DOI:10.14744/bej.2025.04695
Beyoglu Eye J 2025; 10(1): 20-24

Original Article

Anxiety Levels Before Intravitreal Injections

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Abstract

Objectives: In our study, using amsterdam pre-operative anxiety and information scale (APAIS) and visual analog scale anxiety (VASA) analyze the patient's anxiety level about intraocular injection therapy and assess possible risk factors for these levels of anxiety in relation to the patient's sociodemographic, disease, and treatment characteristics.

Methods: Three hundred sixty-nine patients who received intravitreal ranibizumab, aflibercept, bevacizumab, and dexamethasone implants were included in the study. To measure the level of anxiety, APAIS questionnaire and VASA were used. APAIS and VASA were evaluated according to age, sex, indication for the injection, injection drug, previous injection numbers, and lens status in the study eye.

Results: About 15.4% of the patients participating in the study had VASA ≥6. The APAIS anxiety component score of 43.9% of the patients was found to be ≥11. Total information requests were found to be ≥5 in 48.7% of the patients. There was a significant negative correlation between VASA, APAIS, and patient age (spearman r=−0.25, p=0.004, r=−0.22, p=0.001). A significant negative correlation was found between the number of previous injections and anxiety levels measured by VASA (spearman r=−0.35, p=0.02), as well as between the number of previous injections and APAIS scores (anxiety levels and total information request) (spearman r=−0.32, p=0.03). There was a no significant difference between VASA, APAIS, and patient sex (p<0.05). A higher level of anxiety measured by VASA and APAIS has been shown in patients who have not had cataract surgery before, compared to those who have undergone cataract surgery (p<0.05).

Conclusion: The study underscores the importance of improving patient information and conducting further research to alleviate stress levels.

Keywords: Amsterdam pre-operative anxiety and information scale, anxiety, intravitreal injection, visual analog scale anxiety

Introduction

Age-related macular degeneration (AMD), retinal vein occlusion (RVO), and diabetic retinopathy are prevalent eye conditions that significantly impact individuals and society. Over the past decade, the use of vascular endothelial growth factor (VEGF) antagonists (anti-VEGF therapy) has increased, leading to a rise in the number of intravitreal injections administered for various retinal diseases (1).

Numerous large-scale trials have established the safety and effectiveness of anti-VEGF medications in treating neovascular AMD (n-AMD), diabetic macular edema (DME), and macular edema caused by RVO (me-RVO) (2,3). In addition, intravitreal dexamethasone implant injections have been shown to be an effective treatment option for macular edema resulting from other conditions, including RVO (4).

How to cite this article: Ertan E, Simsek M, Dogan M. Anxiety Levels Before Intravitreal Injections. Beyoglu Eye J 2025; 10(1): 20-24.

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Submitted Date: July 31, 2024 **Revised Date:** December 19, 2024 **Accepted Date:** January 01, 2025 **Available Online Date:** March 25, 2025
Beyoglu Eye Training and Research Hospital - Available online at www.beyoglueye.com

In the treatment of these diseases, most patients require multiple injections. The anxiety that patients experience regarding intravitreal injections can significantly impact their adherence to treatment protocols (5). Anxiety may also cause procedural difficulties, such as involuntary head or eye movements, leading to complications such as corneal abrasions, iatrogenic cataracts, and endophthalmitis (6).

The amsterdam pre-operative anxiety and information scale (APAIS) has been previously utilized to assess anxiety in ophthalmic surgeries (7,8). Since its introduction in the 1960s, the visual analog scale has been used to measure pain levels and has been adapted to assess quality of life, anxiety levels, and other emotional states (9,10).

Therefore, the aim of our study is to analyze the anxiety levels of patients undergoing intravitreal injection treatment using APAIS and visual analog scale anxiety (VASA). We also seek to identify possible risk factors associated with these anxiety levels, considering the patients' sociodemographic characteristics, disease profiles, and treatment details.

Methods

This study was approved by the Gaziosmanpasa Training and Research Hospital Ethics Committee (approval number 212, dated January 01, 2021) and conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants. This prospective, consecutive observational non-interventional study included patients diagnosed with n-AMD, DME, and macular edema due to RVO. Subjects with known psychological conditions or anxiolytic medication use were excluded from the study.

All subjects received intravitreal injections of ranibizumab, aflibercept, bevacizumab, or dexamethasone implants administered by the same surgeon in a dedicated injection room. The APAIS questionnaire and VASA were employed to measure anxiety levels. Participants independently completed the surveys immediately before their intravitreal injections. All participants had previously undergone intravitreal injections.

Topical anesthetic proparacaine 0.5% (Alcaine, Alcon-Couvreur, Puurs, Belgium) was administered, followed by the disinfection of the periocular skin and eyelids with 10% povidone-iodine. An eyelid speculum was used to stabilize the eyelids, and two drops of 5% povidone-iodine were applied to the conjunctiva. The conjunctiva was then irrigated with sterile isotonic solution. A 30-gauge needle was used for injections of ranibizumab, bevacizumab, and aflibercept, while a unique 23-gauge needle was used for dexamethasone implants.

