

LETTER

An expected association between low haemoglobin and poor outcome in severe head injury and an insufficiently detailed multivariate analysis

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See related research by Sekhon *et al.*, <http://ccforum.com/content/16/4/R128>

I read with interest the paper by Sekhon and colleagues, 'Association of hemoglobin concentration in critically ill patients with severe traumatic brain injury' (July edition of *Critical Care*) [1]. Whilst the conclusion ('mean 7-day haemoglobin concentration <90 g/L associated with increased hospital mortality in patients with severe traumatic brain injury') is striking, it is plausible, if not likely, that both the haemoglobin deficit and the observed mortality are dependent upon the severity of the initial injury, and therefore an association between these two might be expected.

Given the lack of transfusion trigger and a target haemoglobin concentration post-transfusion in this study, and a generous group upper limit of 90 g/L, would those patients with the lowest initial haemoglobin concentration not be likely to stay below that threshold

despite transfusion? Are not the most severe injuries also likely to be associated with a 7-day mean haemoglobin of less than 90 g/L?

Injury severity was reportedly accounted for in the multivariate analysis, although the details of the model used were not given. What weighting was given to each variable, such as Glasgow Coma Scale, or CT appearance, and on what basis? Of note is the lack of information regarding other injuries, not just in the multivariate analysis but indeed the entire paper. Were only isolated head injuries considered or were polytrauma patients included in this study?

To accept that more than an association exists between two variables - as implied - we must be satisfied of the validity of the multivariate analysis.

Authors' response

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We thank Dr Donnelly for his careful critique of our manuscript [1]. We agree with his assertion that hemoglobin concentration and mortality may be confounded by the severity of illness. In the manuscript, we devote considerable time discussing bias in the context of our results. Despite these concerns, the baseline patient characteristics were remarkably similar between exposure levels. Thus, measured baseline characteristics would be unlikely to account solely for the observed mortality in our study. Although as mentioned in our

discussion, we would be unable to account for unmeasured covariates, which could be a significant source of confounding.

Another concern expressed by Dr Donnelly was the details of the model building. All covariates included in the final model were chosen *a priori* based on subject matter knowledge [2]. Age and admission Glasgow Coma Scale were included in the final model as these are known strong predictors of outcome in traumatic brain injury [3]. Additionally, we included red cell transfusion as did other studies in the area [4,5]. Insertion of an external ventricular drain was chosen because of its association with mortality in our prior study of the same cohort [6]. Although additional variables could have been included in the final model (for example, CT appearance), we were limited in the number of covariates included in the final

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model due to few outcome events present in the study [7]. His question as to the weighting of covariates is unclear. With respect to the modeling itself, all observations were equally weighted.

We disagree with Dr Donnelly's assertion that we implied '...more than an association exists...' between hemoglobin concentration and mortality. Our conclusions were presented in a measured fashion with a careful discussion of the limitations. Despite these limitations, observational studies remain important tools to help generate hypotheses and guide further study design.

Competing interests

The author declares that they have no competing interests.

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