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Comparison of Pain in Different Quadrants while giving Intravitreal Injection

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ABSTRACT

Background: Intravitreal injection is most popular universal intraocular procedure. it is important to consider the discomfort related with this procedure in order to ensure patient compliance and safety.
Objective: To compare the pain in different quadrants correlated to intrvitreal bevacizumab injection.
Material and Methods: Randomized controlled trial of four months was done In-patient Ophthalmology department, Pakistan Institute of Medical Sciences (PIMS) Islamabad between May-2020 to Sep-2020.In this study 120 patients were included (30 patients in each group) to measure the extent of pain while receiving an intravitreal bevacizumab injection. Sample size was calculated by WHO sample size calculator with 5% Level of significance, 80% Power of test.The data analyzed by using SPSS 23.
Results: The results of pain score in our study showed that the mean pain score of the patients in Group ASuperonasal Quadrant was 1.50 ± 0.51, in Group B Superotemporal Quadrant was 4.00 ± 0.91, in Group C Inferonasal Quadrant was 2.70 ± 0.84 and in Group D Inferotemporal Quadrant was 2.87 ± 0.78. The results of p value showed significant difference in pain score in groups. The Pain score is less in Group A Superonasal Quadrant as 1.50 ± 0.51 and more in Group B Superotemporal Quadrant as 4.00 ± 0.91.
Conclusion: Superonasal Quadrant (SN Quadrant) was the less pain site as compared to others site i.e. Superotemporal Quadrant (ST quadrant), Inferonasal Quadrant (IN
Quadrant) and Inferotemporal Quadrant (IT Quadrant). The most pain full site was Superotemporal Quadrant (ST quadrant).
Keywords: Intravitreal injection, visual analog scale, ocular pain, Quadrant of eye

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INTRODUCTION

In an attempt to lower the complication, the ace skill for intravitreal injections is in still under evaluation. Over the past decade, intravitreal injection of "anti-vascular endothelial growth factor" (anti-VEGF) has gained popularity as the most commonly used method to treat variety of ocular diseases.[1] Intravitreal injections were first described in 1911 by Deutschmann and Ohm[2]. In 1944, Von Sallmann first explained the effectiveness of intravitreal antibiotic for the treatment of endophthalmitis[2]. Bevacizumab, Ranibizumab, Aflibircept are the common Anti VEGFs. For age-related macular degeneration intravitreal bevacizumab (Avastin) is a treatment that is the most commonly performed procedures in ophthalmology. In 2013 in USA four million IVIs performed (estimated) and the number is presume to increase.[2] Intravitreal injection is highly targeted drug therapy. Under aseptic measures, intravitreal bevacizumab is injected into vitreous cavity through pars plana. Many drugs can be delivered into vitreous through intravitreal injection: anti-infective (antibiotics, antifungal) anti-inflammatory (NSAIDS, steroids), Gas, Anti VGEF etc.[3] Bevacizumab stops the tying up of VEGF to its receptor.[3] The Food and Drug Administration has proved the bevacizumab for treatment of cancer of metastatic colorectal Area.[4]

In 2005 in a patient, intravitreal bevacizumab firstly used, produced at first week the full resolution of the subretinal fluid and the visual acuity was stable.[3] The result of Diabetic Retinopathy Clinical Research (DRCR) study is of opinion that there is fast depletion in the retinal thickening and improve the visual acuity with the bevacizumab treatment as compared for diabetic macular edema treatment with focal laser (22). Laser treatment are likely to reason for vision loss from the inadvertent foveal burns or the spreading of laser scars over time, especially the patients with the leaking microaneurysms placed near to fovea are at high risk. Even patients still persists the Diabetic macular edema after laser treatment.[4] Ranibizumab was precisely developed for the ocular use; ranibizumab binds all the VEGF isoforms with bond that is 5 to 10 fold higher than that of the bevacizumab.[3] Intravitreal ranibizumab decreases the formation of CNV[4] and also decreases the leakage of neovascular age related macular degeneration in a primate model.[3] Regarding the pain evaluation different studies have been done and none were able to make a clear difference in pain scoring. Usually the pain during intravitreal injection is of mild intensity.[5] The choice of quadrant whether superotemporal or inferotemporal, for injecting intravitreal injections, depends totally upon ophthalmologist choice.