APAIS

The APAIS, developed by the Moermann group in the Netherlands in 1996, is used to assess anxiety related to anesthesia, surgery, and the need for information. Each item is rated on a 5-point Likert scale (1=no severity, 5=extreme severity). The anxiety component is the sum of items 1, 2, 4, and 5, while the need for information component is the sum of items 3 and 6. An anxiety component score ≥11 indicates anxiety, and an information component score ≥5 indicates a need for information.

APAIS Items

1) I am worried about the anesthetics.
2) I always think about the anesthetics.
3) I would like to be informed as much as possible about the anesthetics.
4) I am worried about the procedure.
5) I always think about the procedure.
6) I would like to be informed as much as possible about the procedure.

VASA

The VASA consists of a 10 cm horizontal line with extremities indicating severity, where 0 means "not anxious" and 10 means "extremely anxious." A VASA score of ≥6 indicates a high anxiety level.

Sample Size and Power Analysis

To ensure adequate statistical power, a priori power analysis was conducted using an effect size of 0.5 (Cohen's d), a significance level (α) of 0.05, and a power of 0.8. The analysis indicated that a minimum of 64 participants per group would be required to detect a medium effect size with the desired power and significance levels.

Statistical Analysis

The data were analyzed using PASW Statistics for Windows, Version 21.0 (SPSS Inc., Chicago, IL, USA). Descriptive statistics for continuous data were presented as mean±standard deviation, while categorical variables were shown as counts and percentages. One-way ANOVA and the Student t-test were used to assess parametric data. The Spearman correlation test analyzed the relationship between age, VASA, and APAIS. Statistical significance was set at $p<0.05$.

Results

Of the 369 patients, 198 (53.7%) were men and 171 (46.3%) were women, with a mean age of 64.8±10.3 years (range: 36–92). Diagnoses included 120 n-AMD, 137 DME, and 112 me-RVO patients. Injection drugs were aflibercept (100, 27.1%), ranibizumab (93, 25.2%), bevacizumab (25.7%), and dexamethasone implants (81, 21.9%). Seventy-one patients (57.7%) had previous cataract surgery, while 52 (42.3%) had not. A negative significant correlation was found between VASA and patient age (spearman $r=-0.25$, $p=0.004$). A significant negative correlation was found between the number of previous injections and anxiety levels measured by

VASA (spearman r=−0.35, p=0.02). No significant difference in VASA was observed between sexes (p=0.2). Higher anxiety levels (VASA) were seen in patients without cataract surgery compared to those with cataract surgery (p=0.001). The relationship between patient characteristics and VASA scores is presented in Table 1. Patients with me-RVO had the highest anxiety and information request scores, while those with n-AMD had the lowest (p=0.001). Bevacizumab and dexamethasone implant recipients showed higher anxiety and information request levels compared to aflibercept and ranibizumab recipients (p=0.01). About 15.4% of patients had VASA ≥ 6. The relationship between patient characteristics and APAIS scores is presented in Table 2. Statistically significant lower levels of anxiety and total information requests were found in patients who had undergone cataract surgery before (p=0.001 for both). Patients with me-RVO had higher anxiety levels and total information requests in APAIS scores than other patients (p=0.001 for both). There was a negative significant correlation between APAIS (total anxiety score, total information request), and patient age (spearman r=−0.22 p=0.001). A significant negative correlation was found between the number of previous injections and APAIS (anxiety levels, total information request) (spearman r=−0.32, p=0.03). No statistically significant difference was found between APAIS (anxiety levels, total information request), and sex (p=0.303).

Table 1. Relationship between patient characteristics and VASA

Characteristic	VASA (Mean±SD)	p
Gender		
Female (F)	3.40±2.3	0.2
Male (M)	2.8±2.3	
Past-operation		
Yes (Y)	2.46±2.2	0.001
No (N)	3.9±2.3	
Diagnosis		
n-AMD	1.5±1.6	0.001
DME	3.4±2.1	
RVO-ME	4.9±2.4	
Injection drug		0.42/0.01
Aflibercept	2.4±1.9	
Ranibizumab	1.5±1.9	
Bevacizumab	4.9±1.9	
Dexamethasone implant	4.9±2.7	

SD: Standard deviation; VASA: Visual analog scale anxiety; n-AMD: Neovascular age-related macular degeneration; DME: Diabetic macular edema; RVO-ME: Retinal vein occlusion-macular edema.

