Reviewer's report

Title: Is enucleation a risk factor for the development of cluster headache?

Version: 1 Date: 8 November 2004

Reviewer: Paola Torelli

Reviewer's report:

General
The authors investigated cluster headache (CH) retrospectively in a sample of patients who had had an eye removed for medical reasons (eye trauma, malignant or non-malignant eye diseases). The purpose of their study was to determine whether “removal of an eye is a risk factor for CH”.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

1) The “Methods” section should be moved after the “Background” section and before the “Results” section. In the current manuscript, it is placed after the “Conclusions” section.
2) Title: considering the methodological limitations of the study (see at 4, 5 and 6), the title seems to be overly ambitious. It should be changed to “Enucleation and development of cluster headache: a retrospective study”.
3) Background: in the second paragraph, the authors state: “..several reports described the onset of CH during or shortly after structural brain disease or traumatic brain injury”. Based on the text and the references cited in the text, it is not clear whether they refer only to primary CH cases where there are possible triggering factors (i.e. Refs. 5, 14, and 16; Reik L. Cluster headache after head injury. Headache 1987;27:509-510; or Turkewitz LJ, Wirth O, Dawson GA, Casaly JS. Cluster headache following head injury: a case report and review of the literature. Headache 1992;32:504-506) or they also refer to secondary CH forms. In my opinion, in this context primary CH (with possible triggering factors) should continue to be differentiated from secondary CH, and therefore the authors should refer only to the former.
4) Methods:
a) The authors should indicate which method they used to recruit the 332 patients (i.e., by reviewing all clinical records of patients referred to the Department of Ophthalmology? By identifying them based on diagnosis or surgery – eye enucleation, eye trauma, etc. – in any data bases?)
b) The authors should also indicate exactly when the 332 recruited in the study were seen at the Department of Ophthalmology (from which year to which year).
c) The authors should make it clear whether the 332 patients recruited for the study include all those who were operated on for eye removal in the period considered. If that were not so, there might be a bias in the patient sample selection.
d) Was the questionnaire for CH diagnosis previously validated?
5) Results: The response rate, which is 33.7% (112/332), should be clearly indicated.
6) Discussion:
a) Study limitations: the authors should comment on the methods used, maybe stating that case-control studies and cohort studies are more appropriate for the study of a disease’s risk factors .
b) Study limitations: in addition to the questionnaire-based design the response
rate (33.7%), too, might lead to underestimate the frequency of CH onset in enucleated patients.

c) Study limitations: self-administered questionnaires have often been used in epidemiological studies; however, the presence of CH and its diagnosis according to the International Headache Society classification criteria should better be verified through a face-to-face interview and an objective neurological examination. The authors should comment on this, adding their remarks to the study limitations paragraph.

d) Mean age of the 112 patients at the time of surgery was 48 years ± 21. Based on literature reports, mean age at CH onset is about 29 years (Bahra A, May A, Goadsby P. Cluster headache. A prospective study with diagnostic implications. Neurology 2002;58:354-361; Manzoni GC, Terzano MG, Bono G, Micieli G, Martucci N, Nappi G. Cluster headache - clinical findings in 180 patients. Cephalalgia 1983;3:21-30). The authors should add their comments, indicating a) if they think that enucleation is not a risk factor, regardless of the patient’s age at surgery; or, b) if it can be assumed that enucleation may favour CH onset only if surgery is done in that age range when CH usually occurs spontaneously. (In this connection, it could be interesting to check literature reports to see when CH occurred in patients who developed it following removal of the eye bulb.)

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

1) Methods
   a) The authors should explain what they mean by “temporal course”: does that refer to the duration of attacks (15-180 minutes) or to the periodic time pattern of CH?
   b) How were the filled-in questionnaires returned? Were they returned by mail, or by direct hand delivery to the Department of Ophthalmology, or by any other means?

2) Results
   a) In the first line, I would add the number of females in parentheses (78 men and 34 women).

Discretionary Revisions (which the author can choose to ignore)

1) Results: I recommend that the authors indicate the number of males and of females among the patients who developed CH after eye bulb removal.

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

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

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests: 
I declare that I have no competing interests