



The Effect of Bilateral Intravitreal Ranibizumab Administration on Pain in Diabetic Retinopathy

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Abstract

Aim: To investigate the effect of bilateral intravitreal ranibizumab (IVR) on pain in diabetic patients.

Material and Method: Of the 42 patients who underwent bilateral IVR for diabetic retinopathy and macular edema, 42 eyes injected first were considered as group 1 and 42 eyes injected second were considered as group 2. During the injection, pain was assessed using a numerical scale (NS) and a verbal category scale (VCS).

Results: The mean age of 20 male (47.7%) patients in the groups was 59.90 ± 6.03 years, and the mean age of 22 female (52.3%) patients was 60.72 ± 3.88 years ($p=0.52$). In Group 1, the NS was 3.78 ± 1.11 , while in Group 2 it was 4.14 ± 1.37 , the difference was statistically significant ($p=0.01$). In group 1, VCS was 2.30 ± 0.71 , while in group 2, VCS was 2.73 ± 0.93 , the difference was statistically significant ($p=0.01$).

Conclusion: In diabetic patients who underwent bilateral IVR in the same session, pain sensation in the first injected eye was found to be less. This should be taken into consideration in bilateral IVR application.

Keywords: Ranibizumab, pain, intravitreal injection

INTRODUCTION

Diabetes mellitus (DM) is a disease that causes serious morbidity and mortality, affecting approximately 246 million people worldwide according to the International Diabetes Federation. The prevalence of DM among all age groups was approximately 2.8% as of 2000, and this rate is expected to increase to 4.4% in 2030. Diabetic retinopathy (DR) and cataract are complications of DM that affect vision. DR is a frightening disease as it leads to irreversible loss of vision (1).

Ranibizumab (Lucentis; Genentech, South San Francisco, CA/Roche, Basel, Switzerland, introduced in 2006) is an officially licensed agent containing the Fab fragment of a monoclonal antibody effective on all VEGF-A subtypes, with increased affinity, prepared for intravitreal injection (2).

According to the International Organisation for the Study of Pain, pain is an unpleasant sensory and emotional experience accompanying or identifiable with existing or potential tissue damage (3). One-dimensional scales used in pain assessment are directly aimed at measuring pain

intensity and the patient makes the assessment himself/herself. They are used in the evaluation of acute pain. One-dimensional scales include verbal category, numerical and visual comparison scale. The numerical scale (NS) is a method for determining the intensity of pain and aims to explain the patient's pain with numbers. Numerical scales start with the absence of pain (0) and reach up to the level of unbearable pain (10). The verbal category scale (VCS) is also called simple descriptive scale and is based on the patient's selection of the most appropriate word to describe the pain condition. Pain intensity is ranked from mild to unbearable (4,5).

In bilateral intravitreal ranibizumab (IVR) application, between the first injected eye and the second injected eye The pain sensation may be different, this should not be ignored during the injection.

MATERIAL AND METHOD

Eighty-four eyes of 42 patients who underwent bilateral IVR for DR and macular oedema in the ophthalmology

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department of Karabük University Medical Faculty Training and Research Hospital were evaluated with the approval of the ethics committee. Forty-two eyes of the patients who were injected first were considered as group 1 and 42 eyes who were injected afterwards were considered as group 2. Patients who underwent previous intravitreal injection, underwent any ocular surgery and were not able to co-operate were excluded from the study. During the injection, pain was assessed using a NS (Figure 1) and a VCS (Figure 2).

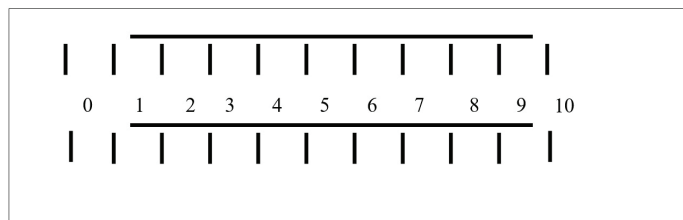


Figure 1. Numerical Scale (Black ve Matassarini 1993)



Figure 2. Verbal Category Scale (Melzack a Katz 1992)

All injections were performed by the same surgeon using the same type of blepharostat. Following topical anaesthesia, ocular surface cleaning was performed with 10% povidone iodine. Following the application of sterile drape and blepharostat, IVR 0.5 mg/0.05 ml was injected using a 30 G syringe tip, marking 3.5 mm from the limbus, without dripping topical anaesthetic again. There was no loss of light sensation in any patient. Following the injection, the entry site was massaged with ear cotton. Patients were asked to evaluate the pain using NS and VCS.

