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Open Access Journal of Ophthalmology

Understanding Patient Perspectives of Anti-VEGF Treatment Experience and Effect in Age-Related Macular Degeneration

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Research Article

Volume 1 Issue 2

Received Date: October 25, 2016

Published Date: December 29, 2016

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Abstract

Purpose: Understand patients' perspectives of intravitreal anti-VEGF therapy efficacy for exudative age-related macular degeneration (eAMD).

Methods: 107 patients receiving intravitreal anti-VEGF injections in an academic retina practice completed a 28-question survey during their clinic visit. IRB approval and patient consent was obtained.

Results: 61 patients (85 eyes) with eAMD were analyzed. Vision improved 3 lines in Snellen acuity in 19% (16/85), remained stable within 3 lines in 66% (56/85), and worsened by 3 lines in 15% (13/85). 38% of patients (23/61) perceived improvement in their vision, 21% (13/61) were uncertain, and 41% (25/61) felt no improvement. There was a statistically significant correlation between the objective effect of treatment on vision and the patients' perception of the effect in bilaterally treated patients (p-value: 0.000) and borderline significance in unilaterally treated patients (p-value: 0.052).

Conclusion: Patients' subjective perceptions of anti-VEGF treatment on visual acuity were consistent with quantifiable changes.

Keywords: Intravitreal; Exudative; Anti-VEGF Treatment; Age-related macular degeneration; STATA t-tests and Fisher's exact test

Introduction

Exudative age-related macular degeneration (eAMD) is a major cause of vision loss in individuals over 55 years of age in the United States. Intravitreal injections of anti-vascular endothelial growth factor (anti-VEGF) agents (bevacizumab, ranibizumab and aflibercept) have revolutionized the care and visual outcomes of these

patients [1,2]. However, the treatment is invasive, must be repeated relatively frequently, and can be considerably anxiety-provoking for patients. Many studies have evaluated patient preferences regarding anesthetic type and the protocol for administering anti-VEGF treatment [3-6]. Additionally, patient perceptions on living with eAMD and the impact it bears on their quality of life with regards to metrics such as mobility, emotional well-being, and access to information have also been examined [7]. However, no studies to date have evaluated the qualitative patient perception of treatment efficacy compared to objective efficacy in the eAMD population. This study aims to describe the patient perspective of the efficacy of anti-VEGF treatment, and correlate this with objective treatment efficacy [8-10].

Patients and Methods

The study protocol was approved by the Institutional Review Board of the Northwestern University Feinberg School of Medicine. A prospective 28-question survey was created by 3 retina specialists (RM, MG, AL) and administered to all patients undergoing intravitreal injection therapy for any diagnosis at Northwestern Medical Faculty Foundation outpatient retina clinic over four consecutive weeks, from June 17, 2013, to July 12, 2013 (Appendix A). All patients over the age of 50 years were included. Patients who were receiving their first intravitreal injection were excluded from this study. Patients anticipated injections at most visits, as a treat-and-extend approach versus a monthly OCT-guided approach was common practice.

All patients were consented by the same investigator (MF) and given the option to complete the survey on their own or with the assistance of the investigator (MF). The patients completed the survey at the end of their clinic visits.

The questions in this survey were designed to qualitatively assess the following categories: factors influencing a patient's treatment choice, the patient's understanding of the diagnosis, the patient's level of anxiety, qualitative experience with the treatment, and perception of the effect of the treatment on the patient's vision. In addition, a chart review was performed on each patient who completed the survey to obtain demographic data including age, gender, and insurance status, as well as clinical information including diagnosis, duration of treatment, vision at presentation, vision at time of survey, vision status of the fellow eye, drug used for treatment, number of injections received since the onset of treatment, and frequency of injections. For the purposes of our analysis, change in vision was defined by the difference in calculated logarithm of the minimum angle of resolution (logMAR, based on the recorded Snellen visual acuity) between vision prior to the first injection and vision at the time the survey was administered after receiving at least one treatment. There were three categories of change: vision improved by at least 3 lines in Snellen acuity (or 0.3 differences in logMAR), vision stable within 3 lines, and vision worsened by at least 3 lines. Perception of treatment was evaluated with the question, "Is the current treatment improving your vision?", with the answer choices of "yes, treatment has made it better", "no, treatment has not made it better", or "unsure".

