Reviewer’s report

Title: Current Practice of Glucocorticoid Replacement Therapy and Patient-Perceived Health Outcomes in Adrenal Insufficiency A Worldwide Patient Survey

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Reviewer: Miguel Debono

This article by Forss et al discusses glucocorticoid replacement in adrenal insufficiency, currently a rapidly evolving area in endocrinology. Patients with adrenal insufficiency have been shown to have a poor quality of life irrespective of treatment and the data in this study, besides agreeing with previous findings, continues to highlight this problem.

Major Compulsory Revisions

1. In your discussion in the third paragraph you mention that multiple daily dosing is a problem in AI and has a negative impact on QOL. You state that 4/10 found multiple daily dosing a problem. Is the problem more related to compliance or to physical health issues? Do we know whether individuals making part of these 40% are on BID or TID regimes?

Is it possible to mention what the other 6/10, which are at a higher percentage, think?

In the same paragraph you rightly mention that those on TID dosing are more satisfied with their treatment then those on BID or OD dosing. This may look contradictory to the rest of paragraph so I think the whole paragraph needs bit more clarification. You might want to reference a recent paper supporting this data where patients preferred four doses of hydrocortisone and had a better QOL (Clinical Endo. 2012 Ekman et al DOI: 10.1111/j.1365-2265.2012.04352.x) and another were a thrice daily regimen was preferred (Clinical Endo Mah et al Volume 61, Issue 3, pages 367–375, September 2004).

Also might be useful to mention the usefulness of physiological glucocorticoid replacement at this point and maybe reference the development of novel formulations which potentially could make a difference.

2. You do mention congenital adrenal hyperplasia and I agree it would have been interesting to analyse the data separately. Important information is available in the literature on quality of life in this group of patients and it should be referenced and discussed. (J Clin Endocrinol Metab. 2010 November; 95(11): 5110–5121 Arlt et al).

Minor Essential Revisions

3. In background
- line 8 after "day/night" I suggest adding the phrase "in keeping with the pharmacokinetics of conventional glucocorticoids" or even better in a sentence or short paragraph giving some information on glucocorticoid pharmacokinetics.

- line 9 - check grammatical mistake

4. Do you have information of associated hormone deficiencies in patients with secondary AI? These will impact on QOL and therefore is an important limiting factor of the paper if not available and will need to be mentioned in discussion.

Discretionary Revisions

5. In results

- Is it possible by using questionnaire information to put down the approximate time range for what you mean by morning, afternoon, evening?

6. Do you have information on what regimes the people complaining of “more fatigue in the morning” as opposed to “more fatigue during the day” were on? It would be interesting to have this data.

Within the limits of what is possible to achieve from a cross sectional survey I think the paper does offer some novel information and should stimulate further research and development in glucocorticoid replacement. I look forward to your views on suggested changes.

Level of interest: An article whose findings are important to those with closely related research interests

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. I have published on adrenal insufficiency and novel treatments for this disorder.