EXPERT OPINION

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Randomized clinical trial of two anesthetic techniques for intravitreal injections: 4% liquid lidocaine on cotton swabs versus 3.5% lidocaine gel

Ninel Z Gregori[†], Matthew J Weiss, Raquel Goldhardt, Joyce C Schiffman, Edgardo Vega, Cherrie-Ann Mattis, Wei Shi, Linda Kelley, Vilma Hernandez & William J Feuer

[†]*University of Miami Miller School of Medicine, Bascom Palmer Eye Institute, Miami, USA*

Objective: To compare same-day and next-day pain control and safety of two anesthetic techniques utilizing 4% liquid lidocaine applied with sterile cotton swabs versus 3.5% lidocaine gel for intravitreal injections. Main outcome measures were: discomfort during anesthetic preparation and needle penetration, 1 and 24 h after injection.

Methods: Patients were randomized to alternate anesthetic method at two consecutive injections in one eye or in different eyes on the same day if requiring bilateral injections. Overall satisfaction, corneal staining, and subconjunctival hemorrhage (SCH) were compared.

Results: Fifty patients were enrolled. Both methods resulted in similar mild discomfort during anesthetic preparation, 1 and 24 h later. The gel resulted in slightly higher discomfort during needle penetration ($p = 0.026$). Patients were satisfied with both techniques ($p = 0.91$), however, 52% patients preferred gel, 33% were indifferent, and 15% preferred cotton swabs ($p = 0.002$). There were significantly less corneal staining ($p = 0.001$) and SCH ($p = 0.004$) after the gel.

Conclusion: Both techniques are equally effective and yield mild discomfort scores during the procedure and the next day. The gel method results in significantly less ocular surface irritation.

Keywords: anesthesia, discomfort, intravitreal injection, lidocaine, lidocaine gel, pain

Expert Opin. Drug Deliv. (2012) 9(7):735-741

1. Introduction

The use of intravitreal injections has become increasingly important for the treatment of many vision-threatening ophthalmic conditions. While this form of treatment has changed the landscape of ophthalmology and improved patients' outcomes across many retinal diseases, repetitive injections are necessary to maintain therapeutic effect. In order for these invasive treatments to be acceptable to patients, the anesthetic method should minimize discomfort during and after the injection.

The American Society of Retina Specialists Preferences and Trends Survey from 2010 revealed that roughly a quarter of retina specialists use one of four techniques: topical anesthetic drops, topical viscous anesthetic, topical anesthetic on a pledget, or subconjunctival injection [1]. Several prospective studies showed equivalent overall pain scores for a multitude of anesthetic preparation techniques for intravitreal injections including proparacaine drops, lidocaine pledgets, lidocaine gel, and subconjunctival injection [2-7]. However, these studies have several drawbacks [2].

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10.1517/17425247.2012.685155 © 2012 Informa UK, Ltd. ISSN 1742-5247

While patients' pain immediately after the procedure has been assessed, their discomfort over the course of the subsequent day has not been studied. In our experience, despite relative comfort immediately after the injection, patients frequently complain of significant discomfort later same day and the following day. Therefore, an anesthetic technique resulting in the least long-term discomfort should be preferred. In addition, these studies failed to utilize a standardized protocol with precisely timed anesthetic application and standardized pain scale validated specifically for patients with ocular disease. Previously published studies adopted pain scales from the pain management disciplines such as verbal rating scale, McGill Pain Questionnaire, and Wong-Baker FACES scale [2]. These pain scales are not directly validated for ocular sensations.

At the Bascom Palmer Eye Institute and the Miami Veterans Administration (VA) hospital, the standard pre-injection preparation includes topical 5% povidone-iodine and topical 4% liquid lidocaine applied on sterile cotton swabs with gentle pressure over the site of injection. The pressure is believed to soften the eye before the injection, thereby reducing post-injection intraocular pressure (IOP) elevations. Newer viscous anesthetic agents, such as 3.5% lidocaine hydrochloride ophthalmic gel, may allow for a more comfortable injection by minimizing manipulation of the eye (no cotton swabs might be required as the gel remains on the eye longer than drops) and allowing for less corneal drying due to better coating of the corneal surface.

We conducted a prospective randomized clinical trial comparing same-day and next-day pain control and safety of the standard Bascom Palmer Eye Institute's anesthetic preparation utilizing cotton swabs soaked in liquid 4% lidocaine with a prep utilizing 3.5% lidocaine hydrochloride ophthalmic gel, similar to the method utilized for topical cataract surgery [3]. We utilized a standardized anesthesia-injection protocol and the Eye Sensation Scale [8] validated in patients with ophthalmic pain to compare discomfort scores during anesthetic preparation and needle penetration, 1 and 24 h later. The effects of both techniques on the corneal surface and the presence of subconjunctival hemorrhage were also compared.

2. Methods

This prospective randomized clinical trial was approved by the Miami Veterans Affairs Medical Center Institutional Review Board and was HIPAA compliant. The study was registered on the ClinicaTrials.gov with the following Identifier NCT01087489. Patients requiring frequent ranibizumab intravitreal injections for various indications as part of their routine clinical care were recruited to partake in this study. Those patients who received at least three prior intravitreal injections were included as it has been shown that perceived pain is reduced with every subsequent injection in a novice patient, especially after the first three injections [4].

2.1 Inclusion criteria

- Able to understand and sign informed consent
- Age ≥ 18 years
- Clinical need for a therapeutic ranibizumab intravitreal injection regardless of the medical indication
- Received at least three prior intravitreal injections as part of clinical care

2.2 Exclusion criteria

- Pregnancy (positive pregnancy test);
- mental disability;
- economically or educationally disadvantaged persons;
- prisoners;
- children;
- patients with fluctuating or impaired decision-making capacity;
- any other condition that the investigator believes would pose a significant hazard to the subject if the investigational therapy were initiated;
- participation in another simultaneous medical investigation or trial;
- inability to comply with study or follow-up procedures;
- previous reaction to the same drug class.

Fifty-three patients were randomized based on power calculations. Three patients were excluded after randomization (one patient withdrew from study due to unreliable telephone connection, one patient died before the second injection, and one patient had been enrolled in another VA study and was not allowed to also enroll in this study).

Patients requiring bilateral ranibizumab injections (n = 19) were randomly assigned to a different preparation method in each eye, and the injections were administered on the same day. Patients requiring unilateral ranibizumab injection (n = 31) were randomly assigned to one of the anesthetic methods and then received the alternate anesthetic prep with the next injection at a future visit.

The 4% liquid lidocaine and 3.5% lidocaine gel anesthesia were administered per standard protocols as described below.

2.3 Liquid lidocaine (4%) preparation

Two drops each of 0.5% proparacaine, 4% lidocaine, and 5% liquid povidone-iodine were instilled, and a 10% povidone-iodine swab was gently applied to the lids and lashes. A standard style sterile speculum was placed between the lids. Five percent liquid povidone-iodine was then applied over the entire ocular surface. Next, three sterile cotton swabs soaked in 4% liquid lidocaine were applied with gentle pressure to the area designated for injection in the inferotemporal quadrant. Each cotton swab was pressed against the eye for 60 s. The cotton swabs were alternated with an additional 5% povidone-iodine applied to the chosen area of injection. An antibiotic (polymixin) was used to wet the

cornea as needed for dryness. The injection was then performed by the same treating physician (NG) according to the routine technique. A sterile caliper was used to mark the distance from the limbus, followed by a drop of 5% betadine to this area, and a 0.05-ml ranibizumab injection into the vitreous cavity using a sterile 32-gauge needle attached to a 1-ml syringe. A sterile cotton swab was then used to cover the site after the needle was withdrawn to limit egress of the vitreous.

