Reviewer's report

Title: Changes of liver enzymes and bilirubin during ischemic stroke. Mechanisms and possible significance

Version: 1 Date: 3 February 2014

Reviewer: Pilar Delgado

Reviewer's report:

In this paper, authors aimed to determine the changes occurring during the first two weeks after stroke admission in liver enzymes, bilirubin, CRP and blood cells (white and red) and to study their possible mechanisms and whether they are related to infarct volume. Admission levels were determined within the first 72 hours after stroke onset.

They found most of the liver enzymes and inflammatory parameters (WBC, CRP) increased during the first week and particularly positive associations were found between GOT and CRP with infarct volume. Results for CRP are in agreement with previous reports on the field and for GOT are partly in opposition to what has been described before.

The description of the changes observed is accurate, however their relevance is limited and the results obtained should be interpreted with more caution, particularly for the increase in GOT (which they claim to be independent from inflammation).

Major compulsory revisions

Methods and results:

1.- One major problem would be the clinical relevance of all the changes described. Although most of the markers are significantly increased/decreased, changes are very mild and probably for most of them, concentrations remain within normal lab ranges, so the biological effect is not very clear to me. Probably the info provided would be much more clear to the reader if it was represented in graphs and the values for the normal range or data from controls were provided. Also, although both CRP and GOT were associated with infarct volume, this multivariate analysis was not controlled for other clinical determinants of outcome such as age or baseline stroke severity (NIHSS scores). I would strongly suggest to include them in the predictive model of infarct volume.

Also, table 4 shows how CRP and GOT are indeed related to each other (beta coefficient 0.18), so probably their interaction should also be considered in the multivariate analysis.

2.- Other major problem would be that missing data was frequent for liver enzymes, bilirubin, blood counts and CRP determinations on admission or seventh day (about 40 cases lost out of 180). Authors should clarify whether baseline characteristics between those patients with available data and those
with missing data were similar. One could think that only more severe strokes (except those who died before the 7th day) remained at the hospital by that time (and therefore they had a blood sample available) whereas mild strokes were discharged earlier and did not.

3.- Figure 1. It is not clear to me why only associations with a beta coefficient higher than 0.3 were chosen to hypothesize the relationship between variables.

4.- Main results are based on data on admission and the 7th day, whereas levels on the emergency department, 3rd day and 14th day are only mentioned on specific parts of the text or just omitted

Also it is not clear why the third day determinations were not used, since it would make more sense to correlate liver changes with infarct volume at the same time, too.

5.- Methods description:

The description of the study variables, in particular the timing for liver enzymes, etc. determinations and their delay relative to the stroke onset is confusing. Please clarify

Also, it is not clear to me which infarct volume was chosen (baseline?, third day?) to calculate correlations with admission and 7th days markers.

6.- Conclusions on other signals different from inflammation leading to the increase in GOT levels might be too speculative, since Table 4 shows indeed that GOT was partly explained by CRP (beta=0.18). I strongly recommend to revise conclusions in the abstract and main text.

Level of interest: An article of limited interest

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests