Author's response to reviews

Title: Long-term outcomes after acute primary angle closure in a White Caucasian population

Authors:

Walter Andreatta (andreattawalter@hotmail.com)
Ibrahim Elaroud (i_melaroud@hotmail.com)
Peter Nightingale (Peter.Nightingale@uhb.nhs.uk)
Maged Nessim (m.nessim@bham.ac.uk)

Version: 3  Date: 17 May 2015

Author's response to reviews: see over
POINT-BY-POINT RESPONSE

We are very grateful to the Editor and reviewers for their thoughtful comments which we feel have made our paper stronger.

REFEREE 1

1. Line 141. Results.
Please clarify why gender is not associated with disease progression. Table 4 shows that 6 out of 7 patients who developed PACG were female. Readers are likely to need additional clarification as to why this is not a relevant finding.
Response: This is based on statistical analysis which was confirmed by our statistician. This is due to the fact that 76% of the cohort was female.

2. Line 152. Results.
please state "5 of the xx eyes" and "4 of the xx eyes" to clarify for the reader what proportion of each group needed topical hypotensive agents.
Response: This was changed as advised.

Please clarify why your approach is more/less valid than the study that excluded cases with uncontrolled IOP after the acute event. It is fine to report these data but if you think your methodology has merits then let the reader know what these are.
Response: This was clarified.

I think this is too vague. "We propose..." should lead to a concrete proposal. Are you proposing that IOPs should be controlled to be lower than the normal population range - if so then please say this. Do your data support a recommendation that <16mmHg is a good target IOP based on the IOPs of the cohort that did not develop PACG - if so then please say this.
Response: We decided to delete that sentence as it is not fully supported by our results (i.e. RNFL thickness). However, based on our data, we could not propose a specific IOP value below which GON could be prevented.
5. Line 192. Discussion.
I would change "by the final visit" to words such as "over a similar time frame to our study". This saves the reader from having to look up the reference to see how valid the comparison is between South East Asians and the population studied.
Response: This was changed as advised.

It may be that taking longer to present for medical attention after developing symptoms is predictive for subsequent poorer compliance or poorer follow-up hampering subsequent treatment. It seems quite likely that poor help-seeking behaviour may correlate with poorer longer-term health outcomes in general. Did the authors see any evidence of this in the chart review?
Response: This is most likely true but it is beyond the scope of our study.

7. Line 207. Discussion.
"significant" may not be the best word to use here.
Response: The word was deleted as advised.

8. General. Discussion:
I would like to see some comment in the discussion about the suitability of current treatment protocols for APAC in the light of these data and the risk factors they have identified. Would the authors continue to treat patients presenting APAC with additional risk factors for PACG in the same manner, now they have this new knowledge? Do their data suggest a subset of patients may be better served by using an alternative treatment strategy, for example needle paracentesis, to rapidly lower IOP and break an episode of APAC?
Response: Further recommendations were made based on the results reported in table 4 concerning the need of a more rapid resolution of the attack. However, the design of our study does not allow us to make recommendations on specific treatment options.

"None" would suffice.
Response: This was amended as advised.
REVIEWER 2

1. Line 63 ‘limited data is available’ should be ‘limited data are available’. MEC
Response: This was changed as advised.

2. Line 69 needs full stop. MEC
Response: This was changed as advised.

3. Line 78 – ‘selected’ implies some potential bias, ‘identified’ would be a better word. MEC
Response: This was changed as advised.

4. Line 85 ‘angle closure on gonioscopy’ needs to be better defined – did you mean iridotrabecular contact over 360 degrees? MEC
Response: This was better defined as advised.

5. Line 87 – ‘origins than’ should be ‘origins other than’ MEC
Response: This was changed as advised.

6. Line 94 discs’ should be disc. MEC
Response: This was changed as advised.

7. Line 96 – subsequent reference to VA being BCVA after VA is first mentioned (line 94) - needs to be phrased more succinctly. MEC
Response: This was changed as advised.

8. Line 98 – ‘All patients had at least one reliable visual field test.’ This sentence reports a result. Do you mean that you excluded patients who could not perform a reliable VF test? MEC
Response: All patients in our cohort had at least one reliable visual field.

9. Line 100 – was the reproducibility of these VF defects assessed in any way? MCR
Response: VF defects were confirmed on at least two separate HVF. A statement was added in the methods.

10. Line 105 (...visual field < 10 degrees) is insufficiently descriptive. Did you mean visual field constriction to within 10 degrees of fixation? MEC
Response: We meant a constriction of more than 5 degrees from the point of fixation. The manuscript was amended accordingly.

