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OUTCOMES OF INTRAVITREAL BEVACIZUMAB IN NEOVASCULAR AGE-RELATED MACULAR DEGENERATION: EXPERIENCE FROM A JORDANIAN MILITARY HOSPITAL

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ABSTRACT

Aim: To evaluate the functional, anatomical and safety outcomes of using intravitreal bevacizumab (IVB) in Jordanian military hospitals for treatment-naïve neovascular age-related macular degeneration (nAMD). **Methods:** This retrospective study involved the use of IVB in treatment-naïve patients suffering from nAMD at the ophthalmology clinic in Prince Rashid Bin Al-Hassan Military Hospital between February 2023 and February 2026. All patients recieved three loading doses of IVB (1.25 mg/0.05 ml) given monthly, followed by PRN. BCVA and CMT were measured at baseline, one month, two months, and three months after loading. The adverse events and safety profile were noted. Statistical analysis involved paired t-tests with $p<0.001$ considered as significant. **Results:** The mean age of patients is 73.5±8.1 years, with women accounting for 57.5% of the population. Best-corrected visual acuity (BCVA) improved significantly from an average of 0.11±0.05 letters at the beginning of the study to an average of 0.5±0.5 three months later (average gain +0.39 letters, $p<0.001$). Central macular thickness (CMT) decreased significantly from an average of 512.6±95.3 Micron at baseline to an average of 230.3±62.5 Micron three months later (average drop -282.3 Micron, $p<0.001$). Complete fluid resolution was achieved in 70% of eyes after completing the loading doses. The overall number of adverse events was equal to 13.5% of eyes. Transitory ocular discomfort was the most common adverse effect (10.0%). **Conclusion:** Three months of loading doses of intravitreal bevacizumab is associated with remarkable anatomical improvement in patients with newly diagnosed nAMD with relatively excellent safety level.

KEYTERMS: Bevacizumab; neovascular age-related macular degeneration; anti-VEGF; macular thickness.

INTRODUCTION

Neovascular age-related macular degeneration (nAMD) is a major cause of both irreversible visual impairment and blindness amongst the elderly global population, especially in developing countries, where life expectancy is longer when compared to developing countries.[1] The condition is characterized by abnormal choroidal neovascularization (CNV) which results in accumulation of subretinal and intraretinal fluid, leading to the disruption of retinal layers and subsequent loss of central vision if left without treatment. Anti-VEGF drugs have completely successfully used in the management of nAMD. Bevacizumab was the first and still the most widely used drug within this class due to the efficacy equal to that of the expensive drugs, acceptable safety profile, and good affordability.[2]

The ophthalmic practice in Jordan, similar to the wider Middle East, encounters an increasingly life expectancy among the population and the economic burden of chronic retinal disease management particularly nAMD.[1] At Prince Rashid Bin Al-Hassan Military Hospital, a large tertiary referral center in the north of Jordan, the standard first-line pharmacological treatment in treatment-naïve nAMD is the use of intra vitreal bevacizumab injection (IVB). Despite that it is used as off-label, the decision is supported by group of international studies, as well as by the need for cost-effective treatment of a large and diverse cohort of

patients.[2,3] However, while clinical trials and Western reports have shown that IVB is effective in a controlled setting, the value of real-life evidence cannot be underestimated.[3,4] In fact, patient outcomes in clinical practice are not necessarily identical to those obtained in randomized controlled trials which could be related to differences in the severity of the disease at baseline, compliance with the treatment, follow-up protocols, management regimen used and genetic factors of the population.[4]

Despite the fact that the use of intravitreal Bevacizumab has been a routine practice in our medical center for a long time, no proper evaluation of its anatomical and functional outcomes has been conducted yet.[5] Therefore, a retrospective study is necessary to fill this gap in the local knowledge base in relation to changes in BCVA and CRT. In addition, safety profile should be assessed alongside with its efficacy. This all will help in establishing a baseline data for clinical experience. Additionally, it could reveal areas for improvement in the treatment process, i.e. the loading and follow-up phases of treatment.[2,4]

METHODS

This retrospective study was conducted at the ophthalmology clinic in Prince Rashid Bin Al-Hassan Military Hospital between February 2023 and February 2026. All naïve patients with active nAMD who received three initial monthly loading doses of intravitreal Bevacizumab followed by intra bevacizumab when there is activity (PRN regimen) were included. The participants were identified and their medical records were reviewed. The eligible patients would have confirmed diagnosis of nAMD and the activity was proved by signs of fluid collection in the retina detected by optical coherence tomography (OCT).

