

Letter-Response to the Editor and Reviewers

Dear Sirs,

We are honored by your considerations.

We hope we have responded to all requests.

The changes throughout the article were marked with yellow.

Below we detail point to point, the questionings.

EDITOR'S COMMENTS:

Please revise the manuscript according to the review report and my comments. And answer all of the reviewers' comments carefully (point-to-point).

Reviewed

Please add a description of the background section of the article in the abstract section. (no more than 100 words)

Description of the background inserted in the abstract section according to orientation.

Severe Acute Liver Failure (IHAG) is a rare, but high-mortality, rapidly evolving syndrome that leads to hepatocyte degeneration with impaired liver function. Thioacetamide (TAA) is a known xenobiotic, which promotes the increase of the formation of reactive oxygen species. Nrf2 activates the antioxidant protection of cells. Studies have evidenced the involvement of inflammatory mediators in conditions of oxidative stress.

REVIEWERS:

Reviewer's code: 02527808

The value of this study was to increase the knowledge in this field as the findings were already studied in previous articles however the study was well designed with good presentation of the data . Some comments was to be considered - many abbreviations was mentioned in the abstract without clarification. - in table (3) what is meant by a & b significance. - It must be considered that this conclusion is limited only to experimental studies , as the use of various antioxidants in clinical studies showed only limited response

Due to the limitation of words to compose the abstract, it is impossible to describe all abbreviations cited, we chose to group them according to the purpose of analysis, so the terms hepatic integrity analysis, oxidative stress and inflammatory process were inserted in the abstract.

The legend of table 3 has been corrected.

The term experimental was inserted in both the abstract and the conclusion to show that the results obtained with glutamine are at the level of experimental studies.

Reviewer's code: 00731613

Discuss the clinical significance of the study as applicable to humans! One factor which needs clarification is the dosage of glutamine and its mode of administration especially if its applied in humans. Discuss the etiopathogenesis of acute liver failure in brief.

At the end of the discussion a phrase on the dosage, modes of administration of glutamine and the applicability of the study to humans were inserted, since glutamine is already used in clinical practice for the treatment of other diseases.

In humans, Gln supplementation has been used in clinical practice especially in diseases of the gastrointestinal tract with daily doses that can reach 20 grams, being administered preferably parenterally.

A short text on the etiopathogenesis of severe acute liver failure was inserted at the beginning of the discussion:

... due to several etiologies: drug-induced liver injury (DILI), xenobiotics, viral hepatitis, diseases metabolic, vascular and autoimmune. In many situations the cause remains unknown.

Reviewer's code: 03647881

Elizângela G Schemitt, etc. presented “Protective action of glutamine in rats with severe acute liver failure”. The title should correct as “Protective action of glutamine in rats with severe acute liver injury” rather than “Protective action of glutamine in rats with severe acute liver failure” according to the definition of liver failure because the elevation of AST/ALT/Alk-p does not mean liver failure.

In addition to the liver integrity parameters (AST, ALT and PA), the other results contributed to characterize hepatic insufficiency in this experimental study, especially the data obtained by the histopathological analysis that presented characteristic aspects of SALF, mainly centrilobular necrosis as presented in the disease in beings humans. All of our study (design, experiment, data collection and analysis of results) was supported by a hepatologist. Thus, to characterize severe acute liver failure, we consider all the results obtained in the study, as well as the technical and scientific advice of a specialist in the area.

Thank you for your availability.

Elizângela G. Schemitt