

January 25, 2014

Title: New prospects in the diagnosis and treatment of immune-mediated inner ear disease.

Authors: David Lobo MD, PhD; José Ramón García-Berrocal MD, PhD; Rafael Ramírez-Camacho MD, PhD.

Name of Journal: World Journal of Methodology

ESPS Manuscript NO: 7607

Dear Editor,

We thank the reviewers and editors of World Journal of Methodology for their constructive review and comments. We believe the manuscript is improved thanks to these comments. We have incorporated the suggestions made by the reviewers and hope the manuscript is now considered suitable for publication.

Reviewer NO 02616129

- 1) Comment 1: “The title is “New prospects in the diagnosis and treatment of immune-mediated inner ear disease”. Intratympanic therapy has not been sufficiently evaluated yet. In spite of all the efforts to find a good marker for the disease, the available tests are not specific or sensitive enough to establish a definitive diagnosis”

Response: We appreciate the reviewer’s comment. The reviewer has undoubtedly grasped the gist of the article. This review deals with the most controversial aspects of AIED and it was our purpose to highlight those aspects that need more research as well.

- 2) Comment 2: “The authors just published a review paper to deal with biologic agents used for immune-mediated inner ear disease. Three among five authors are shown in present review article. Why?”

Response: These three authors have contributed to the present article (preparation, editing, revision and discussion) whereas the other two authors have not participated in this review.

- 3) Comment 3: “I would encourage authors to perform real laboratory works instead of review paper of AIED field”

Response: As first author, I received a cordial invitation as a member of the editorial board of the World Journal of Methodology to write a review about any topic within my area of expertise. Over the last few decades, the authors have contributed to the knowledge of AIED with numerous publications, and we are committed to new basic as well as clinical research in the field of AIED.

Reviewer NO 00506409

- 4) Comment 1: “It might be useful to give some insight in the frequency of the disease”.

Response: This has been addressed in the revised text in a new section ‘Epidemiology’.

- 5) Comment 2: “With respect to the etiology it is not discussed whether infections, in particular, viral infections, could contribute, i.e. by changing molecules from the individual to become self-antigens”.

Response: This had been pointed out briefly in the article and now it has been elaborated more extensively

- 6) Comment 3: “The term “autoinflammatory disease” needs clarification”

Response: We appreciate very much the reviewer’s kind suggestion. It was not our intention to focus on this group of recently characterized diseases, however, differential diagnosis with autoimmune sensorineural hearing loss and differences in their management have now been addressed.

- 7) Comment 4: “Regarding the administration of Rituximab, the term “perfusion” is used: this should be “injection”.

Response: We thank the reviewer for pointing this out. The terminology has now been corrected in the manuscript.

- 8) Comment 6: “It is advised to add explanatory notes to the legend of Figure 1”.

Response: We have proceeded accordingly

- 9) Comment 7: “Regarding table 1 and table 2 it is advised to describe whether all factors/components mentioned have to be present, or only some of these”.

Response: This suggestion has been addressed in table 1. Regarding table 2, it is already mentioned in the text that AIED is suspected whenever three major criteria or two major and two minor criteria are met. However, this has been added to the legend to improve clarity.

- 10) Comment 8: “Regarding table 1 it is advised to present the incidences of various antibodies, if such incidences are available”.

Response: Such incidences are not available in most of the cases. Some of these autoantibodies have been studied in animal models, and most autoantibodies studied in AIED patients have not been tested in large series of patients.

11) Comment 9: “In table 2, is hearing recovery rate >80% meaning recovery after immunosuppressive treatment? Is the 80% indicating the response in the total population of patients?”

Response: The otolaryngologist may be familiar with the term “hearing recovery rate”, but most readers deserve an explanation so it has been given in the legend. Hearing recovery rate is obtained this way: (initial hearing levels – final hearing levels) / initial hearing level – opposite ear hearing levels) × 100 (%). Final hearing levels are obtained after immunosuppressive treatment. 80% indicates the response that must be achieved in a patient so it can be considered a major criterion for the diagnosis of AIED.

3 References have been added.

Thank you again for publishing our manuscript in the *World Journal of Methodology*.

Sincerely yours,

David Lobo, MD, PhD

Hospital El Escorial

Universidad Francisco de Vitoria

San Lorenzo de El Escorial 28200, Madrid

Spain

Fax: +34-918973031