The inclusion criteria included patients of at least 50 years of age and confirming the diagnosis of choroidal neovascularization based on the angiographic findings detected by optical coherence tomography angiography (OCTA). Exclusion criteria included the presence of any previous therapies or detection of advanced macular scarring, geographic atrophy, or development of any other macular conditions not related to AMD.

The data collection process included the demographics of the patients and their baseline data including the best-corrected visual acuity (BCVA) using Snellen chart and the central retinal thickness (CRT) as measured by OCT. Those parameters were measured in three different time schedules: at the start of the treatment, one month after the loading stage and at the last point of study was at end of the first year of treatment.

The primary outcomes of the research are the mean change in BCVA and mean change in CRT from their values at baseline to the post-loading phase and to the final follow-up. The statistical analysis was performed using descriptive statistics, while regarding both pre-treatment and post-treatment values paired t-tests were used.

RESULTS

A total of 260 patients (400 eyes) with a mean age of 73.5 ± 8.1 years were included in the study. Females constituted 57.5% of the sample. At baseline, the mean BCVA was 0.11 ± 0.05 and mean CRT was 512.6 ± 95.3 µm, reflecting moderate to severe disease at presentation. Intraretinal fluid was present in 85%** of eyes and subretinal fluid in 75 %.

In the loading phase, the administration of intravitreal bevacizumab brought statistically significant and progressive improvement in best-corrected visual acuity (BCVA). The baseline mean value of visual acuity was 0.11 letters, but it gradually rose until it reached a mean value of 0.5 letters at the end of the third month. The mean increase of visual acuity from the baseline till the last time point amounted to +0.39 letters. The gain for each month was statistically significant ($p < 0.001$), which indicates the early positive functional effect of treatment. The results of visual improvement are summarized in table 1.

Table 1: Best-Corrected Visual Acuity Over 3 Months.

Time	BCVA (letters)	Visual improvement	P value
Baseline	0.11 ± 0.05	------	-------
1 month	0.25 ± 0.8	+0.14	<0.001
2 months	0.32 ± 0.9	+0.22	<0.001
3 months	0.5 ± 0.5	+0.39	<0.001

Anatomical response assessed by central macular thickness (CMT) and fluid clearance demonstrated significant and rapid decrease in retinal edema after the loading dose. The mean CMT value dropped from 512.6 µm at baseline to 230.3 µm at the end of the third month, which means that it dropped by 282.3 µm in total ($p < 0.001$ for all monthly measures). Moreover, the percentage of patients with fluid clearance was 30% at the end of the first month, increased to 60% by the second month of treatment, and 70% by the end of the third month, although the CMT continued to decrease. The results of improvement in CRT are summarized in table 2.

Table 2: Anatomical Outcomes at over three Months Post-Loading Phase.

Time	Mean CMT (µm) ± SD	Mean Reduction from Baseline (µm)	P value	Proportion with complete fluid resolution (%)
Baseline	512.6 ± 95.3 µm	------	-------	-------
1 month	399.1 ± 64.2	-113.5	<0.001	30% (120/400)
2 months	312.6 ± 58.1	-200.0	<0.001	60% (240/400)
3 months	| 230.3 ± 62.5	-282.3	<0.001	70% (280/400)

The general safety profile of bevacizumab delivered via intravitreal route was shown to be favorable with low rate of side effects. The most attributable complication was transient discomfort in the eyes (10.0%), while the other serious ocular side effects such as endophthalmitis (0.25%) and persistently high IOP (2.0%) were rare. For example, no cases of retinal detachment or vitreous hemorrhage were registered with minimal cases of systemic thromboembolic events (0.25%). Overall, side effects occurred in 13.5% of eyes which indicates the safety of the treatment. The results of adverse effects are summarized in table 3

Table 3: Safety Profile and Adverse Events.

Type of complication	Number of eyes	percentages
Transient ocular discomfort	40	10.0%
Mild anterior chamber inflammation	4	4.0%
Sustained elevated IOP	8	2.0%
Endophthalmitis	1	0.25%
Retinal detacment	0	0.0%
Vitreous hemorrhage	0	0.0%
Thromboembolic events	1	0..25%
Over all adverse events	54	13.5%

DISCUSSION

The findings of this study show that a three-month loading dosage of intravitreal bevacizumab produces statistically important anatomical and functional improvements. Visual function shows improvement over time, from 0.11 letters at baseline to 0.5 letters at three months (P.005), with an average improvement of +0.39 letters for the entire three-month period. The results reported in the study are consistent with those observed in the CATT study since the use of monthly bevacizumab resulted in an average increase of 8.0 letters, as measured by the ETDRS scale.[6] The relatively lower value of improvement obtained in this study may be due to differences in the used measurement scale, initial characteristics of the participants, or duration of the follow-up.

