

August 14, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 12188-review.doc).

**Title:** Combined glucocorticoid and antiviral therapy of HBV-related liver failure

**Author:** Jan-Hendrik Bockmann, Maura Dandri, Stefan Lüth, Nadine Pannicke, Ansgar W. Lohse

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

**ESPS Manuscript NO:** 12188

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated and the manuscript has been reviewed by 2 native speakers.

2 Revision has been made according to the suggestions of the reviewer:

(1) The author should clearly describe the diagnostic criteria of liver failure:

The diagnostic criteria used were defined according to recognized standard procedures. We modified the text on pg.4 as follows: *"Acute liver failure was defined by an international normalized ratio of greater than 1.5 and any degree of encephalopathy."*

(2) The author should explain the reasons of anti-viral therapy for one patient with acute HBV infection in this case report:

This aspect has been clarified on pg.8 as follows: *"Despite the delayed antiviral effects induced by NUCs and their controversial role especially in acute HBV infection we thought that early initiation of entecavir/tenofovir therapy was necessary because of the use of glucocorticoids, since these may potentially augment viral replication, which in turn might even promote further cytotoxic immune responses against infected hepatocytes."*

(3) This type of liver failure is acute on chronic liver failure:

*"Clinical diagnosis: Patient 2A/B: HBV reactivation after Rituximab chemotherapy with acute on chronic liver failure"* (pg.9)

(4) The author should clearly explain how to determine the initial dose of glucocorticoid; how long time to use; when and how to reduce the dose until the glucocorticoid withdrawal:

We thank the reviewer for pointing out the need to specify this. This has been now included in the revised version of the manuscript as follows: *In case of patient N.1: "Thus, high-dose steroid therapy was added after 3 days of antiviral treatment. Prednisolone treatment was started intravenously (i.v.) with 1.5 mg/kg body weight. (...) 2 days after the start of glucocorticoid therapy dropping of transaminases was observed and the prednisolone dose was reduced to 60mg/d per os (p.o.) with further reductions of 10mg per week to a dose of 20mg/day, thereafter reductions of 5mg per week."*

(5) The author should also clearly explain how to prevent the side effects of the drug resulted from high dose steroid therapy:

*"glucocorticoid therapy was accompanied by prophylactic medication with proton pump inhibitors and calcium/vitamin D to prevent steroid-induced gastric ulcers and osteoporosis, respectively. Patients were screened daily for clinical signs and biochemical parameters of infection during their stay in hospital while an antibiotic prophylaxis, f.e. for pneumocystis pneumonia, was avoided due to the short-term treatment with prednisolone."* (pg.8)

(6) Please tabulate levels of lactate and ammonia in blood, gamma-glutamyl transpeptidase, alkaline phosphatase, albumin, ASAT, ALAT, venous pH; shown altered in acute liver

failure [Sijens et al. Eur.Radiol 2008;18:2601-9]:

*Please find table 1.*

- (7) Show results of liver imaging:

*Please find figure 3.*

- (8) Omit "Russian" since not relevant, and write out INR.

This was done as suggested.

3 References and typesetting were corrected.

Thank you to the editorial board and to the reviewers for the constructive comments. We hope that the revised version of our manuscript will be now suitable for publication in the *World Journal of Gastroenterology*.

Sincerely yours,

A handwritten signature in blue ink, appearing to read 'J.-H. Bockmann', followed by a long horizontal flourish.

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