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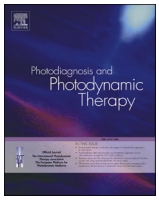

Choroidal Thickness and brolucizumab intravitreal injection: Cause or effect of intraocular inflammation?

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ABSTRACT

Purpose: to analyze the structural changes of choroidal thickness in patients with brolucizumab-related exudative vitritis after intravitreal injection, using EDI-OCT.
Methods: One hundred eyes of one hundred patients, affected by exudative age related-macular degeneration treated with brolucizumab intravitreal injection between January 2022 and august 2023 at Eye clinic of University of Federico II Naples, were enrolled. All eyes underwent macular examination using Enhanced Deep Imaging-OCT (Spectralis, Heidelberg Engineering inc.) preoperatively and at each postoperative check (1, 3, 6, 12 months). Anterior segment evaluation at slit lamp before and after injection was performed.
Results: Of the 100 treated eyes, 4 showed inflammatory signs related to exudative vitreitis, with inflammation signs at slit lamp examination and confirmed by OCT and B scan ecography. EDI-OCT revealed, in all of these 4 patients, a significant increase of choroidal thickness compared to baseline.
Conclusion: choroidal thickness could be correlated in the inflammatory response generated in patients undergoing treatment with brolucizumab.

1. Introduction

Intravitreal injections of anti-VEGF currently represent the gold standard for the treatment of macular neovascularization and several drugs are available to perform these treatments [1]. One of the most recently developed drugs is brolucizumab (Beovu®; manufactured by Novartis) which difference from other molecules consists in its lower molecular weight, due to the absence of fragment crystallizable (fc) portion [2]. Despite numerous trials demonstrated the safety and effectiveness of brolucizumab, numerous evidence support the high rate of intraocular inflammation and side effects after treatment [2,3]. The purpose of this retrospective study has been to analyze the changes of choroidal thickness in patients with brolucizumab-related exudative vitritis after intravitreal injection, assessed with Enhanced Deep Imaging-OCT (EDI-OCT).

2. Methods

One hundred eyes of one hundred naive patients, affected by exudative age related-macular degeneration with type 1 and 2 macular neovascularization treated with beovu intravitreal injection between January 2022 and august 2023 at Eye clinic of University of Federico II Naples, were enrolled. All eyes underwent macular examination using EDI-OCT (Spectralis, Heidelberg Engineering inc.) preoperatively and at each postoperative check (1, 3, 6, 12 months). Anterior segment evaluation by slit lamp before and after injection was performed.

Statistical Package for Social Sciences version 25 software (SPSS, Chicago, Illinois, USA) for Windows (Microsoft, Redmond, Washington, USA) was used for statistycal evaluation.

3. Results

A total of 100 patients were analyzed for the study; 67 underwent 3 beovu injection at least in one eye and 33 underwent to one beovu injection at least in one eye.

The mean patient's age overall cohort was 70.9 ± 6.3 years (50.1 %). Female patients were 65 % of total cohort. The median follow-up time was 16.3 ± 2,1 month.

Of the 100 treated eyes, 4 showed inflammatory signs related to exudative vitreitis, with inflammation signs at slit lamp examination and confirmed by OCT with evidence of hyperreflective spots in vitreous space and B scan ecography.

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EDI-OCT revealed, in all of these 4 patients, a significant increase of choroidal thickness compared to baseline (320.34 ± 59μ vs 230.12 ± $p = 0.001$) (table1) and all of them showed inflammation signs after at least the second beovu injection. The management of intraocular inflammation included topical steroids in three patients and oral and topical steroids in one patient for four weeks.

Best corrected visual acuity returned to baseline after the treatment and inflammation resolved in all patients. The BCVA changed from 1.1 LogMAR before brolucizumab injection to 1.5 LogMAR after, whereas the patients without vitreitis changed from 1.0 before to 0.8 after. (Table 1)

Table 1
Demographics characteristics of the patients.

Feature	*total patients (n = 100)*	*Patients with exudative vitreitis (n = 4)*	*P value*
Age (mean±SD)	66 ± 5.8 years		
		65.9 ± 6.3 years	
Gender			
Male	42 %	15 %	
Female	58 %	85 %	
Mean choroidal thickness before injection	230.12 μ	230.12 μ	<0.001
Mean choroidal thickness after injection	233.15 μ	320.34 μ	<0.001
BCVA before injection (LogMAR)	1.0 ± 0.01	1.1 ± 0.02	<0.001
BCVA after injection	0.8 ± 0.01	1.5 ± 0.01	<0.001

Data are expressed as the mean ± standard deviation (SD) unless indicated otherwise.
p values were calculated using the paired Student's test, with $p < 0.05$ indicating a significant difference.
BCVA Best corrected visual acuity, logMAR logarithm of the minimum angle of resolution.

4. Discussion

In our study, for the first time, we found an increase in choroidal thickness, measured with the EDI -OCT, in patients with inflammation and subsequently reduced after the resolution of the intraocular inflammation. According to previous studies the percentage of intraocular inflammatory reactions in patients treated with brolucizumab appears much higher than that of patients treated with aflibercept and is approximately 4 % of patients treated. furthermore, the onset of inflammatory phenomena seems to arise after the second injection of the drug [1,2,4,5].

This finding could be associated with the capacity of the brolucizumab to penetrate the subretinal space and be carried trought the BBE (external blood retinal barrier) and the onset of inflammation could be related to the high percentage of the population that has preformed anti-brolucizumab antibodies [6].

Following this hypothesis, both the presence of preformed antibodies and the deep penetration of the drug, could be cause an inflammatory state with a vasodilation of the choroidal vessels and a consequent increase in the choroidal thickness itself, as found in our subjects.

Futher and longitudinal studies could be useful in clarifying the etiopathogenesis underlying the high number of inflammatory events linked to this molecule.

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Ethical approval

All procedures performed in studies involving human participants were in accordance with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors.

Informed consent

Informed consent was obtained from all individual participants included in the study.

CRediT authorship contribution statement

Gilda Cennamo: Writing – original draft, Data curation, Conceptualization. **Michele Rinaldi:** Methodology, Writing – original draft. **Emanuele Malvone:** Methodology, Data curation. **Ciro Costagliola:** Conceptualization, Supervision, Validation.

Declaration of competing interest

All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

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