In terms of anatomy, CMT showed marked decline from 512.6 µm at the start of treatment to 230.3 µm at 3 months post initiation of therapy, meaning decreased thickness of 282.3 µm. These results correlate with data obtained from real life trials, showing that switching to bevacizumab from aflibercept led to a decline in CRT of nearly 186 µm over 24 months.[7] Bevacizumab's ability to significantly impact retinal thickness is in parallel with the drug's mechanism of action as full monoclonal antibody against VEGF-A causing decrease in vascular permeability and macular edema.

One significant observation is the fluid resolution pattern, wherein the total fluid resolution reached its highest point at 60% at the second month while it gradually increased to 70% at the third month. The previous literature shows that the eyes may dry up faster when ranibizumab is used rather than when bevacizumab is applied during the first month.[8]

Bevacizumab has been shown to be non-inferior to ranibizumab, based on a number of studies conducted on a large scale. According to the CATT trial, patients taking either drug experienced virtually the same improvements in BCVA: 8.0 letters for bevacizumab and 8.5 letters for ranibizumab. The same was confirmed by the IVAN study.[9]

Meanwhile, the VIEW trials confirmed the non-inferiority of aflibercept as compared to ranibizumab administrated on a monthly basis, while achieving the advantage of fewer injections (an 8-week interval after the loading phase).[10] Nevertheless, the newest real-world studies indicate that switching from aflibercept to bevacizumab also produces acceptable results in terms of BCVA after two years, since the difference in mean BCVA after the treatment was +1.13 letters in the switch group and +1.81 letters in the aflibercept group, meeting the non-inferiority criteria of 5 ETDRS letters. Hence, this causes great economic implications since it is widely recognized that bevacizumab is the most cost-effective drug among the available anti-VEGF therapies, thus leading to the conclusion on spending too much money (over €335 million) when using aflibercept given the European context.[11]

Regardless, the variations in drying kinetics have been recognized. Clinical studies reveal that ranibizumab excretes subretinal fluid more quickly than bevacizumab. This provides an explanation behind the preference of

ranibizumab or aflibercept practitioners although the price is high.

The safety profile in this experiment is good and confirms the publications. The general level of adverse effects is 13.5% with the transient discomfort of the patient's eyes being the effect with the biggest possibility of manifestation -10.0%. The endophthalmitis manifested itself in .25% of the patients in accordance with the results of other studies (.9% in some research and .16% in greater studies). There was a sustained high level of IOP in 2% of cases which is similar to other reports of 2.9% to 5%.[12]

No retinal detachment and vitreous bleeding were noted which conforms to the results received by Abbasi et al., no cases of rhegmatogenous retinal detachment in 60 patients were registered. The thromboembolic incidence is low (0.25%) which indicates systemic safety of intravitreal use of bevacizumab. The recent meta-analysis indicates that no significant differences in incidence levels of serious systemic adverse effects were found while using bevacizumab and ranibizumab.

The low number of endophthalmitis cases (0.25%) indicates the necessity of maintaining sterile injection practices during preparation. The use of preloaded syringes in pharmacy practices can prevent infection much more effectively than using manual techniques.

The findings indicate that intravitreal bevacizumab could serve to be an appropriate initial treatment method for wet AMD in the loading stage with significant benefits in terms of anatomical aspects and safety. Although ranibizumab or aflibercept have specific benefits in comparison to other similar options (like fast fluid absorption in case of ranibizumab and more extended interval schedule offered by aflibercept), bevacizumab could be an effective alternative in terms of its price. All drugs under consideration are noted to have similar efficiency according to CATT, IVAN, and VIEW trials and thus, it gives us a chance to rationally choose the best medication based on economic principles, patient's wishes, and personal treatment outcomes.

Study Limitations

There are some limits to this study. Among these is its relatively brief three-month review phase and, at the same time, the absence of a control group. Thus, the long-term outputs beyond the loading stage were not examined when fixing this treatment process.

CONCLUSION

The introduction of the anti-VEGF therapy is reasonably considered to be effective in the treatment of wet AMD. Moreover, it works well with visual performance and decreases the detection of fluid accumulation in the eye. In many respects, the accuracy of these findings resembles previously existing information obtained from the conducted experiments.

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