	< 0.001
Mean total pain score	0.82 ± 0.34	0.82 ± 0.51	> 0.05

Fig. 1 - *Histogram of the pain scores recorded during anesthesia applications and intravitreal injections. Pain scale: 0 = no pain or touch sensation; 1 = mild pain; 2 = moderate pain; 3 = severe pain.*

in accordance with the ethical standards of the Declaration of Helsinki. Informed consent was obtained from each patient prior to his or her inclusion in the study. Twenty-eight patients with bilateral diffuse diabetic macular edema who were resistant to previously applied grid laser photocoagulation were recruited into the study. In order to avoid hemorrhage, aspirin was discontinued 10 days prior to injection after consultation with an internist. Exclusion criteria were anticoagulant usage, any contraindication for discontinuation of aspirin, and history of previous eye surgery. The intravitreal injections were performed by the same physician (B.K.) under sterile conditions in an operating theater. All patients received topical proparacaine hydrochloride 0.5% (Alcaine®, Alcon–Couvreur, Puurs, Belgium), two drops approximately 10 minutes before patient preparation for injection. Patient preparation consisted of cleaning the eyelids with povidone-iodine 10%, covering the head of the patient with an operation cloth, and placement of the eyelid speculum. Then two drops of povidone-iodine 5% were instilled to the upper and lower fornix. After waiting 5 minutes, anesthesia administration was started. The randomization was stratified so that one half of the first-eye injections and one half of the second-eye injections were assigned to each anesthesia group, with each patient receiving each type of anesthesia once. The anesthesia solution used was 4% solution of lidocaine, which was obtained by diluting unpreserved lidocaine 10% (Aritmal®, Biosel, Istanbul, Turkey) with saline. In topical anesthesia, lidocaine 4% absorbed surgical sponge was placed just behind the inferior nasal limbus with applying slight pressure for 5 minutes. Subconjunctival anesthesia was applied by injecting 0.1 mL of lidocaine 4% solution subconjunctivally just 2 to 3 mm behind the inferior nasal limbus. After waiting 5 minutes for both anesthesias, 0.1 mL solution of 4 mg triamcinolone acetonide (Kenacort®-A, Bristol-Myers Squibb, Princeton, NJ, USA) was injected into the vitreous cavity 3.5 mm posterior to the inferior nasal limbus. A 30-gauge needle was used for both subconjunctival and intravitreal injections. The patients were asked to fixate at a specific target during the anesthesia administration and intravitreal injection in order to minimize eye movements and to achieve the most appropriate gaze position. After the intravitreal injection, the continuance of central retinal artery pulsation was confirmed. Finally, the eyes were closed with antibiotic ointment.

Both after anesthesia administrations and intravitreal injections, the pain experienced was evaluated by a senior nurse who was not involved in the evaluation of the study results and who is not part of the authorship. Each patient was shown a 10 cm visual analogue graphic pain score chart, with a numerical and descriptive rating scale, graded from 0 to 10. Patients were invited to score where on the chart they could grade the pain experienced during the procedures. If patients were unable to read the printed numbers and descriptive text on the pain scale, the nurse read them to the patient. Taking into account not understanding the 10 cm visual analogue graphic pain score chart, each patient was also asked to grade the pain experienced by using a four-point pain scale. Only 11 patients (40%) responded by understanding visual analogue scale. Therefore, in order to grade the intensity of pain, a four-point pain scale was used, which was understood and responded by all the patients. Patients were asked to grade the pain experienced into four levels: 0 = no pain or touch sensation; 1 = mild pain; 2 = moderate pain; 3 = severe pain. The patient's eye movement during intravitreal injection was also evaluated by the physician (B.K.) into three levels: 0 = none or minimal; 1 = not making injection difficult; 2 = making a safe injection difficult. Complications that occurred during anesthesia administrations and intravitreal injections were also recorded.

Statistical analysis

Pain scores and eye movement scores were analyzed using the Wilcoxon signed ranks test. Complications observed during intravitreal injections were compared using the chi-square test. A p value of <0.05 was defined as statistically significant.

