Reviewer's report

Title: Quantitative assessment of Vigabatrin-attributable visual field loss using semi-automated kinetic perimetry

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Reviewer: Miriam Conway

Reviewer's report:

Many thanks for the opportunity of reading the following article. Enclosed are some comments about the study.

Major

• The authors report significant differences for both eyes between the area of isopters and consecutive visits. From the information shown in the Figures 1 to 6 however the significance does not appear to be obvious to the reader. If the authors reported the mean and standard deviation this might help to resolve the problem.

• Significant differences were found for each isopter over time.
  o A post hoc analysis to show between which visit was significant might also be useful
  o Also was a correction to adjust for multiple comparisons applied

• A correlation was found between cumulative dose and I2E and mean daily dose. This information is surprising as to my knowledge the vast majority of researchers report concentric constriction of the peripheral visual field. This means that you might also expect the outer isopters to be affected to a larger extent. In fact Kinirons et al., 2006 only used the III4e isopter to calculate the mean radial degrees. Further discussion is therefore required.

• It is probably quite important to understand how the isopters fluctuate over a 2 year period (using SKP) in a normal population as static visual field loss is routinely adjusted for age. Additionally, would the authors expect cognitive impairment over the 2 year period have an effect reaction time or visual filed size. Is another cohort of patients with epilepsy not receiving VGB required?

• The authors conclude that SKP is an new diagnostic tool for monitoring VAFL however they have not compared SKP against any other investigative techniques to determine if it more or less useful. Instead the main finding appears not to be the technique used (SKP) but how the visual field loss alters with time or how it is correlated with cumulative dose. If this is what they consider to be their main findings then perhaps their title and introduction might also need to alter.

• What was the accuracy of the visual field testing (what were the reliability criteria?). The interweaving of isopters suggests that there may have been some short-term fluctuations not attributed to vigabatrin. It may also have been useful to repeat one of the visual fields tests within the same week to determine how
repeatable each visual field test was.

- Was the learning effect and the fatigue effect accounted for?
- There appears to be significant discussion about the advantages of SKP without any discussion about its disadvantages. This is probably a little biased as it was not compared against another testing techniques to determine for example whether manual Goldmann may have enabled more of the 29 patients to have been reviewed as a human perimetrist can often adjust to the patients needs. In the NHS many hospitals maintain Goldmann’s for paediatric visual field testing as they find that an experienced perimetrist can acquire a field test more easily using the manual form (SKP).
- I think that the Kinirons study may have reported on 93 patients (not 14) over a 10 year period and found no correlation with drug dose. The fact that this group of researchers carried out larger numbers over a longer period and found the opposite results needs a further more detailed discussion.
- Was the daily dose of VGB constant over the 2 year period as this may have affected cumulative dose
- There was no discussion about how maximum VGB dose might also be correlated to VGB attributed field loss (Conway et al., 2008). Maximum VGB dose and cumulative dose are linked therefore some of the power might be due to maximum dose.
- Not sure why only 14% of the population has a defect. A discussion suggesting possible reasons in relation to other research findings might be useful. Again I think Kinirons may have suggested that most of the damage occurs early on.

Minor

V-A is on average 1.00 in the table 0.1 in the text

Did the reading correction vary with the central isopter over the 2 year period (particularly for the presbyopes)?

In the discussion spelling mistake in the Royal College of Ophthalmologists

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