Anxiety about intravitreal injections is a common consideration among physicians and patients. This study asked patients to recall their first injection, and report their current perception of how they felt prior to their first treatment. They were asked to rate their level of anxiety prior to their first injection on a scale of 1 (not anxious) to 5 (very anxious). In addition, the cause of anxiety was elicited with the question, "what made you most anxious?" The answer choices were: "thought of a needle in the eye", "ongoing need to come to the doctor's office", "thought of losing vision", and "other".

With regards to deciding between the three types of anti-VEGF treatment medication, patients were asked to rank in order from 1, most important, to 6, least important, "what is the most important factor in picking your treatment drug?". The options included: "research/clinical trials that have been done", "FDA approval", "cost", "potential interval between injections", "doctor's choice", and "no preference". To investigate opinions about other potential treatment modalities, patients were asked "what would be the ideal treatment for you?" with the following options: "drug is injected monthly but gives you the best vision possible", "drug is injected every 3 months but gives you slight loss of vision", "monthly follow-up in office, which may involve an injection of drug but may give you slight loss of vision", "implantable device requiring surgery once a year with minimal follow-up but gives you the best vision possible", or "eye drops administered at home but still require monthly follow-up with slight loss of vision". Patients were also asked, "how would you feel about getting injections for the rest of your life?"

Statistical analyses were performed using STATA t-tests and Fisher's exact test. Statistical significance was measured at the alpha = 0.05 level. In total this study surveyed 107 patients receiving intravitreal injections for the following diagnoses: exudative age related macular

degeneration (55%), diabetic macular edema (23%), vein occlusion (12%), and non-AMD choroidal neovascularization (CNV)(10%). For the purpose of this paper only those with eAMD were analyzed. The other diagnoses will be analyzed in future papers.

Results

This study included 61 patients with the diagnosis of eAMD, 70% (43 of 61) of whom were female and 30% (18 of 61) of whom were male (Table 1). Ages ranged from 52-96 years, with the average age of 82 years. Baseline visual acuities prior to onset of treatment with anti-VEGF agents ranged from 20/20 to Hand Motion-only vision, with a converted average logMAR value of 0.5 (Snellen equivalent of 20/63).

61% (37 of 61) of these patients were receiving treatment in one eye and 39% (24 of 61) received bilateral treatment for a total of 85 eyes treated. The average number of injections each patient had received prior to completing the survey was 28, with a range from 2-88 per patient. The range of interval between injections was 2 to 12 weeks, with an average interval of 5.8 weeks. All three anti-VEGF agents were used in this cohort (bevacizumab, ranibizumab, aflibercept). The breakdown for the number of medications each patient had used is as follows: 38% (23) patients had been treated with only one medication, 41% (25) had received two medications, and 21% (13) had received three medications during the course of their treatment. At the time of this survey, 60% (37) patients were being treated with aflibercept, 25% (15) were being treated with ranibizumab, and 15% (9) were being treated with bevacizumab.

All the patients in this cohort had insurance, however, coverage for the medications and injections were variable. The insurance providers were: Medicare and Private in 83.5% (51), Medicare only in 10% (6), Private only in 6.5% (4).

Patient's Gender	**n**	**%**	**Number of Injections***	**n**	**%**
Male	18	30	<10	10	16
Female	43	70	11-29	30	49
			>30	21	35
Patient's Age	**n**	**%**	**Frequency of Injections**	**n**	**%**
50-59 years old	2	3	2-3 weeks	5	8
60-69 years old	2	3	4-5 weeks	26	43
70-79 years old	16	26	6-7 weeks	15	25
80-89 years old	29	48	8-9 weeks	11	18
90-99 years old	12	20	10-11 weeks	0	0
			12 weeks	4	6
Patients Receiving Unilateral Treatment					
Baseline Vision	**n**	**%**	**Current Vision**	**n**	**%**
20/40 and better	15	40	20/40 and better	18	49
20/50 – 20/70	11	30	20/50 – 20/70	7	19
20/80 and worse	11	30	20/80 and worse	12	32
Patients Receiving Bilateral Treatment					
Baseline Vision	**n**	**%**	**Current Vision**	**n**	**%**
20/40 and better	18	38	20/40 and better	19	40
20/50 – 20/70	8	16	20/50 – 20/70	9	19
20/80 and worse	22	46	20/80 and worse	20	41

Table 1: Patient Demographics.
*Number of Injections prior to survey administration.

