

MS 28453 - ANSWERS TO THE REVIEWRS

Reviewer 1. In this review article, Clemente et al summarize key points concerning pathogenic mechanisms, diagnosis and treatment of pediatric NAFLD. The article is well written and comprises extensive and updated concepts and bibliography. All in all, the information herein presented is of highly interest.

Several typos can be found throughout the manuscript and need to be fixed.

ANSWERS :

- a. We thank the Reviewer for her/his comments
- b. We fixed the typos throughout the manuscript (highlighted in yellow)

Reviewer 2. The review has summarized comprehensive description of the cause of non-alcoholic liver disease, pathophysiology, diagnosis and treatment, there is not much a review of the field, the author described in detail for us a general overview of the disease in the past and the future.

ANSWER

- a. We thank the Reviewer for her/his comments.

Reviewer 3. In the present review article the authors describe various aspects of NAFLD with particular regard to the pediatric age. The review include several and updated aspects of NAFLD including pathophysiology and pharmacological treatment. The review is clearly written and contains updated informations; therefore it will be of good potential interest for the readers. Only some minor point need to be raised in order to improve the scientific quality of the manuscript:

a.) In the Pharmacological and antioxidant treatment I would suggest to mention the use of silibinin. This information is of particular relevance since its clinical potential has been extensively demonstrated in various experimental models in randomized clinical trial. In addition, such compound is commercially available on most of the markets. To this regard I would suggest to cite and discuss the following references:

1: Salamone F et al. Dig Liver Dis. 2012 Apr;44(4):334-42. PubMed PMID: 22197629.

2: Loguercio C et al. Free Radic Biol Med. 2012 May 1;52(9):1658-65. PubMed PMID: 22343419.

b) There is some minor typo in the manuscript

ANSWERS

We thank the Reviewer for her/his comments

a) We added in the section regarding Pharmacological and antioxidant treatment (pages 23-24) the following sentence: "*Silibinin*, a drug available on most of the markets, is of particular relevance since its clinical potential has been extensively demonstrated in various experimental models^[99bis= new ref 100], and in a randomized clinical trial in adults with histologically documented NAFLD where treatment was associated with improvement in liver enzymes, insulin resistance, and liver histology, without increases in body weight.^[ref. 99 ter= new ref 101]."

b. We fixed the typos throughout the manuscript (highlighted in yellow)