RESULTS

Of 28 patients, 15 were female and 13 were male. The mean age was 59 (range 44–71 years) and the average diabetes period was 14.8 years (range 4–25 years). Intravitreal injections were successfully completed in all cases. No patient refused a further injection. The mean pain score experienced during subconjunctival injection of lidocaine was 0.78±0.62, whereas no anesthesia-related pain was reported in the topical group (Fig. 1). The mean pain score reported after intravitreal injections was 1.64±0.67 in the topical and 0.85±0.52 in the subconjunctival group. The statistical difference between the groups was fairly significant ($p<0.001$). The mean total pain scores of both procedures were 0.82±0.34 in the topical and 0.82±0.51 in the subconjunctival group ($p>0.05$). While moderate pain in 12 eyes (42 %) and severe pain in 3 eyes (10%) occurred in the topical group during intravitreal injections, maximum pain felt in the subconjunctival group was of moderate degree and only occurred in 5 eyes (17%). However, any eye movement that could make safe intravitreal injection difficult was not observed in any patient. The eye movement score observed during intravitreal injection was 0.32 in the topical and 0.25 in the subconjunctival group. The statistical difference between the groups was not significant ($p>0.05$). Nine eyes (32%) developed subconjunctival hemorrhage after subconjunctival injection, whereas no anesthesia-related complication developed in the topical group. Subconjunctival hemorrhage was less than three hour quadrants in eight eyes and more extensive in one eye. After intravitreal injection, limited subconjunctival hemorrhage was observed in 5 eyes (18%) in the topical group and in 11 eyes (40%) in the subconjunctival group ($p>0.05$). The subconjunctival reflux of triamcinolone particles was observed in 2 eyes (7%) in the topical group and in 1 eye (3%) in the subconjunctival group. No eyes developed complications such as retinal detachment, cataract, or endophthalmitis during the follow-up period.

DISCUSSION

Topical and subconjunctival anesthesia are preferable methods for actual intravitreal injection administrations (2, 8, 10, 12, 14-16). The main advantage of topical and subconjunctival anesthesia is that each is a relatively painless application and does not lead to serious complications that retrobulbar and peribulbar anesthesia may cause. Moreover, topical and subconjunctival anesthesia obtained with lidocaine 4% provides sufficient anesthesia for cataract surgery, in which there is further tissue manipulation with respect to intravitreal injection (17). Therefore we have found it appropriate to use and compare these two methods in our series.

Both topically and subconjunctivally administered lidocaine 4% provided an anesthesia of sufficient quality for intravitreal injection in this study. Any eye movement that could make injecting risky was not observed in either group during the injections. Although subconjunctival injection of lidocaine provided better anesthesia than topical administration, total mean pain scores in both groups were similar because of the painful administration of subconjunctival anesthesia. While 16 patients (57%) described mild and 3 patients (11%) described moderate pain related to the subconjunctival injection, no patient in the topical group reported pain related to the contact of lidocaine absorbed surgical sponge. Another problem related with subconjunctival injections was subconjunctival hemorrhage, which occurred in 9 eyes (32%) of our series. Subconjunctival hemorrhage leads to swelling of the conjunctiva which interferes with visualization of the scleral area behind the limbus and makes the fixing of the intravitreal injecting site difficult. It has been suggested that subconjunctival anesthesia may lead to globe perforation and increase the risk of contamination by allowing the newly opened subconjunctival liquid space to have access to the inner aspect of the scleral wound of any injection (12). We did not observe any case of globe perforation or endophthalmitis in the subconjunctival anesthesia group. Another anesthesia method used for intravitreal injections is topical lidocaine 2% gel, which has been found to provide pain control equal to subconjunctival lidocaine 2% anesthesia and cause less chemosis and hemorrhage than subconjunctival anesthesia (18). Topical lidocaine 2% gel also provides better anesthesia than topical lidocaine 4% in clear corneal cataract surgery (19). Lidocaine gel may be considered as an effective and safe alternative to topical drop or subconjunctival anesthesia in intravitreal administrations.

In summary, both subconjunctival and topical anesthesia are effective and reliable in cooperative patients. Although subconjunctival injection of lidocaine provides better pain control during intravitreal injections, its application is painful and leads to subconjunctival haemorrhage. Taking into account that the total main pain scores in both groups are similar, topical anesthesia appears to be the acceptable choice for routine administrations. A further advantage of the topical anesthesia is that it can be applied in patients on coumarin therapy (20). Subconjunctival anesthesia can be preferred in more painful and rare situations such as endophthalmitis and postoperative eyes. Yet, because of a decrease in pain perception in diabetic polyneuropathy (21), the results of this study may not reflect the status in non-diabetics. Further studies are essential to establish the most appropriate anesthesia method for intravitreal injections.