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While comparing superotemporal and inferotemporal injection site, there was no difference notice in the intensity of pain. There was only one study done which compared effect of the site of injection on pain related with the intravitreal bevacizumab injection.[8] In another study publishes in 2018, in Royal College of Ophthalmology a conclusion was made comparing the pain score, stating that the site for injecting intravitreal bevacizumab (IVB) ,Superotemporal was most painful and less painful site was Superonasal.[1] The aim for conducting this study is to observe the pain score of intravitreal injection in different quadrants, to find out which quadrant is less painful and which quadrant is more painful during the procedure because there is no proper conclusion regarding this .Since there is barely any study conducted on this subject in Pakistan. In wet AMD, treatment choices include bevacizumab, ranibizumab, pegaptanib, aflibercept, brolucizumaband another anti-VEGF.[9] For the treatment of AMD all of these drugs are FDA approved. The following image describe the AMD:

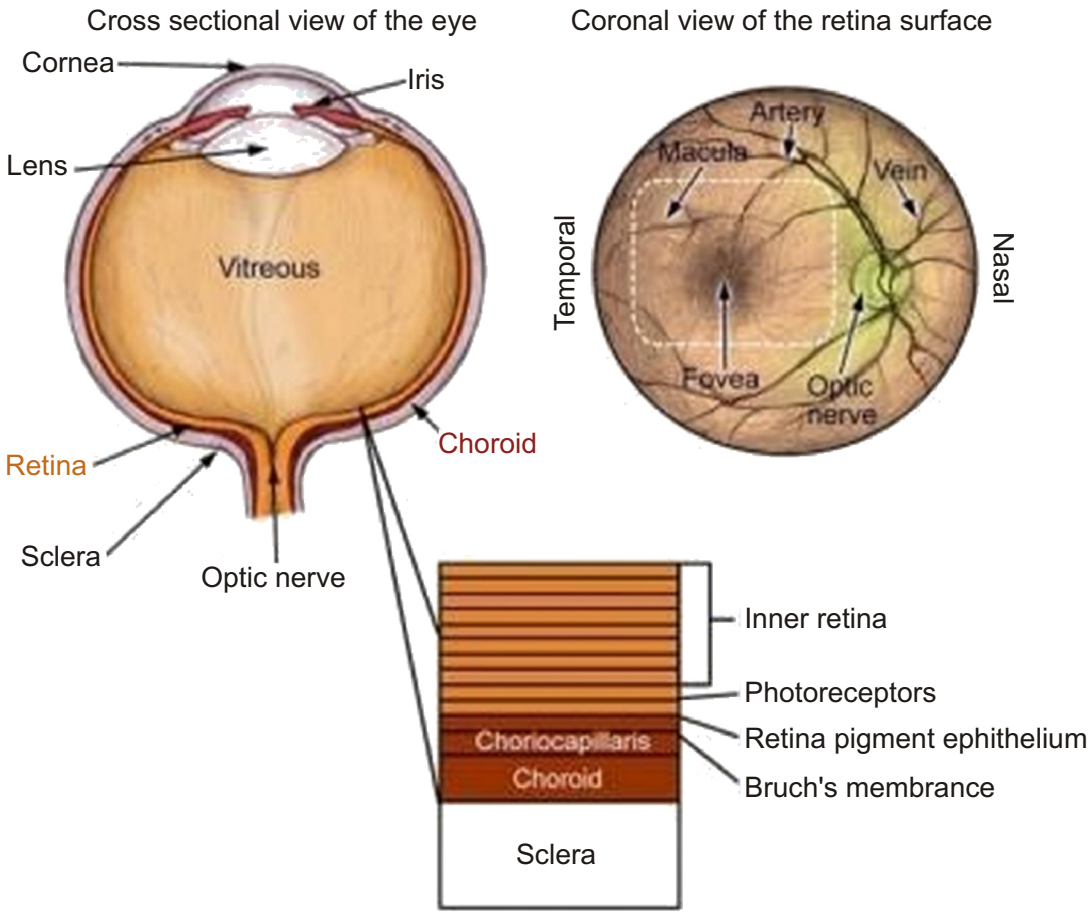


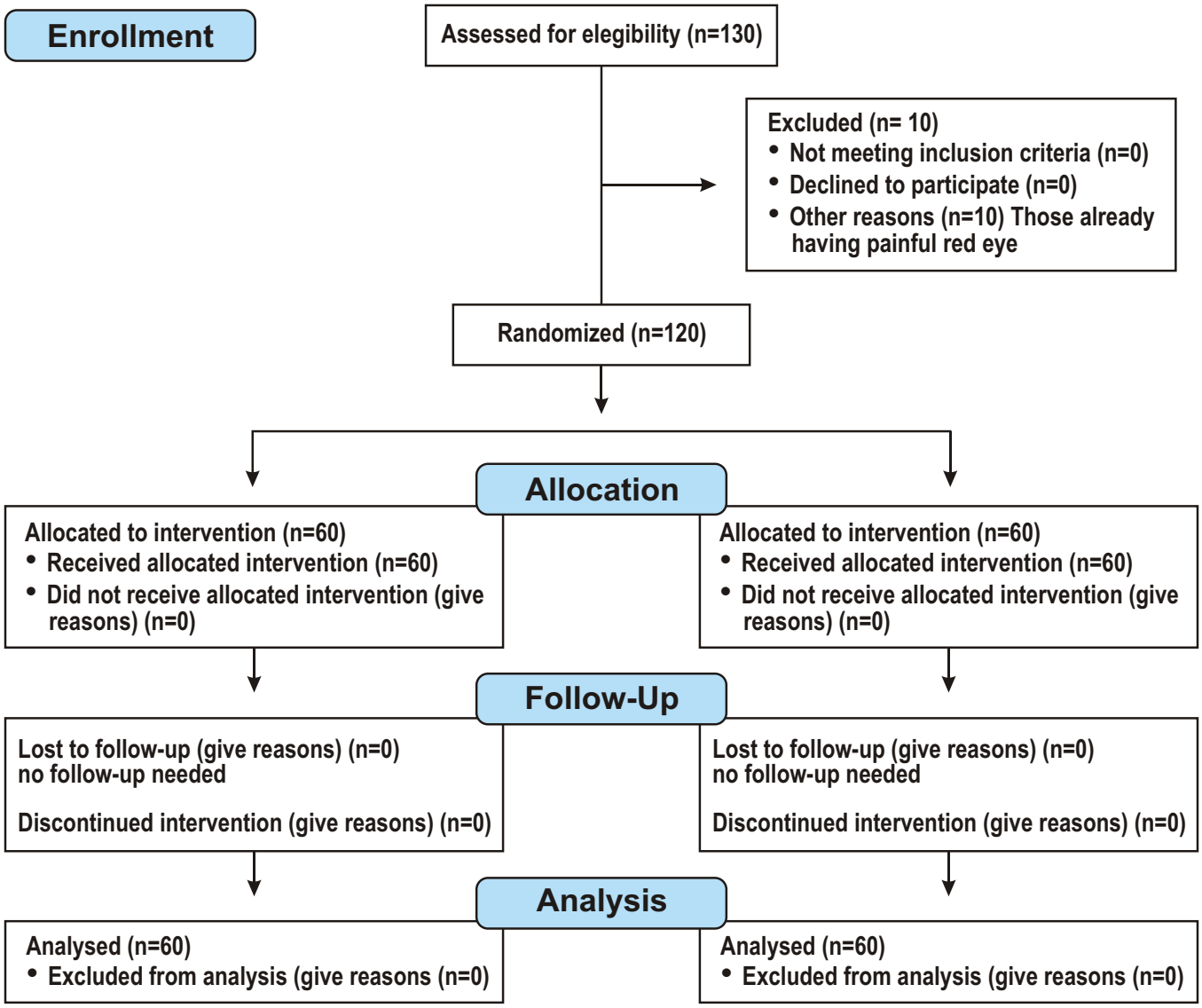
Figure 1: ARMD

MATERIALAND METHODS

Randomized controlled trial of four months was done In-patient Ophthalmology department, Pakistan Institute of Medical Sciences (PIMS) Islamabad from 1st May 2020 to 31st Aug-2020. In this study 120 patients were included (30 patients in each group) to measure the extent of pain while receiving an intravitreal bevacizumab injection.Sample size was calculated by WHO sample size calculator with 5% Level of significance, 80% Power of test.[5] and 3.4 Population standard deviation with following

- Test value of population, mean value of VAS (visual analog scale) score in superior nasal (SN) quadrant group = 1.5
- Anticipated population value, mean value of VAS score in superior temporal (ST) quadrant group = 4.0. Sample size calculated was 30 patients in each group and a total of 120 patients was included in the study. Non-Probability consecutive sampling technique was used.

