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Physical and Emotional Burden on Patients Receiving Intravitreal Administration of Bevacizumab

Abishek Shrestha[1], Sangita Shakya[2], Kiran Shakya[3]
[1]Pharmacy Graduate, National Model College for Advanced Learning (NMCAL), Nepal
[2]Associate Professor, National Model College for Advanced Learning (NMCAL), Nepal
[3]Associate Professor, Nepal Eye Hospital, Kathmandu, Nepal
Corresponding Author: Sangita Shakya | shakyasangita2020@gmail.com | https://orcid.org/0009-0009-4361-2174
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ABSTRACT

Background:
Bevacizumab is intravitreally administered for wide range of vision-threatening retinal diseases.The treatment is effective in stabilizing vision, however repeated injections may impose physical discomfort, emotional stress, and restrictions in daily life and this overall affects quality of life of patients. Evidence on these outcomes in the Nepalese context is very limited.

Objective:
To determine physical and emotional burden on patients receiving intravitreal administration of bevacizumab.

Research Methodology: A cross-sectional, hospital-based descriptive study was conducted at Tertiary Eye Hospital from October to December 2024. A total of 54 patients were included. Data were collected using a validated, questionnaire adapted from the QUALITII tool, covering physical and emotional burden factors.

Results: Physically, 66.67% of patients reported pain during injection and the most common side effects were eye pain (61.1%), light sensitivity (46.3%), and floaters (25.9%). 61.1% of patients reported restrictions on daily activities after injection. Emotionally, anxiety decreased significantly after treatment, which indicates patients feeling more relieved after the injection.

Conclusion: Intravitreal bevacizumab therapy imposes considerable physical and emotional burdens. Addressing pain management and counselling is essential to improve overall patient wellbeing and adherence.

KEYWORDS

Bevacizumab, Intravitreal injection, Macular oedema, Pharmacist role, Treatment burden

INTRODUCTION

Macular oedema is an abnormal increase in thickness of macula normally due to accumulation of fluid in extracellular spaces of the retina.(Kabunga et al., 2022) Macular oedema can be caused by various conditions such as; Age-Related Macular Degeneration (AMD), Diabetic Macular Oedema (DMO), Retinal Vein Occlusion (RVO), Intraocular inflammation (uveitis), and pseudophakia. The most common type of macular oedema is Diabetic Macular Oedema (DMO).(Furino et al., 2021) Intravitreal injection is a common medical procedure used to deliver medication directly into the vitreous humor. Anti-VEGF therapies were first developed in the 1990s to block the vascular endothelial growth factor, which plays a key role in angiogenesis. (Hang et al., 2023) Treatment of these diseases typically involves repeated anti-VEGF IVIs as frequently as every four weeks over an indefinite course to maintain the therapeutic effect. (Ba et al., 2015)

Although intravitreal injection of anti-VEGF drugs can inhibit the further formation of retinal neovascularization to a certain extent, it requires one injection per month to achieve an effective

concentration of the drug in the eye. Repeated intraocular injections cause a heavy economic and mental burden on patients, and with the increase in the number of injections, the risk of ocular and systemic diseases in patients also increases sharply. In addition, some patients showed insensitivity to treatment with anti-VEGF drugs as well as photoreceptor degeneration after long-term repeated treatment. ((Kolar, 2014)

Therefore, evaluating not only the functional outcomes of therapy but also the broader impact on the patients' quality of life, specifically the physical and emotional burdens, is crucial. This study aims to assess the impact of intravitreal bevacizumab on patients with macular oedema. The study focuses on both physical and emotional burdens, to help guide patient-centered care strategies. The data obtained can be used to understand the burden of patients and provide counseling. The strategies include pain management advice (NSAIDs, lubricants, cold compresses), and lifestyle guidance.

METHODOLOGY

Study Design

A cross-sectional, hospital-based study was conducted among patients attending Tertiary Eye Hospital. The study population comprised patients receiving intravitreal administration of bevacizumab.

Sampling Method and Sampling Size

A non-probability convenience sampling method was employed. A total of 54 patients were included in the study during the period from October to December 20 24 at Tertiary Eye Hospital. The relatively small sample size resulted from repeated follow-up visits of the same patients, which limited the recruitment of new participants.

