Author's response to reviews

Title: Clinical validation of S100B use in management of mild head injury

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Author's response to reviews: see over
Dear Dr Rowles,

Thank you for consideration of our manuscript for your journal. Thank you also to the reviewers for taking interest in our work. We have modified the content referring to ethical approval in the manuscript, see methods section. We have also read the reviewers comments and below list my responses to the points.

Reviewer 1

A.
1. We agree. The introduction section has been shortened and we think it is much clearer now.

B.
1. We agree. We have modified the methods section, specifically inclusion and exclusion, to improve clarity.
2. This was based upon the best evidence at the time with the largest study (Biberthaler et al 2006) using a 3 hour window. We were also concerned about the short half-life of S100B in blood. If we would do the same today, we would use a 6 hour window (Zongo et al 2012). We have clarified this choice in the manuscript.
3. In Sweden we follow the Scandinavian Neurotrauma Committee (SNC) guidelines for initial management of these patients. S100B was introduced into these in 2007 (into the intermediate risk group of patients, i.e. unconsciousness and/or amnesia and GCS 14-15). The result is the guidelines presented in figure 1, essentially the SNC guidelines with the addition of S100B. This has been clarified in the text.
4. We agree that this should be included. We have added this in the text.

C.
1. We are sorry, but we do not understand the question. We did record clinical findings in patients but this was not an endpoint of the study. We will possibly use this data to form a hypothesis for future studies.

D.
1. We have modified the text to clarify this.
2. We agree. This is a complicated issue. The evidence today seems to indicate that a 6 hour window is reasonable and most patients seek health care within this time. We have added discussion concerning this in the text.

Reviewer 2

3. We agree that this was unclear. We have clarified this in the text. 44 patients were over-triaged when S100B levels were low. 15 had a CT, 20 were admitted and 9 patients had a CT and were admitted.

Reviewer 3

1. We agree. We refer to the evidence available at the time (early 2007). We have clarified this in the text. Recently, evidence seems to show that S100B should be useful in children as well. This patient group is more difficult to manage and also have the obvious problems with
radiation from CT scans to a greater extent than adults. We are currently systematically reviewing the evidence for S100B introduction into paediatric head injury management. 2. We did make a sample size calculation for the health economic aspect of this (250 patients). However, the endpoint of the present report was to show the actual use of S100B clinically and we did not know what compliance to expect. We suspected that compliance would be quite poor since this referred to a new blood test never used before in the hospital. We therefore agreed upon 500 patients as an arbitrary number based upon consensus. 3. Since we only take S100B on a selected subset of patients (see inclusion and exclusion criteria), the numbers are smaller when compared to other studies. Since we wanted to examine clinical impact, it was important to only take S100B in patients with real diagnostic uncertainty. In minimal head injury, patients should not have a CT scan and in patients with certain high-risk factors (such as clinical signs of basal skull fractures and neurological deficits) a CT is obviously warranted. With respect to the size of the hospital, our numbers are adequate and we “missed” very few patients. If this would be an exploratory study, this would be a selection bias. However, since we are reporting clinical use, we feel this selection is adequate. 4. We agree that in retrospect the figure could have been made clearer. The dotted line did not re-join the “CT pathology” pathway since these patients are a different group with regard to risk and we wanted to keep these separate. However, as you correctly suggest, we should have made this clearer. We are presently updating our guidelines as will consider this aspect carefully. 5. We agree, this would have been very interesting. However, we did not register these reasons in a systematic manner and so we cannot report any data for this. We are planning a validation study of updated guidelines where a “clinical judgement” arm will be compared to the guideline. 6. We agree - the health economic aspect is important if this is to have impact on our health care. We are working on this paper presently and hope to publish later this year. Combing everything into one paper would probably be confusing, particularly to people not involved in this type of research. We wanted first to show how S100B is used in the clinical setting and how compliance is in “real life”, despite the good performance of S100B (similar to the previous studies). 7. Thank you, we have corrected the abbreviation of CT.

We would like again to thank the editor and reviewers for their interest in our paper. We feel that the manuscript has been greatly improved after revision and that it may be considered for publication in BMC Emergency Medicine.

Warm regards,

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