Treatment Efficacy

Of the 85 eyes treated, vision objectively worsened by at least 3 lines in 15% (13/85), remained within 3 lines in 66% (56/85), and improved by at least 3 lines in 19% (16/85). Subjectively, the 61 patients reported perceptions along a similar trend. When asked whether they perceived their vision to be improving from treatment, 41% (25/61) reported "no," 21% (13/61) were "unsure," and 38% (23/61) said "yes."

Unilateral Treatment: The analysis was further subdivided into unilateral versus bilateral treatments in patients. 37 patients received unilateral injections for eAMD. In these eyes, the visual acuity: worsened by at least 3 lines in 11% (4/37), remained stable within 3 lines in 67.5% (25/37), and improved by at least 3 lines in 21.5% (8/37). 75.7% (28/37) of the patients receiving unilateral treatment had better vision in their fellow eye.

For patients receiving treatment in one eye only, the response to the question "do you think your treatments are improving your vision?" was "no" in 50% (2/4) of those whose eyes worsened by 3 lines. For those whose vision remained stable within 3 lines, patients responded 48% (12/25) "no", 20% (5/25) "unsure", and 32% (8/25) "yes" to this question. In patients whose vision improved by 3 lines, 75% (6/8) perceived that their treatment was improving their vision (Figure 1). Correlation analysis in STATA revealed a borderline statistically significant positive correlation of 0.32 (p-value: 0.052, at the alpha=0.05 level) between the objective effect of the treatment on vision and the subjective perception of treatment's effect on vision in those patients who received unilateral treatment (Figure 1).

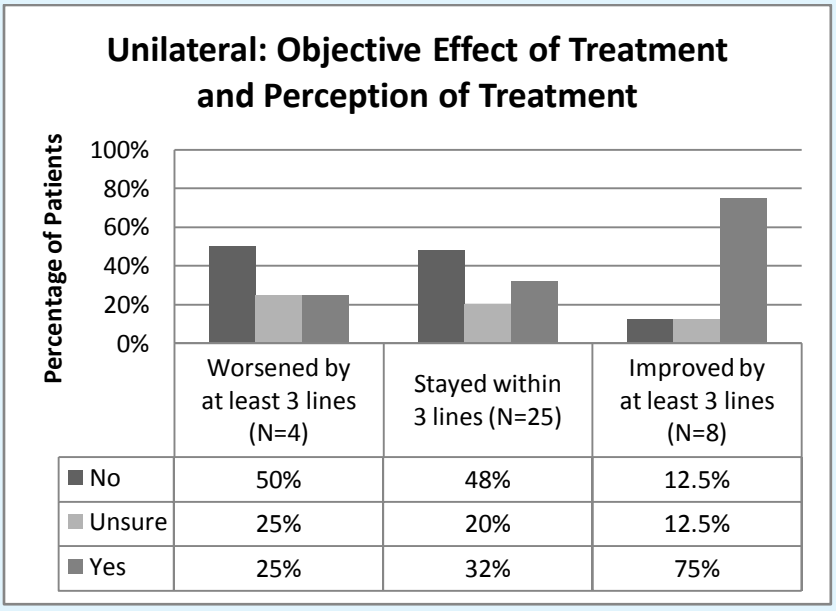

Figure 1: Change in visual acuity in those receiving unilateral treatment after initiation of treatment and perception of treatment improving vision.

Bilateral Treatment: 24 patients (48 eyes) received bilateral injections. Patients only completed one survey regardless of whether they had one or both eyes treated. The answers to the survey were counted once per patient, regardless of whether they received bilateral or unilateral treatment. The objective changes in vision for both eyes were as follows: one eye that was stable (remained within 3 lines) and one eye that worsened by at least 3 lines in 37.5% (9/24); both eyes remained within 3 lines in 37.5% (9/24); one eye that was stable (remained within 3 lines) and one eye that improved by at least 3 lines in 16.7% (4/24); and both eyes improved by at least 3 lines in 8.3% (2/24).

In the 9 patients with stable vision in one eye and vision that worsened in the other eye, the perceptions of whether treatment improved vision were: "no" in 89% (8/9) and "unsure" in 11% (1/9). For the 9 patients whose vision in both eyes remained within 3 lines, the perceptions of whether treatment improved vision were: "no" in 22% (2/9), "unsure" in 44% (4/9), and "yes" in 33% (3/9). For the 4 patients with one eye that did not

change and the other eye that improved, the perceptions of whether treatment improved vision were: "unsure" in 25% (1/4) and "yes" in 75% (3/4). For the 2 patients in whom both eyes improved by at least 3 lines, 100% (2/2) perceived their treatments as improving their vision (Figure 2). Overall, there was a positive correlation identified between objective vision change and subjective perception of vision change among those patients who had both eyes treated (correlation of 0.77 with a p-value: 0.0000 at the alpha=0.05 level) (Figure 2).

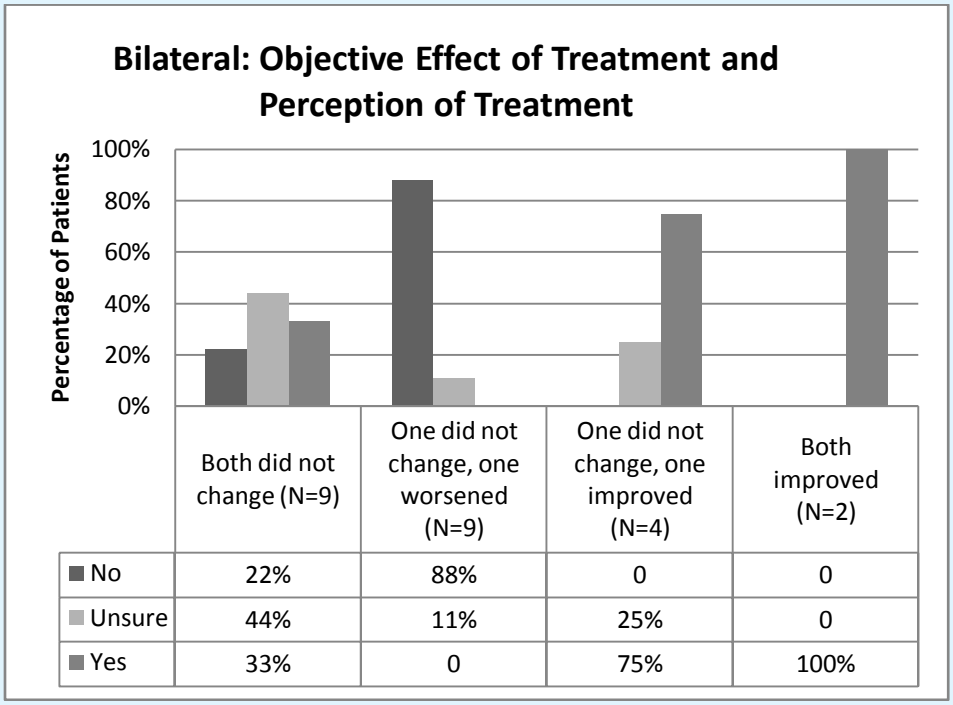

Figure 2: Change in visual acuity in those receiving bilateral treatment after the initiation of treatment and perception of treatment improving vision.

Neither the number of prior injections received nor the patient's gender was found to have a statistically significant correlation with the patient's perception of their treatment's efficacy (p value of 0.59 and 0.45, respectively).

Treatment-related Anxiety

The most common level of anxiety patients recalled feeling prior to their first injection was level 1 (no anxiety) (36%; 22/61). The second most common was level 5 (very anxious) (28%; 17/61). The most common etiology of anxiety was the "thought of losing vision" in 56% (34/61). The "thought of the needle in the eye" was the second most common source of anxiety in 33% (20/61).

Treatment Preferences

Patients were asked to indicate what the most important factor was in their choice of medication. 75% (46/61) of patients reported that the "doctor's choice" was the most important factor, followed by 15% (9/61) "research/clinical trials that have been done", 7% (4/61)"cost", 2% (1/61) the "interval between injections", and 2% (1/61) with "no preference". "FDA approval" was not chosen by any patient 0% (0/61). It is important to note the highly insured status of this cohort as "cost" was a choice in the survey.