Instruments and Instrumentation

A validated 50-item questionnaire, QUALITII (Questionnaire to Assess Life Impact of Treatment by Intravitreal Injections), was adapted from the existing literature. The original tool was reviewed and modified with guidance from the research supervisor and an expert panel, which resulted in a 38-item questionnaire. This included 35 close-ended questions and 3 open-ended questions. The final instrument covered the following domains: Demographic information of patients, Details related to eye disease and treatment, physical and emotional burden associated with the treatment, and Quality of life–related factors.

Data Collection Process

Data collection was carried out Tertiary Eye Hospital Kathmandu. The study participants were patients with macular oedema who had received intravitreal bevacizumab and were attending follow-up consultations 15 days after administration.

Prior to data collection, informed consent was obtained from each participant. In cases where patients faced difficulty responding to certain questions, assistance was sought from their escorts, who were requested to support the participants in providing accurate responses.

Scoring System

For scoring satisfaction level, patients were asked to rate 0-6, where for scoring how patients were bothered with side effects, 0= Very Bothered and 6= Not bothered at all. For scoring pain

and discomfort that resulted from injection, 0= Insignificant and 6= Very significant. For scoring anxiety before, during and after the injection, 0= Very anxious and 6= Not at all anxious.

Ethical Approval

The research was started after obtaining approval from the Ethical Committee of Tripureswor Eye Hospital.

Informed Consent

Written informed consent was taken from each patient participating in research and properly informed about research objectives and importance.

Data Analysis

Data were analyzed in the computer using descriptive quantitative analytical statistics in MS. Excel 2013 and Statistical Package for Social Sciences (SPSS) version 26 and the results were represented in tables and figures.

Selection Criteria

Inclusion Criteria

1. Patients who are above 18years old
2. Received at least one intravitreal bevacizumab injection in the study eye
3. Attending follow-up visit 15 days after injection to align data collection workflow.
4. Patients who can understand and respond the questionnaire.

Exclusion Criteria

1. Patients younger than 18 years with the rational of study focusing only on adults.
2. Patients unable and unwilling to give informed consent.
3. Patients who are unable to understand the questionnaire.
4. Patients who are undergoing concurrent ocular therapy other than intravitreal bevacizumab.

RESULTS AND DISCUSSIONS

Demographic Characteristics and clinical profile of patients *Age*

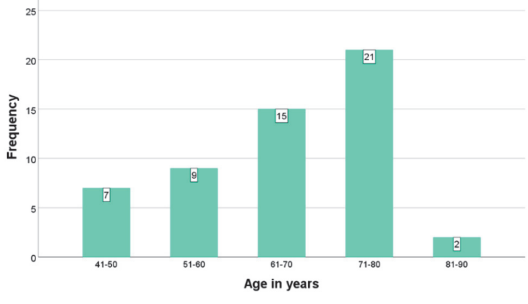

Figure 1: Frequency distribution of patients based on Age

Out of 54 patients, the highest number of patients were found to be of age group 70-80 years which accounted for 21(38.9%) followed by age group 61-70 years (27.8%), age group 51-60 (16.7%), age group 41-50 (13.0%) and age group 81-90(3.7%).

Many of the chronic retinal conditions necessitating intravitreal injections, such as age-related macular degeneration (AMD) and retinal vein occlusion (RVO), are strongly associated with older age.(Pradhan et al., 2018) Ba, Jun et al. on their study on neovascular AMD treatment identified patient mean ages ranging from 73.0 to 80.3 years.(Ba et al., 2015) Also, Kubin et al. in a real-world study on nAMD patients reported a mean age of 78 ± 8 years, with a significant majority (71%) being 75 years or older.(Kubin et al., 2024) Shrestha Arjun et al. in a study assessing intravitreal bevacizumab (IVB) use in Nepal, found the mean age for patients with AMD was 72.04 (±8.62) years.(Shrestha et al., 2021) Kolačko et al. in their study concluded older patients, especially those over 60 or 75, often report a reduced quality of life due to poorer general health, more significant visual impairment, and limitations in social roles, which is a natural consequence of aging. (Kolačko et al., 2023)

Gender

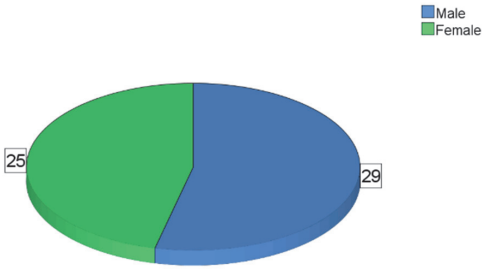

Figure 2: Distribution of patients based on Gender

Out of 54 patients, 29(53.7%) were male and 25(46.3%) were female.