CONSORT FLOW CHART



SAMPLE SELECTION

Inclusion Criteria:

1. Either sex
2. Age >40 years
3. Diagnosed with Age-related Macular degeneration (AMD), choroidal neovascularization, Macular edema due to "Branch Retinal Vein Occlusion" (BRVO) or DME, Diabetic Retinopathy PDR.
4. Ability to report and score pain perception.

Exclusion Criteria:

1. Any other ocular surgery other than catarct.
2. Active ocular infection
3. Glaucoma
4. Stroke and MI in last 6 months
5. Uncontrolled hypertension
6. Using any analgesics or sedative.
7. Dry eye syndrome
8. History of eye drops that may have an effect on eye surface sensitivity
9. Contact lens users
10. Poor cooperation in the visual analog (VAS) scale.

The study was conducted after approval from the Institutional Ethical Review Committee on 18-05-2020 (No F.1-1/2015/ERB/SZABMU/564. All the study candidates fulfilling the including criteria was taken up for the treatment group only after their written consent. All the data was entered in and analyzed using SPSS 23.0. The descriptive statistics was presented as mean ± standard deviation for quantitative variable i.e. Age, Pain. The categorical variables i.e. Gender, was presented in the form of frequency and percentages. The efficacy of treatment was compared on the basis of VAS score by applying ANOVA in four groups. The p-value less than = 0.05 was considered as significant.

RESULTS

The objective of our study was to compare the pain score in different quadrants correlated to intravitreal bevacizumab injection. The study was conducted at in-patient Ophthalmology department, Pakistan Institute of Medical Sciences. The sample size of our study was 120 patients (30 in each group). In our study we divide the patients in four groups according to the quadrant of eye (Group A Superonasal Quadrant, Group B Superotemporal Quadrant, Group C Inferonasal Quadrant and Group D Inferotemporal Quadrant). The results of our study showed that the mean age of the patients in Group A Superonasal Quadrant was 59.87 ± 9.45 years, in Group B Superotemporal Quadrant was 58.37 ± 8.29 years, in Group C Inferonasal Quadrant was 59.83 ± 9.08 years and in Group D Inferotemporal Quadrant was 61.67 ± 9.41 years. The overall mean Age of patients in our study was 59.93 ± 9.03 years.

According to age groups the results showed that in Group A Superonasal Quadrant 22 (73.3 %) patients were from ≤ 65 Years age group and 8 (26.7 %) were from > 65 years age group. In Group B Superotemporal Quadrant 23 (76.7 %) patients were from ≤ 65 Years age group and 7 (23.3 %) were from > 65 years age group. In Group C Inferonasal Quadrant 21 (70.0 %) patients were from ≤ 65 Years age group and 9 (30.0 %) were from > 65 years age group. In Group D Inferotemporal Quadrant 17 (56.7 %) patients were from ≤ 65 Years age group and 13 (43.3 %) were from > 65 years age group. In our study Overall 83 (69.2 %) patients were from ≤ 65 Years age group and 37 (30.8 %) were from > 65 years age group. According to gender the results showed that in Group A Superonasal Quadrant male patient were 14 (46.7 %) and female patients were 16 (53.3 %). In Group B Superotemporal Quadrant male patients were 13 (43.3 %) and female patients were 17 (56.7 %). In Group C Inferonasal Quadrant male patients were 12 (40.0 %) and female patients were 18 (60.0 %). In Group D Inferotemporal Quadrant male patients were 13 (43.3 %) and female patients were 17 (56.7 %). In our study overall male patients were 52 (43.3 %) and female patients were 68 (56.7 %). The results of pain score in our study showed that the mean score of the patients in Group.

A Superonasal Quadrant was 1.50 ± 0.51, in Group B Superotemporal Quadrant was 4.00 ± 0.91, in Group C Inferonasal Quadrant was 2.70 ± 0.84 and in Group D Inferotemporal Quadrant was 2.87 ± 0.78. The results of p value showed significant difference in pain score in groups. As the p value is less than level of significance. The Pain score is less in Group A Superonasal Quadrant as 1.50 ± 0.51 and more in Group B Superotemporal Quadrant as 4.00 ± 0.91.

Table 1: Distribution of Gender and age Groups in study Groups

Gender	Groups				Total	Age Groups	
	Group A (Superonasal Quadrant)	Group B (Superotemporal Quadrant)	Group C (Inferonasal Quadrant)	Group D (Inferotemporal Quadrant)		>65 Years	>65 Years
Male	14	13	12	13	52	83	37
	46.7%	43.3%	40.0%	43.3%	43.3%		
Female	16	17	18	17	68		
	53.3%	56.7%	60.0%	56.7%	56.7%		
Total	30	30	30	30	120	120	
	100.0%	100.0%	100.0%	100.0%	100.0%		

Table 2. Comparison of Pain Ccore among Four Study Groups and Comparison of Pain between both Genders

Groups	N	Mean	SD	Minimum	Maximum	F-Test	Sig.	T Test
Group A (Superonasal Quadrant)	30.00	1.50	0.51	1.00	2.00	52.59	0.000*	
Group B (Superotemporal Quadrant)	30.00	4.00	0.91	3.00	5.00			
Group C (Inferonasal Quadrant)	30.00	2.70	0.84	2.00	4.00			
Group D (Inferotemporal Quadrant)	30.00	2.87	0.78	2.00	4.00			
Male	52	2.77	1.23				.983	0.021
Female	68	2.76	1.13				.983	0.021

*significant (p value < 0.05)
**p-value based on ANOVA

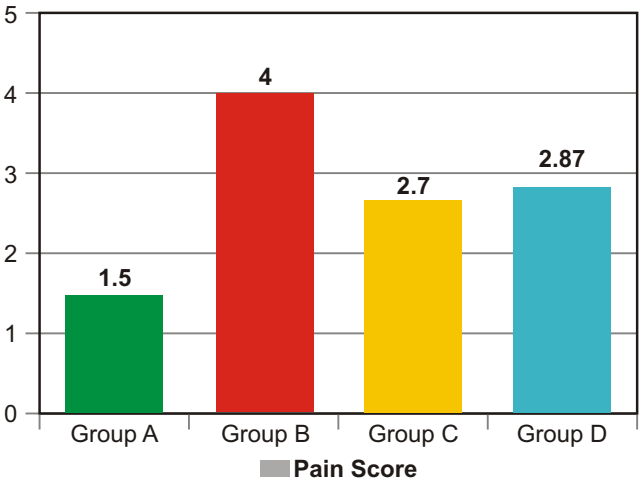


Figure 01. Pain Score in Different Quadrants

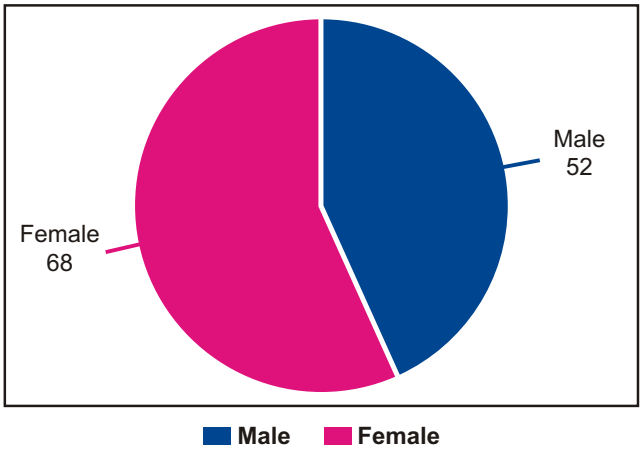


Figure 02. Gender

DISCUSSION

In near future, intravitreal injection will become most popular universal intraocular procedure[17]. As a consequence, it is important to consider the discomfort related with this procedure in order to ensure patient compliance and safety. The SN quadrant was related with the less pain during the IVB injection, according to our findings. Intravitreal injections used to treat a number of ocular disorders "neovascular AMD, diabetic macular edema (DME), and retinal vascular occlusions (RVO)". The mostly used anti-VEGF agents are bevacizumab and ranibizumab.[4] There may also be a relationship between the administered drug and the severity of pain. Since the chemical structures of intravitreal medications are different, they may cause varying degrees of pain in the eye (18). In order for the drug to be dispersed evenly throughout the eye, local anesthetic drops were instilled in supine position and patients were also instructed to close eyes slowly, move their eyes, and avoid squeezing or rubbing. Nonetheless, despite ocular motions to diffuse the drug, pooling remains a considerable potential, particularly in the supine posture and only the two drops were administered. The exact causes for the changes in pain scores between the four anatomical quadrants are unknown, and future research should map the sensory nerves of sclera, episclera and conjunctiva in the all quadrants within 34 mm of the limbus, which is the normal intravitreal injection location.