11. Line 109 – how is glaucomatous optic neuropathy defined? Did you mean increased disc cupping? If so there needs to be some description/discussion regarding any difficulty in detecting disc cupping in short eyes which tend to have small discs. It may be the best way to determine whether there was glaucomatous optic neuropathy was the presence of reproducible field defect. There needs to be some discussion of whether field defects detected were reproducible. MCR
Response: We feel that the explanation of GON is too complex to be included in the methods and therefore we referenced the following paper: Foster PJ, Buhrmann RR, Quigley HA, et al. The definition and classification of glaucoma in prevalence surveys. Br J Ophthalmol. 2002; 86:238–242.
Nevertheless, every disc was measured and its size taken into account when considering whether or not this was a case of GON. In addition, all cases that were thought to have GON also had a corresponding VF defect.

12. Line 113 – statistical analysis needs to be described in more detail in the methods section along with cut-off used to indicate statistical significance MEC
Response: This was changed as advised.

13. Line 124 ‘none...showed a glaucomatous visual field defect’ This is unnecessary as you have stated you have excluded patients with established glaucoma. It would be more useful to state how many were screened and how many were excluded because of established field defects or unreliable fields. MEC
Response: The sentence was deleted. The patients with previous glaucoma were excluded at the time of data collection and therefore it would be difficult to determine their precise number.

14. Line 160 – ‘While’ should be ‘whilst’. ‘Studies investigated’ should be ‘studies have investigated’ MEC
Response: This was changed as advised.

15. Line 166 – GON – write out in full at first use. MEC
Response: This was changed as advised.

16. Line 167 – can you really state that APAC results in NFL defects? Did these studies have nerve fibre layer imaging before and after APAC? MEC
Response: These studies measured the RNFL shortly after APAC and then at subsequent follow up appointments. The healthy fellow eye was used as control. They found progressive RNFL thinning.

17. Line 168 – see note above re difficulty seeing increased CDR in these eyes. There really needs to be some discussion of the limitation of using CDR in a retrospective study – presumably the patients were seen by a number of different clinicians with a range of experience. MCR
Response: This was added in the discussion as one of the limitations (lines 237-239).

18. Line 175 – how can you propose this from your data? You have not reported any findings on RNFL defects. How is GON defined? What evidence is there that RNFL defects progress to GON? MEC
Response: We agree with your comment and that statement was removed.

19. Line 183 – ‘be accountable’ should be ‘account’ MEC
Response: This was changed as advised.

20. Line 188 – the difference is only 2.5 % which would constitute one eye in your sample. Not worth discussing reasons for such a small difference. MEC
Response: The sentence was removed as advised.

21. Line 192 – al should have full stop after it unless journal guidance states otherwise. Consider this for all subsequent uses of al. Presumably Tan et al. excluded eyes not affected by glaucoma at presentation – need to state explicitly.
MEC
Response: This was changed as advised.

22. Line 195 – ‘had glaucoma’ should be ‘developed glaucoma’. MEC
Response: This was changed as advised.

23. Line 196 – ‘linked’ should be ‘associated with’ as this is a statistical statement. MEC
Response: This was changed as advised.

24. Line 201 – what is the aetiology of pigment release? Are we talking about after LPI? If so why would there be more pigment release in cases suffering longer APAC. MEC
Response: Pigment release occurs during angle closure and it is believed to be due to iris ischemia and contact between the iris and the cornea and/or the lens. This leads to iris atrophy. Post mortem microscopy of the trabecular meshwork showed extensive pigment deposition which could result in reduced aqueous filtration (Sihota R, Lakshmaiah NC, Walia KB et al. The trabecular meshwork in acute and chronic angle closure glaucoma. Indian J Ophthalmol. 2001 Dec;49(4):255-9).

25. Line 203 – ‘find any predictor’ should be ‘identify risk factors for’. MEC
Response: This was changed as advised.

26. Line 209 - what is mechanism by which APAC causes poor VA if not through PACG? MEC
27. Line 211 – (the VA ranged..) should be (the VA cut-off ranged..)
Response: This was changed as advised.

28. Line 215 – ‘justify’ should be ‘explain’. MEC
Response: This was changed as advised.

29. Line 220 – do you mean less than 20 degrees from fixation? MEC
Response: This was changed as advised. We meant 10 degrees from fixation.

30. Line 226 – should read ‘in our sample of white Caucasian patients delayed presentation…’ MEC
Response: This was changed as advised.

31. Line 232 – raise should be rise. MEC
Response: This was changed as advised.