Disease condition of patient

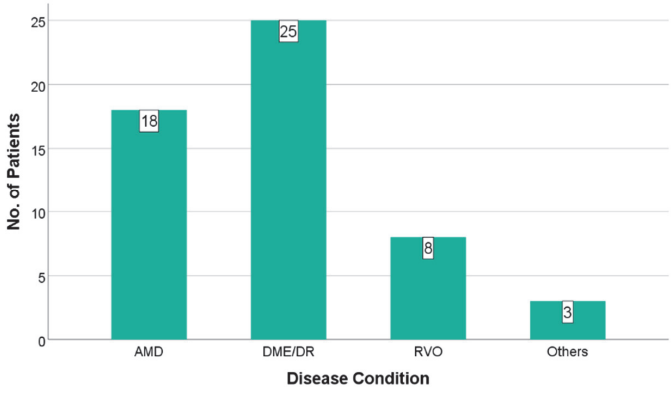

Figure 3: Frequency distribution based on disease condition of Patients

Out of 54 patients, the highest number of patients were found to be diagnosed with Diabetic Macular Oedema/Diabetic Retinopathy 25(46.3%), followed by Age Related Macular Degeneration/Age Related Macular Oedema 18(33.3%), Retinal Vein Occlusion 8(14.1%) and others 3 (5.56%).

Shrestha, Arjun et al. in a study conducted in Nepal found that Diabetic Retinopathy patients received 32.6% of intravitreal bevacizumab injections.(Shrestha et al., 2021) Similarly, Kabunga et al. in their study on macular oedema in Uganda reported DR as the commonest cause of MO, accounting for 53.1% of cases. The "others" category typically includes a range of less common conditions that can also cause neovascularization or macular oedema and thus benefit from anti-VEGF injections.(Kabunga et al., 2022)

Out of 54 patients, 18(33.3%) patients administered bevacizumab every 4-5 weeks, 5(9.3%) patients administered every 6-8 weeks, 10(18.5%) patients administered every 10-12 weeks, 1(0.19%) patient administered every 13-16 weeks.9(16.7%) patients administered only as needed and 11(20.3%) patients administered bevacizumab for the first time.

Every 4-5 weeks (33.3%): This frequency aligns with monthly dosing regimens, which have historically been a common approach in clinical trials and practice for anti-VEGF therapies.(Bahr & Bakri, 2023) Monthly injections have shown significant visual acuity improvements and reductions in macular thickness.(Martin et al., 2012) Every 6-8 weeks (9.3%) and Every 10-12 weeks (18.5%): These longer intervals are characteristic of "Treat-and-Extend" (T&E) regimens or less frequent fixed dosing schedules.(Bahr & Bakri, 2023) This approach aims to reduce the treatment burden on patients and healthcare systems by decreasing the number of required visits while maintaining efficacy.(Anguita et al., 2021)

The "as-needed" regimen means patients are monitored at regular intervals (e.g., monthly), but injections are only administered when there is evidence of disease activity. This reduction in injection frequency directly contributes to a lower treatment burden for both patients and physicians. Significant proportion of new patients 20.3% suggests a continuous influx of individuals requiring anti-VEGF therapy to preserve their vision.

Physical Burden on Patients

Aspect of Pain

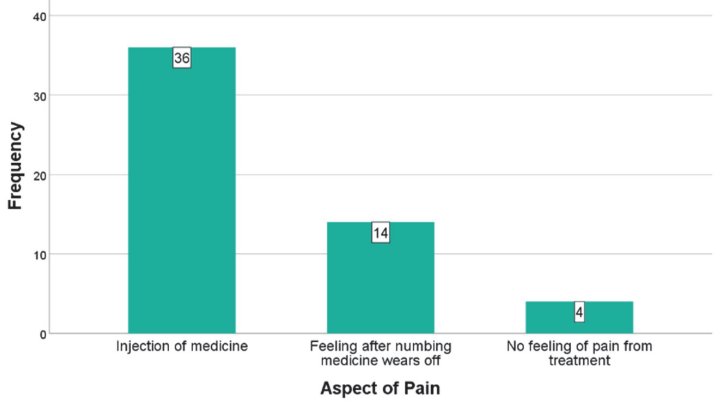

Figure 4: Distribution of patients based on aspect of pain on treatment

Out of 54 patients, 36(66.7%) patients reported "injection of medicine into the eye" as an aspect of treatment that caused most pain while 14(25.9%) patients reported "feeling after numbing medicine wears off" as an aspect of treatment that caused most pain.4(7.4%) patients didn't feel pain from the treatment.

