Format for ANSWERING REVIEWERS

October 19, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 5498-review.doc).

Title: Psychometric Hepatic Encephalopathy Score for Diagnosis of Minimal Hepatic Encephalopathy in China

Author: Su-Wen Li, Kai Wang, Yong-Qiang Yu, Hai-Bao Wang, Yuan-Hai Li, Jian-Ming Xu

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 5498

The manuscript has been improved according to the suggestions of reviewers:
1 Format has been updated.

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

Thanks for experts' time to review our manuscript. The answers to the experts' questions are list below.

Answers to Expert 00181501

Dear expert, thanks for your time to review our manuscript. The answers to your questions are list below.

(1) The sample size is small.

Answer:

The PHES has been standardized in several countries, such as Germany, Italy, Spain, India, Korea and Mexico, further validation is needed in China. The number of patients seems small, but we will increase the sample size in subsequent research. This preliminary study aimed to construct a dataset of normal values in a healthy Chinese population and evaluate the usefulness of PHES for the diagnosis of MHE among Chinese patients with liver cirrhosis. The sample of control group and cirrhosis group in our study is 146 healthy volunteers and 53 patients, respectively.

(2) The reason about defining the cut-off of -4 as base for diagnosis of MHE should be explained.

Answer:

In the healthy volunteer group of our research, the lower boundary of the 95% range between mean-2SD and mean+2SD was -4.0. So, the cutoff between normal and abnormal was set at -4. And most studies focused on PHES for diagnosis of MHE used the sutoff of -4, such as studies from Germany and Italy. The cutoff of our research is consistent with previous studies.

Answers to Expert 01588404

Dear expert, thanks for your time to review our manuscript. The answer to your question is list below.

Major suggestion it would have been interesting to have evaluated CFF in both volunteers and Cirrhotics administered PHES and seen the correlation between results and the sensitivity and specificity of PHES and its component tests.

Answer:

This is a good suggestion. Many studies proved the CFF is a simple and usefull tool for screening of MHE. Because the CFF is not available, our study foucsed on the normal values of subtests included in PHES and the usefulness of PHES for the diagnosis of MHE. If possible, the CFF will be evaluated in

both controls and patients with live cirrhosis in further research.

Answers to Expert 01800318

Dear expert, thanks for your time to review our manuscript. The answers to your questions are list below.

(1). Did the authors perform power calculation in order to find the necessary number of patients included in the different groups for safe results? As the authors main aim is to present a study representative for Chinese population, the number of total 56 cirrhotic patients seems to me small. Also the number of 7 patients with child C cirrhosis is also small. Greater number of patients are necessary, according to other similar studies (more than 200 participants) referenced by the authors. So it should be advisable to increase the number of patients in the present study.

Answer

We estimated that about 178 patients of cirrhosis are needed to obtain a safe result. This is a preliminary study, we constructed a dataset of normal values in a healthy Chinese population. And we calculated the PHES score of cirrhotic group based on the normal values of healthy volunteer group, it seemed reasonable. The sample of control group and cirrhosis group is 146 healthy volunteers and 53 patients, respectively. The patients if Child C in this study is small, it might be caused by the exclusion criteria. Patients with Child C are prone to experience upper gastrointestinal hemorrhage and OHE. The patients with history of UGIB and OHE were excluded. And patients who took lactulose to prevent OHE were excluded too. The sample size of our study is small, the number of patients will be increased in subsequent research.

(2). It is important to comment more on the PHES score between the control group and cirrhotic group first. Then to use a formula for the cirrhotic group and then to clearly compare, comment and discuss the differences between MHE and non-MHE subgroups of the cirrhotic group.

Answer

In present study, the score of PHES was compared between healthy volunteers and liver cirrhosis group. The final score of PHES was generated from the sum of the scores of five tests. The score of PHES in the healthy volunteer group was -0.6±3.7 (median, 0; range -11~+5). The score of PHES in liver cirrhosis group was -5.6±4.9 (median, -4; range -13~+4), and was significantly lower than in the volunteer group ($P<0.05$).

(3). The authors should explain why they define the cut-off of -4 as base for diagnosis of MHE?

Answer

In the healthy volunteer group of our research, the lower boundary of the 95% range between mean-2SD and mean+2SD was -4.0. So, the cutoff between normal and abnormal was set at -4. And most studies focused on PHES for diagnosis of MHE used the sutoff of -4, such as studies from Germany and Italy. The cutoff of our research is consistent with previous studies.

(4). In some areas in Discussion there is plagiarism. Validation adjusted to age and education has been also reported to other similar studies referenced by the authors. The authors spent a lot of time on age and education adjusted validation. The authors should focus on their own results and compare them to other similar studies.

Answer

We have revised the discussion of our manuscript. We referenced about thirty papers, which were listed in the manuscript. The results of subtests included in PHES can be influenced by age, educational status and sex. So, adjusted normal values are recommended. In this research, we found that all five subtests of PHES are influenced by age and education years. And one of our aims was to constuct the normal values of subtests of PHES. So a lot of time was spent on discussing the age-and-education corrected normograms. The time spent on age-and-educaion adjusted normograms was cut down in the revised manuscript.

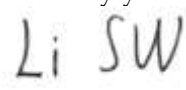
(5). English language is very good although some minor mistakes.
Answer
The expression in English had been edited by a professional English editing company.

Answers to Expert 00182548
Dear expert, thanks for your time to review our manuscript. The answer to your question is list below.
The expression in English is not the best. The article should be reviewed in this regard.
Answer
The expression in English had been edited by a professional English editing company.

3 References and typesetting were corrected

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

Sincerely yours,



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