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Reprint requests to:
Berkant Kaderli, MD
Uludag University Hospital
Department of Ophthalmology
16059 Gorukle–Bursa
Turkey
drkaderli@yahoo.com

REFERENCES

1. Kresloff MS, Castellarin AA, Zarbin MA. Endophthalmitis. Surv Ophthalmol 1998; 43: 193-224.
2. Baudouin C, Chassain C, Caujolle C, Gastaud P. Treatment of cytomegalovirus retinitis in AIDS patients using intravitreal injections of highly concentrated ganciclovir. Ophthalmologica 1996; 210: 329-35.
3. Palestine AG. Intraocular therapy for cytomegalovirus retinitis. J Int Assoc Physicians AIDS Care 1996; 2: 25-8.
4. Tornambe PE, Hilton GF. The Retinal Detachment Study Group. Pneumatic Retinopexy. A multicenter randomized contrdled clinical trial comparing pneumatic retinopexy with scleral buckling. Ophthalmology 1989; 96: 772-84.
5. Hattenbach LO, Klais C, Koch FH, Gumbel HO. Intravitreous injection of tissue plasminogen activator and gas in the treatment of submacular hemorrhage under various conditions. Ophthalmology 2001; 108: 1485-92.
6. Kokame GT. Vitreous hemorrhage after intravitreal tissue plasminogen activator (t-PA) and pneumatic displacement of submacular hemorrhage. Am J Ophthalmol 2000; 129: 546-7.
7. Krepler K, Kruger A, Tittl M, Stur M, Wedrich A. Intravitreal injection of tissue plasminogen activator and gas in subretinal hemorrhage caused by age-related macular degeneration. Retina 2000; 20: 251-6.
8. Antcliff RJ, Spalton DJ, Stanford MR, Graham EM, ffytche TJ, Marshall J. Intravitreal triamcinolone for uveitic cystoid macular edema: an optical coherence tomography study. Ophthalmology 2001; 108: 765-72.
9. Benhamou N, Massin P, Haouchine B, Audren F, Tadayoni R, Gaudric A. Intravitreal triamcinolone for refractory pseudophakic macular edema. Am J Ophthalmol 2003; 135: 246-9.
10. Martidis A, Duker JS, Greenberg PB, et al. Intravitreal triamcinolone for refractory diabetic macular edema. Ophthalmology 2002; 109: 920-7.
11. Spaide RF, Sorenson J, Maranan L. Combined photodynamic therapy with verteporfin and intravitreal triamcinolone acetonide for choroidal neovascularization. Ophthalmology 2003; 110: 1517-25.
12. Aiello LP, Brucker AJ, Chang S, et al. Evolving guidelines for intravitreous injections. Retina 2004; 24: 3-19.
13. Jager RD, Aiello LP, Patel SC, Cunningham ET Jr. Risks of intravitreous injection: a comprehensive review. Retina 2004; 24: 676-98.
14. Danis RP, Ciulla TA, Pratt LM, Anliker W. Intravitreal triamcinolone acetonide in exudative age-related macular degeneration. Retina 2000; 20: 244-50.
15. Penfold PL, Gyory JF, Hunyor AB, Billson FA. Exudative macular degeneration and intravitreal triamcinolone. A pilot study. Aust NZ J Ophthalmol 1995; 23: 293-8.
16. Jonas JB, Kreissig I, Sofker A, Degenring RF. Intravitreal injection of triamcinolone for diffuse diabetic macular edema. Arch Ophthalmol 2003; 121: 57-61.
17. Jafee NS, Jafee MS, Jafee GF. Anesthesia, wound healing, sutures and needles. In: Jafee NS, Jafee MS, Jafee GF, eds. Cataract Surgery and its Complications, 6th ed. St. Louis: CV Mosby; 1997; 18-47.
18. Kozak I, Cheng L, Freeman WR. Lidocaine gel anesthesia for intravitreal drug administration. Retina 2005; 25: 994-8.
19. Bardocci A, Lofoco G, Perdicaro S, Ciucci F, Manna L. Lidocaine 2% gel versus lidocaine 4% unpreserved drops for topical anesthesia in cataract surgery: a randomized controlled trial. Ophthalmology 2003; 110: 144-9.
20. Jonas JB, Pakdaman B, Sauder G. Cataract surgery under systemic anticoagulant therapy with coumarin. Eur J Ophthalmol 2006; 16: 30-2.
21. Nielsen NV, Lund FS. Diabetic polyneuropathy: corneal sensitivity, vibratory perception and Achilles tendon reflex in diabetics. Acta Neurol Scand 1979; 59: 15-22.