Boyle et al. in their study involving 1416 patients, the most frequently reported uncomfortable aspects of treatment were the injection of the medication into the eye (29%), followed by the feeling after the topical anesthetic wears off (17%), and the use of betadine (12%) . (Wang et al., 2022)

Duration of Pain

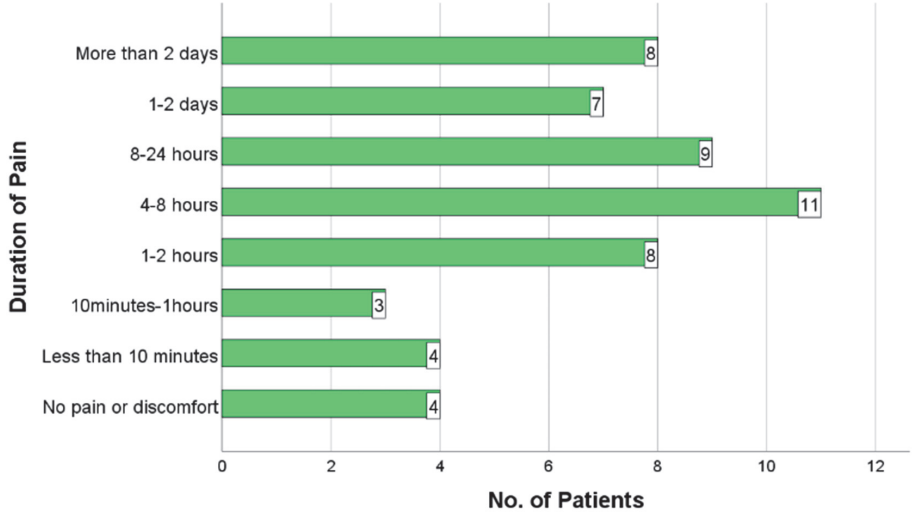

Figure 5: Distribution of patients based on duration of pain after treatment

Out of 54 patients, 4(7.4%) patients reported pain lasted less than 10 minutes after injection, 3(5.56%) reported 10minutes-1hour, 8(14.8%) patients reported 1-2 hours, 11(20.3%) patients reported 4-8 hours, 9(16.7%) patients reported 8-24 hours, 7(13%) reported 1-2 days, 8(14.8%) reported more than days and 4(7.4%) patients didn't feel pain or discomfort after injection.

Pain from Injection

Table 1: Patient's rating on pain from Injection

Rating	Frequency	Percentage
0	1	1.9
1	15	27.8
2	10	18.5
3	16	29.6
4	9	16.7
5	3	5.6

0 =Insignificant 6 = Very Significant pain

The mean rating of pain from injection was found to be 2.48 ± 1.27.

Wang et al. in their study found the most frequently reported uncomfortable aspects of treatment were the actual injection of the medication into the eye (29%), followed by the feeling after the topical anesthetic wore off (17%), and the use of betadine (12%). Patient age was associated with pain perception; the mean discomfort score was 2.22 among patients younger than 63 years, compared with 1.56 among patients older than 80 years, suggesting a potential decrease in tactile sensitivity with age.(Wang et al., 2022) Granström et al. In their study using the 25-item National Eye Institute Visual Function Questionnaire NEI VFQ-25), "Pain in the eyes" had a median score of 100 (interquartile range 75–100) on a 0–100 scale, where 100 indicates best functioning (i.e., least pain) Male respondents in this study reported significantly less intensity of pain compared to female respondents (median 100 vs. 87.5).(Granström, n.d.)

Counselling from Healthcare Professionals for Pain Management

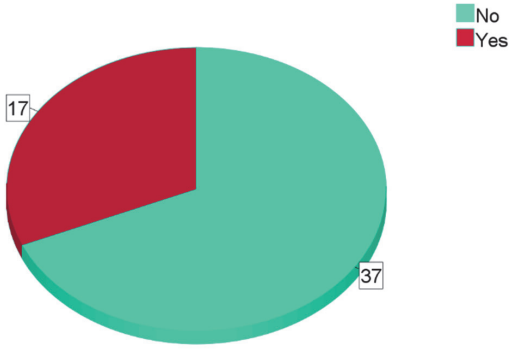

Figure 6: Distribution of patients based on counselling from healthcare professionals for pain management

Out of 54 patients, 17(31.4%) patients reported they received counselling from healthcare professionals and pharmacists for pain management while 34(68.6%) patients reported they didn't receive counselling for pain management after injection.

