Reviewer’s report

Title: Advanced Age, Altered Level of Consciousness and a New Diagnosis of Diabetes are Independently Associated with Hypernatremia in Hyperglycaemic Crisis

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Reviewer: Susan Braithwaite

Reviewer’s report:

By retrospective analysis of 273 admissions, this report identifies each of three factors, namely age 60 or older, altered consciousness, and new diagnosis of diabetes, to be independently associated with hypernatremia at the time of presentation with hyperglycemic crisis. Hypernatremia was defined as uncorrected serum sodium at presentation above 145 mmol/L. The prevalence of hypernatremia among hyperglycemic crisis patients was relatively high, at 11.7%. When hyperosmolality was defined to be a value >320 mosm/Kg by calculation, then all cases of hypernatremia also had hyperosmolality.

Minor Essential Revisions:

There is a typographical error in the abstract about Age 60 or older.

Compulsory Revision:

In the "methods" section, it should be stated whether readmissions of the same individual were excluded from data analysis. The types of hyperglycemic crisis collected were: ketoacidosis (including the subtypes with and without hyperosmolality), hyperosmolar non-ketotic state (with hyperglycemia?), and hyperglycemia, defined in reference 10. It is not clear on first reading whether "hyperosmolar non-ketotic state" and "hyperglycemia" are two different conditions, or whether the authors refer to one condition with use of the term "hyperosmolar non-ketotic state and hyperglycemia." This condition "hyperosmolar non-ketotic state and hyperglycemia" is often referred to as "HHS" in other literature, to differentiate it from other types of hyperosmolar non-ketotic states that are not associated with hyperglycemia. Please reiterate the definitions of each category and change the punctuation or number the categories so that all readers will understand the categorization.

The results should state the numbers of each type of hyperglycemic crisis that were found.

Later, in the discussion, a percentage of patients having hypernatremia is associated with each of the following three categories: ketoacidosis, hyperosmolar non-ketotic state and hyperglycemia. Therefore, I assume "hyperglycemia" was a recognized category. Why is hyperglycemia considered to be a crisis, if there is neither hyperosmolality nor ketoacidosis? Please describe
the characteristics that define hyperglycemia as a crisis, for purposes of this classification.

Discretionary Revisions:

The concept of combined hyperosmolality and ketoacidosis needs a bit of discussion. How often is the combination seen in other studies focused on hyperglycemic crisis? On page 4 of the first-reviewed draft, in the first paragraph of the discussion, a comparison to one other study is made with respect to the prevalence of hypernatremia. For comparison, additional literature about hyperglycemic crisis might be considered, some of it quite old. Not only the prevalence of hyperosmolar ketoacidosis, but also the prevalence of ketoacidosis itself (as a fraction of cases of hyperglycemic crisis), or the prevalence of pure hyperglycemic hyperosmolar state without significant ketoacidosis (as a fraction of the cases of hyperglycemic crisis), should be discussed, as a point of comparison in the older studies. The older reports that might be used for comparison go back quite far in time, and can be found from different parts of the world. It would be very interesting to tabulate them, with emphasis on the frequency of each type of hyperglycemic crisis. A further point is that the relationship of hyperosmolality with altered consciousness in the context of hyperglycemic crisis has been observed previously, but the original reports of the relationship have not been acknowledged fully in this paper. These are just a few examples for consideration by the authors:


Fulop. Lancet 1973, p 635. "Hyperosmolarity may... be the main factor responsible for the lowering of consciousness in patients with diabetic ketoacidosis, as it is in patients with "nonketotic hyperosmolar diabetic coma".


Pinies. Diabe and Metabolisme 1994; page 43. Older age, low blood pressure, low sodium, pH, and bicarbonate....were related to mortality.


In making some of these comparisons with older literature, it is worth remarking on whether the findings of the current paper extend analyses to a population for which there is contrasting data, compared to other populations, as already is done in making the comparison to the Newton paper.

The conclusion as stated might be reworded. The conclusion presently reads: "Great attention must be paid to fluid therapy in hyperglycaemic crisis patients who are elderly, unconscious, or newly diagnosed with diabetes as they are particularly predisposed to hypernatremic dehydration." Perhaps this implication belongs in the discussion. Since the report does not examine the conduct of
therapy, the conclusion instead should focus on what was actually studied, i.e. the relationship between epidemiologic and diagnostic findings on presentation with hyperglycemic crisis in the population that was studied.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests.