Reviewer’s report

Title: Complete Atrioventricular Block due to Timolol Eye Drops: A Case Report and Literature Review

Version: 1 Date: 08 Oct 2019

Reviewer: Emanuel Raschi

Reviewer's report:

This case report describes an unusual presentation of a patient without apparent cardiovascular contraindications to beta-blockers, who developed complete AV block after timolol eye drops after 13 years of use.

There are several aspects to be carefully considered by the authors:

- Overall, it is important to underline the novelty of this case report, both in the abstract and in the text (discussion and conclusion), especially in comparison with literature data (see below).

- The title implies that literature review was undertaken, but this issue appears to be only marginally addressed in the text. It is unclear how (search strategy) and where (MEDLINE?) literature review was carried out. The reader might appreciate a table summarizing collected evidence from literature in order to fully understand the unusual aspect of this case report (the manuscript just quoted "some research suggest"… and "the longest latency according to literature").

- I agree that the drug might have triggered the AV block in a patients with underlying conduction defect (independent on timolol). The unclear aspect is that the patient recovered (increased heart rate) after 48 h from timolol discontinuation. The authors should discuss whether this timeline is in line with pharmacokinetics and pharmacodynamics of timolol. For instance, It might be that the drug had accumulated because of impaired metabolism and/or reduced elimination. Because renal/liver function were apparently normal, the issue of genetics should be discussed in more detail as a plausible mechanism (poor metabolizer).

- In order to assess causality, the authors should consider to apply recognized algorithms such as Naranjo and WHO.

- The authors should consider to place ECG figures as supplementary material. Conversely, for a reader, it would be useful to have an explanatory figure providing the timeline of events.
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Unable to assess

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

Not relevant to this manuscript

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

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