Management of Pain

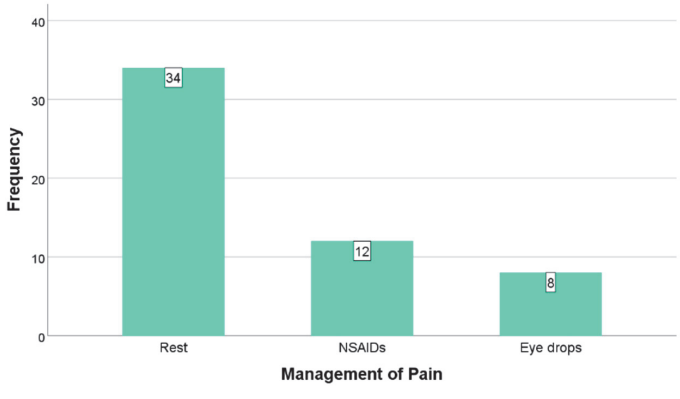

Figure 7: Distribution of patients based on pain management

Out of 54 patients, 34(63%) patients reported to have rest or no management for pain while 12(22.3%) patients reported to have used NSAIDs for pain management and 8(14.8%) patients reported to use eye drops for pain management.

Rest (63%) is the most reported patient-initiated strategy for managing pain or discomfort. Only 17 out of 54 patients (31.4%) reported receiving counselling for pain management from healthcare professionals and pharmacists. This relative lack of formal counselling could contribute to patients relying on general coping mechanisms like rest or not actively managing the pain if they are unsure of appropriate actions. Some of the patients are using OTC NSAIDs to relieve pain or discomfort after injection. 14.8% patients used artificial tears to manage pain or discomfort after injection.

Side Effects

Table 2: Side Effects after administration of injection

S.N	Side effects	Frequency
1.	Eye Pain	33
2.	Increased floaters	14
3.	Increased Sensitivity to Light	25

Patients could choose multiple options as side effects. Out of 54 patients, 33(61.1%) patients reported eye pain as a side effect, 14(25.9%) patients reported increased floaters, and 25(46.3%) patients reported increased sensitivity to light.

Wang et al. in their study reported a slightly lower figure of 49.7% of patients experiencing eye pain as a commonly reported side effect and increased sensitivity to light affecting 37.1% of patients.(Wang et al., 2022)Floaters" or "vitreous floaters" are explicitly listed as potential ocular adverse events associated with intravitreal anti-VEGF injections.(Hang et al., 2023) Patients may also complain of "vitreous opacities or bubbles" after the procedure.(Rijal et al., 2021) These are generally considered "less serious" side effects compared to vision-threatening complications like endophthalmitis or retinal detachment.(Ehlers et al., 2022)

Frequency of side effects

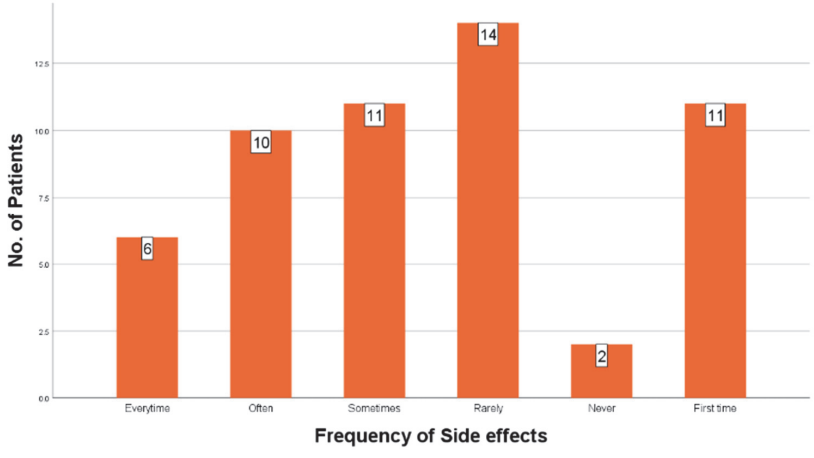

Figure 8: Distribution of patients based on frequency of side effects

Out of 54 patients, 11 patients reported side effects to occur sometimes, 10 patients reported "often", 6 patients reported "every time", 14 patients reported "rarely", and 2 (3.7%) patients reported "never".11 (20.3%) patients received injection for the first time so frequency couldn't be calculated.

