Author's response to reviews

Title: Acetylcysteine for prevention of contrast-induced nephropathy after intravascular angiography: A systematic review and meta-analysis.

Authors:
- Sean M Bagshaw (smbagsha@ucalgary.ca)
- William A Ghali (wghali@ucalgary.ca)

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Biomed Central Nephrology

Dear Editors:

Regarding: MS: 1057270635047940 - Acetylcysteine for prevention of contrast-induced nephropathy after intravascular angiography: A systematic review and meta-analysis.

Thank you for giving us the opportunity to resubmit this manuscript. We have revised the manuscript in accordance with the reviewer comments that were provided in your letter dated July 12, 2004. Below, we provide an itemized summary of the changes made to the paper. Reviewer comments are in bold, followed by our responses. You will see that we have responded to each of the reviewer comments that you provided.

In addition, we conducted a supplementary literature search to update our meta-analysis with any additional trials of acetylcysteine for prevention of contrast-induced nephropathy that have been published since we initially submitted our paper to you. That search update has revealed four additional trials that fulfill our inclusion/exclusion criteria. We have thus updated our meta-analysis with these trials. The overall results and conclusion of our meta-analysis do not change after inclusion of these four studies, and as a result of this update, this meta-analysis is likely to now be the most comprehensive and up to date meta-analysis available of peer-reviewed trials of acetylcysteine for prevention of contrast-induced nephropathy.

Reviewer 1 (Marc De Kock).

I think the doses and the timing of administration of NAC is of primary interest.

The reviewer has raised an interesting question. Clearly the timing and total dose of administered acetylcysteine are variable across trials, as shown in Table 1. Despite this, no clear pattern has emerged to suggest that any particular dose or schedule is more efficacious than others. We now explicitly mention the NAC dosing and timing algorithms on page 8, paragraph 2 of the Results section, and as mentioned above, also show this information in detail in Table 1.
Do you think that creatinine is the best way to monitor tubular cells oxidative injury?

The reviewer raises an important question. On page 8, paragraph 3 in the results section we discuss the variability in the definitions of contrast-induced nephropathy across trials. This information is also presented in Table 1. Further, on page 9, paragraph 2 we comment on the overall need for dialysis across all trials as an important outcome, but one that could not be meaningfully assessed in any of the individual trials due to lack of power. Finally, in our discussion on page 15, paragraph 1 we suggest that use of surrogate outcomes of renal dysfunction such as serum creatinine may not be the most important outcome for trials of contrast-induced nephropathy. We hope that future clinical trials will address more clinically important outcomes such as change in GFR, need for dialysis, length of hospitalization, health-care costs and long-term recovery of renal function.

Reviewer 2 (Shereif H Rezkalla).

This reviewer had no specific comments or questions.

Reviewer 3 (Antonio C Seguro)

This is an important paper. In a meta-analysis the authors concluded that the efficacy of acetylcysteine for prevention of contrast-induced nephropathy remains unproven. An interesting finding was obtained by the meta-regression analysis. This analysis suggests that the heterogeneity across studies may be partially explained by whether the angiography was performed electively or emergently. (Minor Compulsory Revisions) Similar results have been recently published by Kshisagar et al. (JASN 2004;15:761).

We have added mention of the recently published meta-analysis by Kshisagar et al. to our Discussion section on page 12, paragraph 2 (cited as reference number 44).

We thank the reviewers for their reviews and thoughtful comments. We recognize that the paper has improved through the requested revisions, and hope that the editors will be satisfied with our revisions.

We look forward to hearing from you.

Yours sincerely,

Sean M. Bagshaw, MD

William A. Ghali, MD, MPH