The stroma of conjunctiva has the morphology similar to end bulbs of the Krause, and half of the bulblike compact nerve terminals are present in the superior lateral quadrant of the bulbar conjunctiva, which may confirm our conclusion. Most of these structures were seen in narrow 1 mm wide annular zone of the conjunctiva beginning around 0.5 mm from the corneoscleral edge, far from the intravitreal injection site. It would have been interesting to use a standard technique to measure conjunctival sensitivity in the each quadrant for each subject.[1] In order to standardize the sense of drug-induced pain, only patients who received intravitreal ranibizumab injections were included in a study[18].

About 100,000 intravitreal injections are administered in United States monthly, according to estimates. This procedure could become the most public intraocular procedure in the world. Intravitreal injection can be done in a variety of ways, with different aseptic methods, prophylactic antibiotics, anesthetics use, treatment protocols and post-injection monitoring. In our study we used VAS for the pain determination. VAS used widely in the research of ophthalmology. It has previously been tested in studies examining extreme postoperative pain, and it is simple to use for both patients and health-care providers.[19] The findings of the research that have been conducted to assess pain levels during intravitreal injection have been mixed. Many factors involved with pain in intravitreal injection like sex, age, anxiety, needle size, technique of anesthetic, eye drop ketorolac, previous injection number.

A study was conduct to check the effect of intravitreal injection into different quadrants on pain score and injection comfort. The results showed that no difference was found between the quadrants in terms of pain score.[5] Therefore, the physicians may prefer the most comfortable quadrant for themselves and for their patients in intravitreal injection. Doguizi et al[6] also investigated the pain score in injection of intravitreal aflibercept in the 119 patients with the variables sex, age, injection site (ST or IT quadrant), during injection position (supine or sitting), previous number of the intravitreal injections, hypertension or DM presence and status of lens. With all these studied variable pain not showed significant relation site of injection. They demonstrated that pain associated with intravitreal aflibercept injection is generally mild with low pain scores. Various anesthesia methods were compared in intravitreal injection. In a study comparing topical proparacaine, topical tetracaine, lidocaine impregnated cellulose sponge and subconjunctival lidocaine anesthesia, no difference was found in terms of pain scores.

Another study compared proparacaine drop, proparacaine drop plus subconjunctival lidocaine, lidocaine gel anesthesia methods in intravitreal injection and subconjunctival lidocaine was found to be the most effective method to prevent pain and eye movements.[20] Intravitreal injection after topical proparacaine anesthesia has been reported to be highly effective and inexpensive. Blaha et al. found that topical tetracaine patients had a mean pain score of 2.8.[21] For topical proparacaine patients, Andrade et al. posted a pain score of 3.2 ± 1.7. Despite the fact that our study's mean pain score was 2.76 ± 1.17. Patients' pain scores during intravitreal injections of ranibizumab and aflibercept were compared in a study focused on patient feedback. In this study, 72 eyes from 72 patients who had never had any intravitreal injection procedures before were included. A total of 38 patients were given ranibizumab and 34 were given aflibercept injections. A visual analogue scale was used to assess pain (VAS). Patients were asked to rate their pain on a VAS scale from “0 (no pain) to 10 (worst pain ever felt)” immediately after the injection. Ranibizumab and aflibercept classes had VAS pain ratings of 3.28 ± 2.45 and 4.20 ± 2.30, respectively. The mean VAS scores varied significantly between groups (P = 0.04). The aflibercept group's VAS pain scores were found to be substantially higher than the ranibizumab group's. However, there was no connection between the severity of pain during intravitreal injection and age. The majority of the participants in our sample were under the age of 65 years, which may explain why we didn't find a significant association between age and pain score. In our study Overall 83 (69.2 %) patients were from $\leq$ 65 Years age group and 37 (30.8 %) were from > 65 years' age group. These findings match with the study.[9]

Doguizi et al [6] reported low pain score in females than males, and study by Haas et al[10] reported more pain score in female than males. The results of our study showed that the mean pain score was similar in males and females. Previous studies have found that some factors that may be associated with pain in intravitreal injection. Shin et al[11] described higher pain scores in women than

men. Injection comfort and safety scores were lower in female than male. The nerves density decreases with the age, especially after age of 70, meaning that elder patients must feel less in pain during the intravitreal injection. However, there was no connection between the severity of pain during the intravitreal injection and the age. The majority of the participants in study[1] were under the age of 70 and find no relation with age and pain severity. The mean age of the patients in Group A Superonasal Quadrant was 59.87 ± 9.45 years, in Group B Superotemporal Quadrant was 58.37 ± 8.29 years, in Group C Inferonasal Quadrant was 59.83 ± 9.08 years and in Group D Inferotemporal Quadrant was 61.67 ± 9.41 years. These results also confirmed by a study.[13]

