

15.04.2014

Dear Editor,

We want to thank you and all the Reviewers for the evaluation and valuable comments that will definitely improve the text. Below we answer the queries in order. Suggested changes were highlighted in different color in the revised manuscript. Please find enclosed the edited manuscript in Word format (file name: 9719-edited.doc).

**Title:** NAFLD: What has changed in the treatment since the beginning?

**Author:** Bulent BARAN, Filiz AKYUZ

**Name of Journal:** World Journal of Gastroenterology

**ESPS Manuscript NO:** 9719

Reviewer 1 (02822388)

Query 1. Please normalize the format before published.

Answer 1. The format of the manuscript and references was revised according to the Editor's suggestions. Also Figure 1 is improved accordingly.

Reviewer 2 (02890067)

Query 1. What is with angiotensin-converting enzyme inhibitors (ACE-I) and angiotensin receptor blockers (ARBs)? Namely, according to some studies ACE-I and ARBs could be useful therapeutic approach for the patients suffering from NAFLD. I suggest that authors add this in their manuscript in order to improve this manuscript.

Answer 1. A paragraph which summarizes the utility of ACE-I and ARBs in treatment of NAFLD was added. Also relevant references were added to the references section.

Reviewer 3 (02541859)

Query 1. Incretin based therapies in the treatment of NAFLD should be mentioned.

Answer 1. A paragraph about incretin-based therapies and relevant references were added as suggested by the Reviewer.

Query 2. In the definition of metabolic syndrome, waist measurement should be given: A waistline of 40 inches or more for men and 35 inches or more for women (measured across the belly)

Answer 2. Suggested changes and additions were done.

Query 3. Genetic factors like PNPLA3 gene polymorphism leading to NAFLD should be mentioned.

Answer 3. Suggested changes and additions were done.

Query 4. In the summary, individualized treatment has been mentioned but not elaborated to the readers.

Answer 4. The summary was improved as suggested.

Reviewer 4. (02541689)

Query 1. The review provides mainly general informations and sometimes repeated, adding little novelty. E.g. - the pathogenesis section is redundant and not clear. Moreover some relevant concepts have not been treated: e.g. the emerging role of free cholesterol accumulation, SNPs... - therapy section: they omitted to say that physical exercise per se may improve NAFLD, they do not state that rosiglitazone has been withdrawn from the market because increased acute myocardial infarction risk, novel drugs such as incretin-mimetics have not been mentioned.....

Answer 1. In this paper, we aimed to review the general principles of therapy and to summarize previously investigated pharmacological treatment options in NALFD in the light of recent advancements on the pathogenesis of the disease. However, we are very grateful for the suggestions that we agree. Suggested changes regarding cholesterol accumulation, SNPs were added as suggested. Physical exercise has already been mentioned in the general principles section. FDA has recently changed and removed the restrictions regarding rosiglitazone prescription: <http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm376683.htm>

Another section including information about the incretin-mimetics and relevant references were added as suggested.

Query 2. English should be deeply revised throughout the manuscript by an English native speaker.

Answer 2. Revised accordingly.

Sincerely yours,

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