In an attempt to gauge patient prioritization of treatment efficacy (best potential visual acuity) versus treatment burden (fewer visits, but poorer outcomes), patients were asked, "What would be the ideal treatment for you?" Answer options were: "Drug is injected monthly but gives you the best vision possible"; "Drug is injected every 3 months but gives you slight loss of vision"; "Monthly follow-up in office, which may involve an injection of drug but may give you slight loss of vision";"Implantable device requiring surgery once a year with minimal follow-up but gives you the best vision possible"; and "Eye drops administered at home but still require monthly follow-up with slight loss of vision." 59%

(36/61) of eAMD patients chose monthly injections with best possible vision results over the other scenarios. The second most common choice (18%; 11/61) was "implantable device". The survey also inquired whether patients with eAMD would be willing to undergo anti-VEGF injection indefinitely: 84% (51/61) reported they would, to minimize the risk of losing vision.

Discussion

The data from this study support the finding that anti-VEGF therapy is effective in maintaining visual acuity within 3 lines of the baseline in the majority of patients with eAMD. The majority of treated eyes in this study (66% or 56/85) remained within 3 lines of pre-treatment visual acuity, and 19% (16/85) improved by 3 lines. Although anti-VEGF treatment is not curative nor can it erase irreversibly lost vision, it does offer a promising mechanism that patients recognize may slow their disease and maintain their sight.

Patients' perception of the treatment effect on their vision is statistically significantly correlated with the actual effect treatment had on their vision. Patients in whom vision worsened by 3 lines or improved by 3 lines had perceptions consistent with the actual effect on their vision (either "no" improvement or "yes" improvement, respectively). In patients receiving injections in one eye and whose vision remained stable within 3 lines, 48% perceived their treatments as not improving their vision. In patients receiving bilateral injections and whose vision in both eyes remained within 3 lines, 44% were unsure if their treatments were improving their vision. Of note, for the patients who received bilateral injections and the vision in one eye remained within 3 lines and the fellow eye changed (either improved or worsened), the eye with vision that changed drove the overall patient perception of the treatment. For patients whose vision improved in one eye, 75% reported that their treatments were improving their vision. In patients whose vision worsened in one eye, 80% reported that treatments were not improving their vision.

Prior to their first injection patients report disparate levels of anxiety. 36% of patients remember not being anxious at all (level 1) and 28% remember being very anxious (level 5). The greatest cause for their anxiety was the thought of "losing their vision" (56%) followed by the thought of a "needle in the eye" (33%). This gives us the insight that the majority of patients (56%) were more anxious about the consequences of the disease process rather than the procedure itself.

84% of all patients surveyed reported that the treatment was effective in minimizing the risk of losing further vision, and so would choose the best visual outcome, including continuing treatment indefinitely. When presented with alternative options, the majority of patients (59%) prefer the current standard of monthly injections with proven efficacy versus perhaps less frequent visits or less invasive administration but worse visual outcome. This shows that patients value treatment efficacy over treatment burden or convenience.

Finally, it is important to note the crucial role of the practitioner. 75% of patients stated that ultimately they value their physicians' advice for their treatment drug over any other factor. With this potential influence comes the responsibility on the part of the physician to ensure that the treatment is most in line with, not only scientific evidence-based data, but also the patient's quality of life, priorities, goals, and expectations.

Limitations of this study include a relatively small sample size and recall bias of patients. Another limitation is the demographic population surveyed at this urban, academic retina practice. The cohort generally had insurance that covered the majority of the medication and procedure, and this may not be generalizable to other practice settings. However, these treatments are the standard of care and assistance programs may make this therapy more available to those less well insured. The information gained from this study is useful in providing some understanding of patient's experience with anti-VEGF treatment, and offers a starting point for future, larger scale studies aiming to improve the patient experience, and ultimately the quality of clinical care delivered to this patient population.

Acknowledgement

Supported in part by an unrestricted grant from Research to Prevent Blindness.

Competing Interests Statement

The authors declare that they have no conflict of interest.

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