The overall mean age of patients in our study was 59.93 ± 9.03 years. These findings match with the study in which the mean age of the patients was 61.3 ± 10.4 years. Some studies have found a relationship between pain and needle diameter during the injection. In a previous study, we found that the use of 30 gauge needles instead of 27 gauge significantly reduced pain scores in patients. However, another study reported that the use of a 30-gauge needle instead of a 27-gauge needle did not have any superiority in reducing pain. Nevertheless, 30 gauge needles were preferred by all surgeons. We preferred 30 gauge needle for injection because we thought it was easier to exceed the scleral resistance during the injection. The results of pain score in our study showed that the mean score of the patients in Group A Superonasal Quadrant was 1.50 ± 0.51, in Group B Superotemporal Quadrant was 4.00 ± 0.91, in Group C Inferonasal Quadrant was 2.70 ± 0.84 and in Group D Inferotemporal Quadrant was 2.87 ± 0.78. The results of pain score in study[1] showed that the mean score of the patients in Group A Superonasal Quadrant was 1.50 ± 1.7, in Group B Superotemporal Quadrant was 4.00 ± 2, in Group C Inferonasal Quadrant was 3 ± 2.3 and in Group D Inferotemporal Quadrant was 3 ± 2.1.

Similar to our study, Karimi et al[1] divided the eyes of the patients into superotemporal, superonasal, inferotemporal, and inferonasal quadrants to evaluate the relationship between the injection site and pain severity following intravitreal injection. They used a 10-degree visual pain scale to assess pain severity. The researchers reported that injection into the superior temporal quadrant causes the most severe pain [15]. This finding is consistent with our research. Compared to this study, the number of participants was lower in our study. On the other hand, the authors did not separate the eyes as right and left eyes. We formed groups with equal number of patients for each quadrant of the right and left eye in our study. Pain during intravitreal injection is usually mild [16]. When our injections were evaluated as a whole, our pain scores were generally low. Our study showed that that pain score was significantly linked with injection site.

CONCLUSION

In conclusion, we concluded that Superonasal Quadrant (SN Quadrant) was the less painfull quadrant as compared to other quadrants i.e. Superotemporal Quadrant (ST quadrant), Inferonasal Quadrant (IN Quadrant) and Inferotemporal Quadrant (IT Quadrant). The most pain full site was Superotemporal Quadrant (ST quadrant). We suggest use Superonasal Quadrant (SN Quadrant) site for the intravitreal injection for the treatment of eye diseases and in patients who feel more pain in their last intravitreal injection.

Limitations and Recommendations:

1. It was a single hospital trial with few numbers of patient.
2. Study only based on VAS score.
3. In this study unable to carry out a double-blind RCT.
4. The number of patients was not enough to detect uncommon medications side
5. effects
6. Not specify one surgeon's discretion because of administrative issues.

REFERENCES

1. Karimi S, Mosavi SA, Jadidi K, Nikkhah H, Kheiri B. Which quadrant is less painful for intravitreal injection? A prospective study. Eye. 2019;33(2): 304-12.
2. Shikari H, Samant PM. Intravitreal injections: A review of pharmacological agents and techniques. Journal of Clinical Ophthalmology and Research. 2016;4(1):51-9.
3. Peyman GA, Lad EM, Moshfeghi DM. Intravitreal injection of therapeutic agents. Retina. 2009;29(7): 875-912.
4. Gunther JB, Altaweel MM. Bevacizumab (Avastin) for the treatment of ocular disease. Survey of ophthalmology. 2009;54(3):372-400.
5. Güler Ö, URFALIOĞLU S, Güler M. The effect of intravitreal injection into different quadrants on pain score. Cumhuriyet Tıp Dergisi. 2019;41(3):653-7.
6. Doguizi S, Sekeroglu MA, Inanc M, Anayol MA, Yilmazbas P. Evaluation of pain during intravitreal aflibercept injections. European journal of ophthalmology. 2018;28(1):63-7.