2.4 Viscous lidocaine (3.5%) ophthalmic gel preparation

Two drops each of 0.5% proparacaine and 5% povidone-iodine were placed on the eye. Sixty seconds later, two drops of preservative-free 3.5% lidocaine hydrochloride ophthalmic gel (Akten™, Akorn, Inc.) were placed over the ocular surface and into inferior fornix. The patient was asked to close the eye gently for 7 min. A 10% povidone-iodine swab was gently applied to the lids and lashes. A standard-style sterile speculum was placed between the lids and the gel was rinsed from the eye with an antibiotic (polymixin) to allow access of povidone-iodine to the conjunctiva in the next step. Five percent liquid povidone-iodine was then applied over the ocular surface and allowed to remain in contact with the eye for 60 s. An antibiotic (polymixin) was used to wet the cornea as needed for dryness. Next, the injection was performed by the same treating physician (NG) in the infero-temporal quadrant according to the routine technique as described in the previous preparation.

The patients were prepped by the same two technicians certified for the study. Time required for each preparation for each eye was recorded to compare the length of the two methods. Both preparations were performed by the same technician on the same patient to avoid variability in technique. Same speculum style was utilized in both methods. The injections were given by the same treating physician. For both preparations, optic nerve perfusion was assessed by confirming post-injection finger-counting vision. Immediately after the injection, a physician masked to randomization graded the extent (corneal quadrants, 1 – 4) and density (0 = none, 1 = mild, 2 = moderate, 3 = severe, 4 = corneal epithelial defect) of corneal staining as visualized by fluorescein staining, and the size (in clock hours) of subconjunctival hemorrhage.

Following the injection, a masked staff member administered a standard questionnaire to evaluate the patient's discomfort level. The patient was asked to grade discomfort during anesthetic preparation and needle penetration on a scale from 1 to 5 (1 = none, 2 = mild, 3 = moderate, 4 = severe, 5 = extremely severe) according to the published Eye Sensation Scale specifically designed and validated in patients with ophthalmic pain [5]. Subjects also graded their satisfaction with the entire injection experience on a scale from 1 to 5 (1 = very unsatisfied, 2 = unsatisfied, 3 = neutral, 4 = satisfied, 5 = very satisfied). Patients were asked to list the type and the timing of any pain medications used, in order to rule out the effect of systemic pain medications on the ocular discomfort they perceived.

Within 24 h of the injection, subjects were contacted via telephone by a staff member masked to randomization to assess discomfort felt 1 h after and the day after the injection on the same Eye Sensation Scale. Patients were also asked to report presence of sharp pain, dull ache, gritty sensation, burning, stinging, light sensitivity, watery eyes, pressure sensation, and decreased vision. Once again, they were asked to grade their satisfaction level with the injection process. Patients were asked to apply polymixin drops four times daily for 4 days after the injection.

Patients requiring unilateral injection were given alternate method the next time they required an injection with the same questionnaires repeated. In addition, the patients were asked about adverse events in the intervening month. Those patients requiring bilateral intravitreal injections were randomly assigned to a different preparation in each eye. One last follow-up was then completed at the next visit about 1 month after the second injection to document any adverse outcomes. After patients completed the second injection, they were asked to directly compare the two preps and to choose their preferred anesthetic method.

The study was designed for paired analysis, since each patient received one injection with each anesthesia. If we expect a 25% difference between eyes, with an alpha error of 0.05 and a beta error of 0.1, the estimated sample size is 47. An estimated 10% loss to follow-up increased the sample size to 53 patients. The results were then analyzed with t-tests (paired or unpaired) or a McNemar's chi-square test as appropriate. A p-value of 0.05 was considered statistically significant. Software utilized for statistical analysis is IBM SPSS PASW Statistics Version 17.0.

3. Results

Fifty-three patients were randomized based on power calculations. Three patients were excluded after randomization (one patient withdrew from study due to unreliable telephone connection, one patient died before the second injection, and one patient had been enrolled in another VA study and was not allowed to also enroll in this study). The results presented are based on 50 patients. One patient had only received two prior (rather than at least three) injections but was included. Omitting this patient from the analyses did not change the conclusions. Patient demographics are shown in **Table 1**. Nineteen patients received bilateral ranibizumab injections on the same day and 31 patients received unilateral ranibizumab injections with anesthetic method randomly assigned at the first visit and the alternate method given at the next injection.