Table 2. Relationship between patient characteristics and APAIS

Characteristic	APAIS (Mean±SD)	p
Gender		
Female (F) (anxiety)	9.38±4.1	0.3
Male (M) (anxiety)	8.5±4.6	
Female (F) (information)	4.8±2.1	0.2
Male (M) (information)	4.3±2.4	
Past-operation		
Yes (Y) (anxiety)	7.77±4.1	0.001
No (N) (anxiety)	10.53±4.2	
Yes (Y) (information)	4±2.1	0.001
No (N) (information)	5.4±2.31	
Diagnosis		0.001/0.001
n-AMD (anxiety)	6.4±3.6	
n-AMD (information)	3±1.5	
DME (anxiety)	9.6±4.1	
DME (information)	4.8±2.02	
RVO-ME (anxiety)	11.3±4.4	
RVO-ME (information)	6.5±2.4	
Injection drug		0.212/0.001
Aflibercept (anxiety)	7.9±3.9	
Aflibercept (information)	3.9±1.9	
Ranibizumab (anxiety)	5.9±2.9	
Ranibizumab (information)	3±1.5	
Bevacizumab (anxiety)	11.7±4	
Bevacizumab (information)	6.2±1.9	
Dexamethasone (anxiety)	11.7±4.7	
Dexamethasone (information)	6.6±3.0	

SD: Standard deviation; APAIS: Amsterdam preoperative anxiety and information scale; n-AMD: Neovascular age-related macular degeneration; DME: Diabetic macular edema; RVO-ME: Retinal vein occlusion-macular edema.

Discussion

In our study, we found that 43.9% of patients experienced pre-operative anxiety according to the APAIS score, and 15.4% had a VASA score of ≥6. The use of both APAIS and VASA scales provided a comprehensive assessment of anxiety levels in patients undergoing intravitreal injections. This dual approach allowed us to capture a broad spectrum of anxiety manifestations, which is critical given the procedural context.

The results of our study are consistent with those of Segal et al.,(11) who reported that 25% of patients undergoing intravitreal injections had VASA scores of 6 or above. However, contrary to Segal et al., (11) who found higher anxiety levels in female patients, our study found no signif-

icant difference between male and female patients in terms of anxiety levels ($p<0.05$). This discrepancy could be due to differences in sample size, demographic characteristics, or cultural factors affecting anxiety expression.

Martel et al.(12) also used the APAIS scale and found no significant differences in anxiety levels between sexes, supporting our findings. This consistency across different studies using APAIS suggests that this scale is reliable for assessing preoperative anxiety in ophthalmic procedures.

Our study demonstrated a significant negative correlation between age and anxiety levels measured by both APAIS and VASA. This indicates that younger patients tend to have higher anxiety levels. Heras et al.(13) also found that younger age was associated with higher anxiety levels. The increased anxiety in younger patients may be due to a lack of previous medical experience or a greater fear of the unknown.

Patients who had undergone previous cataract surgery exhibited significantly lower anxiety levels compared to those who had not had such surgery ($p=0.001$). In addition, in our study, a significant negative correlation was found between the number of previous injections and anxiety levels measured by VASA as well as between the number of previous injections and APAIS scores (anxiety levels and total information request). The prior experience of patients with injections reduced their information needs and anxiety scores. This finding aligns with the results of Chaudhary et al.,(14) who concluded that prior exposure to surgical procedures can reduce anxiety. The familiarity with surgical environments and procedures likely reduces the fear and uncertainty that contribute to anxiety.

When analyzing anxiety levels by diagnosis, we found that patients with me-RVO had the highest anxiety scores, whereas those with n-AMD had the lowest ($p=0.001$). Kayikcioglu et al. (15) reported higher anxiety levels in patients with AMD compared to those with DME, which contrasts with our findings. This discrepancy may be due to differences in patient populations or the chronicity and perceived severity of the diseases.

The type of injection drug also influenced anxiety levels. Patients receiving bevacizumab and dexamethasone implants reported higher anxiety compared to those receiving aflibercept and ranibizumab ($p=0.01$). The thicker 22-gauge needle used for dexamethasone implants, compared to the 30-gauge needle used for the other drugs, might contribute to this increased anxiety due to the anticipated pain or discomfort. This observation aligns with the findings of Rodrigues et al., (16) who noted that smaller gauge needles are associated with less discomfort during intravitreal injections.

Our study has several limitations. The relatively small sample size limits the generalizability of our findings. Future studies with larger patient populations and diverse demographic backgrounds are needed to validate our results. In addition, we did not examine the relationship between visual acuity and anxiety levels, which could be an important factor in understanding the full impact of these treatments on patient anxiety. Investigating this relationship in future studies could provide deeper insights into patient experiences and inform more targeted interventions to reduce anxiety.

Conclusion

Our study highlights that anxiety associated with intravitreal injections is significantly influenced by age, diagnosis, injection drug, previous cataract surgery, and previous injection numbers. There was no significant difference in anxiety levels between sexes. These findings underscore the importance of improving patient information and conducting further research to alleviate stress levels, particularly among younger patients and those receiving specific types of injections.

Disclosures

Ethics Committee Approval: This study was approved by the Gaziosmanpasa Training and Research Hospital Ethics Committee (approval number 212, dated January 01, 2021) and conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants.

Peer-review: Externally peer-reviewed.

Conflict of Interest: The authors declare that they have no competing interests.

Use of AI for Writing Assistance: Not declared.

Authorship Contributions: Concept – E.E., M.D.; Design – E.E.; Supervision – E.E., M.D.; Resource – M.S.; Materials – M.S.; Data Collection and/or Processing – M.S.; Analysis and/or Interpretation – E.E.; Literature Search – E.E., M.S., M.D.; Writing – E.E., M.S., M.D.; Critical Reviews – E.E., M.S., M.D.

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