7. Barthelmes D, Walton R, Campain AE, Simpson JM, Arnold JJ, McAllister IL, et al. Outcomes of persistently active neovascular age-related macular degeneration treated with VEGF inhibitors: observational study data. British Journal of Ophthalmology. 2015;99(3):359-64.
8. Boyle J, Vukicevic M, Koklanis K, Itsiopoulos C. Experiences of patients undergoing anti-VEGF treatment for neovascular age-related macular degeneration: a systematic review. Psychology, health & medicine. 2015;20(3):296-310.
9. Pinheiro-Costa J, Freitas-da-Costa P, Falcão MS, Brandão EM, Falcão-Reis F, Carneiro ÂM. Switch from intravitreal ranibizumab to bevacizumab for the treatment of neovascular age-related macular degeneration: clinical comparison. Ophthalmologica. 2014;232(3):149-55.
10. Haas P, Falkner-Radler C, Wimpissinger B, Malina M, Binder S. Needle size in intravitreal injectionspain evaluation of a randomized clinical trial. Acta ophthalmologica. 2016;94(2):198-202.
11. Shin SH, Park SP, Kim YK. Factors Associated with Pain Following Intravitreal Injections. Korean J Ophthalmol. 2018;32(3):196-203. doi: 10.3341/kjo.2017.0081. Epub 2018 May 15. PMID: 29770638; PMCID: PMC5990646.
12. Dugel PU, Koh A, Ogura Y, Jaffe GJ, Schmidt-Erfurth U, Brown DM, et al. HAWK and HARRIER: phase 3, multicenter, randomized, double-masked trials of brolucizumab for neovascular age-related macular degeneration. Ophthalmology. 2020; 127(1):72-84.
13. Scott IU, Flynn Jr HW. Reducing the risk of endophthalmitis following intravitreal injections. Retina. 2007;27(1):10-2.
14. Yamashiro K, Tsujikawa A, Miyamoto K, Oh H, Otani A, Tamuara H, et al. Sterile endophthalmitis after intravitreal injection of bevacizumab obtained from a single batch. Retina. 2010;30(3):485-90.
15. Moss JM, Sanislo SR, Ta CN. A prospective randomized evaluation of topical gatifloxacin on conjunctival flora in patients undergoing intravitreal injections. Ophthalmology. 2009;116(8):1498-501.
16. Shiroma HF, Takaschima AKK, Farah ME, Höfling-Lima AL, de Luca Canto G, Benedetti RH et al. Patient pain during intravitreal injections under topical anesthesia: a systematic review. Int J Retina Vitreous. 2017;3:23.doi:10.1186/s40942-017-0076-9. PMID: 28680703; PMCID: PMC5494853.
17. Rezaei KA, Wen JC. Intravitreal Injection Technique. MedEdPORTAL. 2016;12:10502. doi: 10.15766/mep_2374-8265.10502. PMID: 30984844; PMCID: PMC6440421.
18. Güler Ö, URFALIOĞLU S, Güler M. The effect of intravitreal injection into different quadrants on pain score. Cumhuriyet Medical Journal. 2019;41(3): 653-7.
19. Güler M, Bilgin B, Çapkın M, Şimşek A, Bilak Ş. Assessment of patient pain experience during intravitreal 27-gauge bevacizumab and 30-gauge ranibizumab injection. Korean Journal of Ophthalmology. 2015;29(3):190-4.
20. Andrade GC, Carvalho AC. Comparison of 3 different anesthetic approaches for intravitreal injections: a prospective randomized trial. Arquivos Brasileiros de Oftalmologia. 2015;78:27-31.
21. Blaha GR, Tilton EP, Barouch FC, Marx JL. Randomized trial of anesthetic methods for intravitreal injections. Retina. 2011;31(3):535-9.
22. Arevalo JF, Lasave AF, Wu L, Maia M, Diaz-Llopis M, Alezzandrini AA, et al. Intravitreal bevacizumab for proliferative diabetic retinopathy. Retina. 2017;37(2):334-43.

DATA SHARING STATEMENT: The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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AUTHOR'S CONTRIBUTION
The following authors full fill authorship criteria as per ICMJE guidelines;

Khan I, Zaib HMJ:	Idea conception, data acquisition, final approval, agreed to be accountable for all the work.
Khalid A, Noor M:	Design of the work, drafting the work, critical rivision, final approval, agreed to be accountable for all the work.
Armoghan N, Khadija H:	Data analysis, drafting of the work, final approval, agreed to be accountable for all the work.
Nazir F:	Data interpretation, critical revision, final approval, agreed to be accountable for all the work.