3.1 Discomfort experienced the day of injection

The analysis of pooled data from bilateral and unilateral patients revealed that discomfort associated with anesthetic administration was mild and the same with both methods

Table 1. Demographics and ocular history.

Variable	N (%) Unilateral (n = 31)	N (%) Bilateral (n = 19)	N (%) Total (n = 50)
Age			
Mean (SD)	73 (11)	76 (13)	74 (12)
Median (range)	77 (42 – 90)	82 (48 – 91)	78 (42 – 91)
Gender			
Male	29 (94%)	19 (100%)	48 (96%)
Race/Ethnicity			
White non-Hispanic	22 (71%)	17 (89%)	39 (78%)
African American	2 (6%)	1 (5%)	3 (6%)
Hispanic	7 (23%)	1 (5%)	8 (16%)
Ocular diagnosis			
Age-related macular degeneration	20 (65%)	15 (79%)	35 (70%)
Diabetic macular edema	1 (3%)	4 (21%)	5 (10%)
Retinal vein occlusion	6 (19%)	0	6 (12%)
Central serous retinopathy	1 (3%)	0	1 (2%)
Irvine-Gass syndrome	1 (3%)	0	1 (2%)
Idiopathic choroidal neovascular membrane	1 (3%)	0	1 (2%)
Other form of macular edema	1 (3%)	0	1 (2%)
Number of previous injections in either eye			
Mean (SD)	16 (13)	22 (17)	18 (15)
Median (range)	12 (3 – 52)	19 (2 – 72)	14.5 (2 – 72)

*Pre-existing glaucoma includes those with ocular hypertension on glaucoma medications; it does not include other glaucoma suspects.

Table 2. Questionnaire scores (asked same day as injection): mean (SD).

Question		Unilateral (n = 31)	p-value*	Bilateral (n = 19)	p-value*	All patients (n = 50)	p-value*
Discomfort‡ during preparation	Gel	1.9 (0.8)	0.6	2.1 (0.8)	0.7	2.09 (0.8)	0.5
	Cotton swabs	2.0 (1.1)		2.2 (1.1)		2.1 (1.1)	
Discomfort‡ during needle penetration	Gel	2.0 (1.0)	0.15	2.0 (0.8)	0.083	2.0 (0.9)	0.026
	Cotton swabs	1.7 (1.0)		1.7 (0.8)		1.7 (0.9)	
How satisfied are you with entire prep and injection§	Gel	4.5 (0.8)	0.3	4.4 (1.0)	1.0	4.5 (0.8)	0.4
	Cotton swabs	4.3 (1.1)		4.4 (0.9)		4.3 (1.0)	

*Paired t-test.

‡1 – 5 (1 = none, 2 = mild, 3 = moderate, 4 = severe, 5 = extremely severe).

§1 – 5 (1 = very unsatisfied, 2 = unsatisfied, 3 = neutral, 4 = satisfied, 5 = very satisfied).

(**Table 2**). Discomfort during needle penetration was also mild, however, it was slightly higher after the gel, and the difference was statistically significant (p = 0.026, paired t-test). Patients were equally satisfied with both anesthetic preparations when asked immediately after each injection (p = 0.4, paired t-test).

3.2 Discomfort experienced the day after injection

One hour after the injection, the mean (SD) discomfort scores were slightly above mild in the gel (2.1 (1.1)) and in the lidocaine-soaked cotton swab (2.4 (1.0)) groups (p = 0.13, paired t-test) (**Table 3**). The morning after the injection, the mean discomfort (SD) scores were between none and mild after the gel (1.6 (0.8)) and the cotton swabs (1.8 (0.8)), p = 0.063 paired t-test (**Table 3**). Patients reported to be equally satisfied with both methods (p = 0.91, paired t-test), however, when asked to directly compare the two anesthetic preparations and choose the method of preference, the majority preferred the gel method. Fifty-two percent preferred the gel, 33% were indifferent, and 15% preferred cotton swabs (p = 0.002, McNemar's test). The reasons given by the patients were less discomfort the next day and shorter speculum time.