The frequent occurrence of side effects, even if mild, contributes to the "humanistic burden" of intravitreal injection therapy. (Hashimoto et al., 2023) Despite the high prevalence of side effects and the associated burden, many studies indicate that patients adapt over time. (Wang et al., 2022)

Restriction after Injection

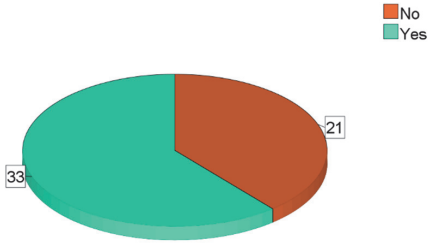

Figure 9: Distribution of patients based on restrictions from daily activities after Injection

Out of 54 patients, 33 (61.1%) patients reported restrictions from daily activities after injection while 21 (38.9%) patients reported no restrictions after injection.

Wang et al. in their study found 42.1% of patients reported restrictions from usual activities due to discomfort after intravitreal injections. This difference highlights that the impact on daily life can vary significantly, potentially influenced by your specific patient population, the nature of their conditions, or the local care context. (Wang et al., 2022)

Relation between Gender and Restrictions on Daily activities

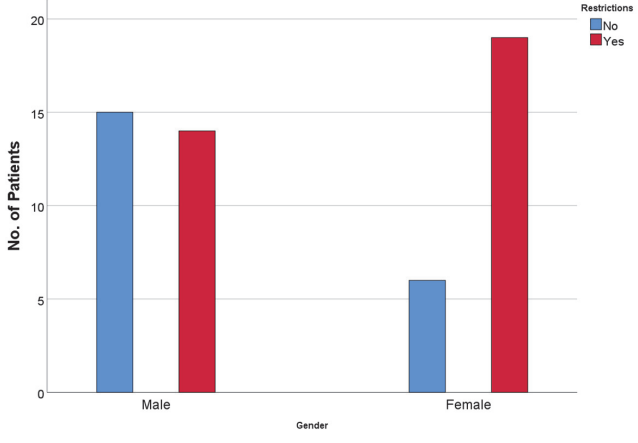

Figure 10: Relation between Gender of patients and restrictions on daily activities

The Chi-square analysis was conducted to examine the association between the two categorical variables

$\chi^2 = 4.342$
$p = 0.037$

Since $p < 0.05$, the result is statistically significant.
There is a significant association between the two variables.

Emotional Burden

Table 3: Anxiety Before During and After the Injection

Rating	Before	During	After
0	2	0	1
1	15	6	1
2	7	6	4
3	2	5	3
4	3	6	3
5	0	3	6
6	25	28	36

0 = Very anxious 6 = Not anxious at all

The mean anxiety before, during and after the treatment was found to be 3.65±2.84, 4.44±1.88 and 5.11±1.55 respectively.

The result indicates declining anxiety as the patients move through the treatment procedure. The findings suggest anticipation of procedure provokes more anxiety than the procedure.The immediate relief after the completion of procedure resulted rapid reduction in anxiety level.

Anxiety before treatment: The finding can be compared with the study finding by Spooner, Kimberly L et al. where 67% of patients experienced high anxiety for their first injection .(Spooner et al., 2019) The lower level of anxiety in present study may be due to differences in patient populations, pre-procedure patient education and how anxiety was perceived.

Anxiety during and after the treatment: The gradual increase in the mean score from "before" (3.65) to "during" (4.30) to "after" (5.11) indicates that patients' anxiety levels continue to decrease as they go through the treatment procedure. This suggests that the patients feel more relief once the injection procedure starts, especially when it is completed.

The highest proportion of patients, 36 out of 54 patients (66.7%) reported an anxiety score of 6 (“not anxious at all”) after treatment. The large population felt relieved and emotionally calm after the treatment procedure was completed. The patients might experience fear or anxiety before the treatment because of the uncertainty or anticipated pain. This indicates need of adequate counselling besfore the treatment to reduce the emotional distress.

CONCLUSION

Intravitreal bevacizumab therapy is effective and generally well-accepted, but it imposes meaningful physical discomfort, emotional stress, and functional limitations. There is need of supportive interventions aimed at improving patient experience and maintaining long-term adherence. Enhancing counselling, managing pain proactively, and reducing emotional burden before injection may improve overall quality of life for patients undergoing repeated intravitreal treatment.

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