Reviewer's report

Title: The Prevention of Anaphylactoid Reactions to Iodinated Radiological Contrast Media: A Systematic Review of Randomised Controlled Trials

Version: 1 Date: 5 March 2006

Reviewer: Raymond Liu

Reviewer's report:

General

Dr. Delaney’s article is a systematic review of the use of H1 antihistamines and steroids prior to iodinated radiological contrast media administration. While Dr. Delaney’s methods are thorough and transparent, I do not believe his analysis of the data support his conclusions. In particular, I worry about the heterogeneity of the data and the lack of high quality randomized trials on which he bases his conclusions.

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

Page 2: The analysis for H1 blockers should not include the study from Ring et. al, unless that paper separated the patients receiving only H1 blockers. In that study, some patients received steroids, and some received more than one anti-histamine. Dr. Delaney should mention if they only analyzed the subset receiving clemastin alone.

Page 3: Dr. Delaney’s conclusion that “methylprednisolone 32mg be given at least 6 hours prior and two hours prior to the administration of contrast” is based on one study alone – please see later comments for page 12 and 13.

Page 4: The author needs to elaborate on the difference in allergic reactions between non-ionic and ionic contrast agents. The numbers he quotes for the difference between the two types of contrast agents would suggest that using non-ionic contrast agents reduces the risk of allergic reactions more than the interventions he is studying. One might wonder if his meta-analysis should focus more on the difference between non-ionic and ionic contrast agents rather than pre-medication in the prevention of allergic reactions.

Page 9: The author mentions that only one study clearly met all of the predefined validity criteria. In fact, at least two of the studies included in the meta-analysis met NONE of the validity criteria. Given that these studies are not deemed to be of high quality based on these criteria, shouldn’t they be excluded from the meta-analysis? Excluding the low quality studies seems reasonable, but that leaves too few studies to analyze. Therein lies the problem with this meta-analysis – there are too many poor quality studies with too much heterogeneity to make any sound conclusions.

Page 9: Dr. Delaney states that there is “significant heterogeneity amongst the included studies….it was not possible to explore further reasons for the heterogeneity.” I think it would be important for Dr. Delaney to elaborate on this more. Could he in the discussion, describe exactly what was heterogeneous between the studies, and whether there should be a standard for future studies? If there should be a standard, what should be tested?
Page 12: “strongly suggestive of a protective effect of corticosteroids.” I’m not sure how the author can come to this conclusion when there were not enough studies to analyze. His conclusion is based on only one trial, and that is not sufficient for a meta-analysis.

Page 12: “The protective effect of H1 antihistamines and corticosteroids in high-risk patients has been demonstrated in non-randomized studies.” In the absence of good randomized data, data from non-randomized studies needs to be elaborated on (probably in the background section).

Page 13: “the results of this review would suggest that two doses of corticosteroids be used as prophylaxis, especially in light of the results of the Lasser study…” As mentioned previously on Page 12, conclusions of a meta-analysis should not be based on one trial, in this case the Lasser trial.

Page 14: Conclusions: Once again, I don’t think the authors can conclude that their meta-analysis shows that the use of steroids is supported by available trials, especially when there was only one good quality trial that they are basing this conclusion on. In addition, the heterogeneity of the trials makes it impossible to support the routine use of H1 and corticosteroids without further studies.

Discussion: I think that the author should state that more high quality studies are necessary before any meta-analysis conclusions can be made, and describe what he thinks these future studies should look like.

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

Page 4, line 7: Spelled “focused” wrong.

Page 7: The author should indicate what he means by “pseudo-randomized” and why he allowed pseudo-randomized trials to be included in the analysis.

Discretionary Revisions (which the author can choose to ignore)

Page 4: The background section should focus more on the morbidity and mortality of contrast agents. There is a recent article published that describes some U.S. statistics:

x-ray contrast media on u.s. Death certificates.
PMID: 16498085 [PubMed - in process]

Page 4: It would be interesting to have a description of the spectrum of allergic reactions that can occur with contrast agents in the background section.

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

Level of interest: An article of importance in its field

Quality of written English: Acceptable
Statistical review: No

Declaration of competing interests:

I declare that I have no competing interests.