3.3 Ocular surface findings

The gel method resulted in significantly fewer clock hours of subconjunctival hemorrhage (p = 0.004, paired t-test),

Table 3. Questionnaire scores (asked day after injection): mean (SD).

Question		Unilateral (n = 31)	p-value*	Bilateral (n = 17)	p-value*	All patients (n = 48)	p-value*
Discomfort‡ 1 h after injection	Gel	2.1 (1.1)	0.15	2.2 (1.1)	0.6	2.1 (1.1)	0.13
	Cotton swabs	2.5 (1.0)		2.4 (1.1)		2.4 (1.0)	
Discomfort‡ day after injection	Gel	1.5 (0.9)	0.13	1.7 (0.7)	0.19	1.6 (0.8)	0.063
	Cotton swabs	1.8 (0.8)		1.9 (0.8)		1.8 (0.8)	
How satisfied are you with entire prep and injection yesterday§	Gel	4.4 (0.8)	1.0	4.2 (1.1)	0.8	4.3 (0.9)	0.91
	Cotton swabs	4.4 (1.0)		4.1 (1.0)		4.3 (1.0)	

*Paired t-test.

‡1 – 5 (1 = none, 2 = mild, 3 = moderate, 4 = severe, 5 = extremely severe).

§1 – 5 (1 = very unsatisfied, 2 = unsatisfied, 3 = neutral, 4 = satisfied, 5 = very satisfied).

Table 4. Ocular surface examination (immediately after injection).

Variable	3.5% lidocaine gel	Cotton swabs with 4% lidocaine	p-value*
Subconjunctival hemorrhage (clock hours) n = 48			
Mean (SD)	0.65 (0.70)	1.1 (0.85)	0.004
Median (range)	1 (0–3)	1 (0–4)	
Corneal staining (quadrants) n = 49			
Mean (SD)	2.3 (1.3)	3.0 (1.0)	0.001
Median (range)	2 (0–4)	3 (0–4)	
Corneal staining (density‡) n = 49			
Mean (SD)	1.3 (0.7)	1.9 (0.7)	< 0.001
Median (range)	1 (0–3)	2 (0–3)	

*Paired t-test.

‡0 = none, 1 = mild, 2 = moderate, 3 = severe, 4 = corneal epithelial defect.

less density of corneal staining ($p < 0.001$, paired t-test), and fewer quadrants of corneal staining ($p = 0.001$, paired t-test) (**Table 4**). There were no corneal abrasions with either method.

3.4 Ocular symptoms the day after injection

Analysis of symptoms reported by patients the next day revealed that frequencies of these symptoms were not statistically different after gel vs. cotton swabs (**Table 5**). At least one symptom was present in all eyes, and the mean (SD) number of symptoms was similar after the gel (2.7 (1.6)) and cotton swabs (3.3 (1.8)), $p = 0.071$ (paired t-test).

We compared patients who were taking pain medication to those who were not. For this analysis, we included only patients who had the same pain medication status at the time of both injections. There were 18 patients taking pain medications and 22 patients who were not at the time of both injections. Interestingly, patients taking medications to relieve various systemic pain reported more symptoms than those not taking pain medications (3.3 ± 1.6 vs. 2.3 ± 1.5, $p = 0.037$, t-test) after gel and (4.0 ± 1.9 vs. 2.8 ± 1.6, $p = 0.033$, t-test) after cotton swabs. However, none of the discomfort scores or satisfaction scores was statistically different between pain medication takers and non-takers.

Based on the final examination approximately 1 month after the second injection, there were no cases of endophthalmitis, retinal detachment, or vitreous hemorrhage.

4. Discussion

Intravitreal injections have become the most common in-office procedures performed in the vitreoretinal practices. Minimizing discomfort during and after the injection is paramount for patients to readily accept this repetitive treatment modality, but the preferred preparation method had not been previously determined. We present results of a prospective, randomized clinical trial comparing same-day and next-day pain control efficacy and safety of two anesthetic methods, utilizing 0.5% proparacaine plus topical 4% liquid lidocaine applied with cotton swabs versus 0.5% proparacaine plus 3.5% viscous lidocaine ophthalmic gel. We show that both topical 4% liquid lidocaine on cotton swabs and topical 3.5% lidocaine gel applied according to a standardized protocol result in similarly mild discomfort during the anesthetic application, 1 h after the

Table 5. Ocular symptoms reported the day after injection (n = 48).

Variable	n (%)	p-value*
Sharp pain		
Gel eye	6 (12%)	0.11
Cotton swabs eye	12 (25%)	
Dull ache		
Gel eye	17 (35%)	0.8
Cotton swabs eye	19 (40%)	
Gritty/sandy sensation		
Gel eye	14 (29%)	1.0
Cotton swabs eye	15 (31%)	
Burning/stinging sensation		
Gel eye	21 (44%)	0.064
Cotton swabs eye	30 (63%)	
Light sensitivity (n = 46)		
Gel eye	26 (57%)	1.0
Cotton swabs eye	25 (54%)	
Watery eyes		
Gel eye	38 (79%)	
Cotton swabs eye	39 (81%)	1.0
Pressure sensation		
Gel eye	1 (2%)	0.4
Cotton swabs eye	4 (8%)	
Decreased vision		
Gel eye	7 (15%)	0.4
Cotton swabs eye	11 (23%)	
At least one symptom		
Gel eye	44 (92%)	1.0
Cotton swabs eye	45 (94%)	
Number of symptoms		
Gel eye		
Mean (SD)	2.7 (1.6)	0.071‡
Cotton swabs eye		
Mean (SD)	3.3 (1.8)	

*McNemar's test.
‡Paired t-test.

injection, and the day after the injection. The gel resulted in slightly more discomfort during needle penetration (mild versus less than mild with cotton swabs), most likely due to the fact that closing the lids expressed the gel out of the conjunctival sac while the liquid lidocaine was held directly over the site of injection for several minutes. Nevertheless, patients reported equal satisfaction with both anesthetic techniques, and 52% preferred the gel method while 33% were indifferent, and only 15% preferred the 4% lidocaine prep. When asked why, most patients reported shorter speculum time (average of 5 min vs. 2 min) and less irritation the next day as their main reasons for preferring the gel. This is most likely due to milder ocular surface irritation (corneal staining and subconjunctival hemorrhage) documented with the gel prep in the current study.

To date, few studies have assessed patient comfort with an anesthetic gel for intravitreal injection. In 2005, Kozak *et al.* compared 2% lidocaine gel to 2% subconjunctival lidocaine and demonstrated no significant difference in pain reported immediately after intravitreal injections in 28 patients. Less extensive subconjunctival hemorrhage and chemosis was documented in the viscous lidocaine group [6]. This finding was later confirmed with a 100-patient population in a 2006 paper by Friedman *et al.* [7]. In 2010, Pollak and Davis demonstrated no difference in pain scores obtained immediately after the injection associated with lid speculum insertion, povidone-iodine application, and needle insertion after topical 0.5% proparacaine, topical 0.5% proparacaine plus two 4% lidocaine-soaked cotton swabs applied to the eye, and 3.5% lidocaine ophthalmic gel [9]. The authors estimated that the gel was applied for 20 – 70 s before the injection.

