Reviewer’s report

Title: Predictive factors of adrenal insufficiency in patients admitted to acute medical wards: a case control study

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Reviewer: Bertil Ekman

Reviewer’s report:

Comments to the Author

Oboni et al investigated Predictive factors of adrenal insufficiency in patients admitted to acute medical wards: a case control study

This study evaluates clinical and biological determinants associated with adrenal insufficiency of any kind admitted to an acute medical ward. The main finding was that 32 of 11300 patients admitted to the actual acute medical ward between 2008-2010 responded less than 550 nmol/l in cortisol peak after stimulation with 250 µg Synachten. This was judged adrenal insufficiency and treated. No further diagnostic analyses were done. Furthermore the only significant predictive factor for adrenal insufficiency found was glucocorticoid withdrawal. Low blood pressure was surprisingly not associated with adrenal insufficiency. The control group used was not defined.

I agree that the issue is important but the paper is not ready for publication at this stage.

The paper needs a significant amount of revision.

Specific comments.

Introduction: Adrenal insufficiency has to be defined more: primary, secondary, iatrogen etc.

The second sentence in not so easy to understand and come back in the end of the second paragraph.

Second paragraph:
A lot of symptoms/signs and biological markers. Define, “hypotension symptoms”,
“history of glucocorticoid withdrawal (syncope)”???

Hyperkaliemia=hyperkalemia. Several places in the paper.

Why are basal cortisol levels inaccurate to assess adrenal function? Reference from 1953?. No other literature? Combined ACTH and cortisol measurements in plasma for primary adrenal insufficiency are often diagnostic.
Discuss more about cut of levels for cortisol levels on basal conditions and in the critical ill situation or like the patient population described in this paper, probably a large proportion with pneumonia or other bacterial infections.

Is a cut off of 550 nmol/l in cortisol after 250 µg Synachten appropriate in the acute setting?

What is the difference of 1 µg and 250 µg? Is it important for this study?

In the study by Patel et al 1991 (14) "In acute hospital admissions, baseline serum cortisol between 0800 and 0900 hours should exceed 250 nmol/l. Peak serum cortisol after 250 micrograms intramuscular tetracosactrin should exceed 600 nmol/l. Calculation of the increment is of no value"

Results: In all 6 are under glucocorticoid treatment and excluded. How many of these had an adrenal crisis or sign of adrenal insufficiency? Nothing is said about follow up of the 32 patients with abnormal response to Synachten? You must have the exact diagnosis on every patient? And all symptoms? Or?

Nothing is said about the 32 patients or the controls (281-32) like demographics, diagnoses, results of the Synachten tests, outcome etc.

Discussion

The first Paragraph is a combined introduction/methods and result section and could be omitted.

The statement: Low blood pressure is not a useful sign to discriminate adrenal insufficiency from other diseases. “Still, according to the literature this is a typical sign of acute adrenal insufficiency”.

Do the authors really mean that low blood pressure is not associated with adrenal insufficiency because it did not discriminate against other serious diseases.

Etc:

The control group is not healthy and probably even more ill than the adrenal insufficient patients so the only hint the clinician got is to ask the patient if they have used glucocorticoids. All patients with primary or secondary adrenal insufficiency are missed.

The part about logistic regression is sophisticated, but in this case a systematically description of the 32 cases should have give much more of valuable information.

**Level of interest:** An article of limited interest

**Quality of written English:** Not suitable for publication unless extensively edited

**Statistical review:** Yes, and I have assessed the statistics in my report.
Declaration of competing interests:

I declare that I have no competing interests