Ethics committee approval was received with the decision of Karabük University Non-Interventional Clinical Research Ethics Committee No. 2020/155.

Statistical Analyses

Statistical analyses were performed using SPSS version 16.0 (SPSS Inc, Chicago, Illinois, USA). p values below 0.05 were considered statistically significant. In the normal distribution test (Kolmogorov Smirnov test) performed before the analysis, it was seen that the variables fit the normal distribution. Mean and standard deviation values of the groups were calculated. Paired t test was used to compare the numerical variables of two groups.

RESULTS

The mean age of 20 male (47.7%) patients in the groups was 59.90 ± 6.03 years, and the mean age of 22 female (52.3%) patients was 60.72 ± 3.88 years ($p=0.52$). In Group 1, the NS was 3.78 ± 1.11 , while in Group 2 it was 4.14 ± 1.37 , the difference was statistically significant ($p=0.01$). In group 1, VCS was 2.30 ± 0.71 , while in group 2, VCS was 2.73 ± 0.93 , the difference was statistically significant ($p=0.01$) (Table 1).

Table 1. NS ve VCS values in groups

	Group 1	Group 2	P value
NS	3.78 ± 1.11	4.14 ± 1.37	0.01
VCS	2.30 ± 0.71	2.73 ± 0.93	0.01

DISCUSSION

Since intravitreal injections require repeated doses, it is important that the procedure is painless and easy in terms of patient compliance. If there is severe pain, subsequent injections may not be desired by the patients. Although intravitreal drug administration is one of the most common intraocular procedures, there is no consensus on which anaesthesia technique should be used for the procedure (6). There are anaesthesia studies for intravitreal injections with needles of different diameters (27-30 G) (7). It has been reported that pain will decrease as the needle tip width decreases (7). In all patients in our study, a 30 G needle was used and pain between the two eyes was evaluated independently of the needle diameter.

The ideal intravitreal injection should be fast, effective, safe, easy, cost effective and as painless as possible. There is a consensus on what should be done to reduce the risk of infection in intravitreal injections, but there is no consensus on which anaesthetic technique should be chosen to reduce the pain felt during injection. Studies have suggested that topical anaesthesia is preferable for intravitreal injections because it is fast, inexpensive and easy to administer (7). In our study, we applied topical anaesthesia to all patients because of these advantages.

One-dimensional scales are self-assessment methods that directly measure the severity of pain. In our study, bilateral IVR was performed in the same session. We asked the patient to compare the procedures performed on both eyes using the numerical scale and verbal categorisation scale, which are one-dimensional scales.

In the literature, 162 patients were compared with visual analogue scale (VAS) and no difference was found between aflibercept ranibizumab and dexamethasone implant in terms of pain (8). Pain was found to be less in cases of advanced age, male gender and pseudophakic (8). Patients undergoing eye surgery were not included in our study and we aimed to eliminate the effect of age and gender on pain assessment by comparing two eyes of the same patient in the same session.

In previous studies, most patients who underwent repeated injections reported that they felt that the pain was similar to the pain experienced during the previous injection or that it was reduced. However, increased waiting time may also be associated with increased discomfort in repeated injections (9,10). We excluded patients with previous injections from our study and tried to reduce the factors that may have an effect on pain as much as possible by performing bilateral injections in the same session.

CONCLUSION

In conclusion, in our study, pain in the later eye was found

to be higher in patients who received injection in two eyes in the same session. We believe that within the same individual, during a single session, assessing the pain in both eyes before and after injection will make a valuable contribution to the existing literature. Although the pain is slightly higher, we think that injection in two eyes in the same session should not be avoided.

Although only two eyes were compared, the limitations of our study are that we did not evaluate parameters such as gender and age and the number of patients was not larger.

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