One concern using gel for anesthesia prior to invasive ocular procedures is that, if applied prior to povidone-iodine, it may prevent povidone's access to conjunctival flora and potentially increase risk for endophthalmitis [9,10]. Infectious endophthalmitis is the most serious complication after intravitreal injections. A recent paper by Inman and Anderson reported no cases of endophthalmitis after 4,690 consecutive antivascular endothelial growth intravitreal injections factor using 2% topical lidocaine gel anesthesia [11]. The authors used a standard technique where lidocaine gel was administered from a multi-use tube within 15 s after 5% povidone-iodine, and was allowed to remain on the eye for at least 5 min. The eye was then always prepped with additional 5% povidone-iodine to the entire eye surface and the lid margins [11]. In the present study, povidone-iodine was applied to the entire surface of the eye and allowed to sit for 60 s prior to applying the lidocaine gel to assure adequate microorganism kill time as no data are available on the time required to sterilize conjunctival surface. The gel was then rinsed from the eye and additional 5% betadine was applied prior to injection. In Inman's study and the current study, polymixin/trimethoprim drops were prescribed QID for 3 days, however given the recent data showing increase in bacterial resistance with repetitive antibiotic use after intravitreal injections, we do not advocate antibiotic use but stress the importance of povidone-iodine use [12]. Similar to the Inman study, no cases of endophthalmitis were encountered in our study. The present study, however, was not designed to compare rates of endophthalmitis between different anesthesia methods.

A particular strength of the current study is the assessment of the discomfort experienced the day after injection. This was done based on our clinical experience that patients often leave the clinic pain-free but complain of discomfort over the next several days. To our knowledge, this is the first study to evaluate the effect of injections on patients' symptoms over the next 24 h.

A second strength of the study lies in the careful design of study protocols for anesthesia administration and discomfort assessment. We utilized the Eye Sensation Scale, which was specifically designed and validated in patients with ocular pain [5]. To minimize influence of variation in technique,

only two senior technicians (VH and LK) administered anesthetic according to a standard protocol with precisely timed anesthetic administration. While each cotton swab was applied for 60 s in the study, we feel that shorter application might be adequate and would minimize the time required for the prep. The same investigator (NG) performed all injections. Patients who had received at least three prior intravitreal injections were recruited to minimize the influence of anxiety many individuals experience during their initial injections. Same subjects graded both preps during consecutive injections, and many (19/50) patients receiving bilateral injections on the same day were recruited allowing direct comparison of ocular discomfort experienced. Masked staff members administered discomfort questionnaires and performed ocular surface assessments.

5. Conclusions

The present study provides prospective evidence that the 4% liquid lidocaine applied with cotton swabs and 3.5% lidocaine gel result in mild discomfort during the anesthetic–antiseptic preparation and 1 h after and the day after intravitreal injection. Despite slightly more discomfort during the needle penetration after gel, the majority of patients prefer the gel method when asked to directly compare the techniques. The gel method results in significantly less keratopathy and subconjunctival hemorrhage. Overall, both methods of anesthesia are well tolerated and accepted by patients undergoing intravitreal injection.

Acknowledgements

The study was registered on the ClinicaTrials.gov with the following Identifier NCT01087489. The data outlined in this manuscript were partially presented at the 2011 Angiogenesis meeting, Miami, February, 2011; the Association for Research in Vision and Ophthalmology, Fort Lauderdale, May, 2011; the American Society of Retina Specialists, Boston, August, 2011.

Declaration of interest

Research supported by an unrestricted grant from Research to Prevent Blindness, Inc. and NEI core center grant P30 EY014801. The sponsor or funding organization had no role in the design or conduct of this research.

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Affiliation

Ninel Z Gregori[†1,2] MD, Matthew J Weiss[2] MD, Raquel Goldhardt[1,2] MD, Joyce C Schiffman[2] MS, Edgardo Vega[1] PA, Cherrie-Ann Mattis[1] MD, Wei Shi[2] MS, Linda Kelley[1] COA, Vilma Hernandez[1] COMT & William J Feuer[2] MS
[†]Author for correspondence
[1]Miami Veterans Affairs Medical Center, 1201 NW 16th Ave, Miami, 33125, USA
[2]University of Miami Miller School of Medicine, Bascom Palmer Eye Institute, 900 NW 17th Street, Miami, 33136, USA
Tel: +1 305 326 6000;
Fax: +1 305 326 6417;
E-mail: ngregori@med.miami.edu