Reviewer’s report

Title: Magnesium supplementation and high volume hydration reduce the renal toxicity caused by cisplatin-based chemotherapy in lung cancer patients; a toxicity study.

Version: 7 Date: 21 July 2014

Reviewer: Christine N Metz

Reviewer’s report:

Oka and colleagues report their findings from a historical prospective cohort study examining the effects of hydration and magnesium supplementation on renal injury in adult lung cancer patients treated with cisplatin. It is a fairly small study with approx 85 subjects total – receiving one of three treatment regimens (low volume+Mg vs. high vol-Mg vs. high vol+Mg) during their first cycle of cisplatin treatment. Outcomes measured were serum creatinine and creatinine clearance. They report an improvement in renal function (based on serum creatinine and creatinine clearance in patients receiving Mg.

Major suggested revisions:

1. These data are consistent with the postulate that cisplatin leads to hypomagnesemia which promotes renal injury and support previous findings that Mg supplementation is useful for protecting against renal injury in humans (Willox et al, 1986; Bodnar et al, 2008; Muraki et al, 2012; Hirai et al, 2013; and Yoshida et al, 2014) and in rodents (Solanki et al, 2014). References should include the most recent paper by Yoshida et al in 2014 because this was a large retrospective study of 496 thoracic cancer patients (treated with cisplatin +/- Mg) over 3 years. The authors should compare their dose of Mg (8mEq) with those used in these previous human studies?

2. Please clarify – lung cancer patients (as described in abstract) vs. patients with malignant chest tumors (as described in the methods).

3. Please clarify ‘electrolyte-containing solution’ line 114

4. Please clarify that serum (vs. urine or plasma) creatinine was measured in the methods section.

5. Why limit this study to the first round of cisplatin – was the Mg or hydration treatment restricted to the first round of cisplatin only. Cisplatin results in cumulative nephrotoxicity (and that is what ultimately matters for the patient); therefore, one might expect better results in later cycles. Justification should be provided.

6. Please define what is meant by Mg-based medications (do you mean Mg-containing medications or medications associated with Mg depletion)-provide examples.
7. The % of males in each group are not similar (hi vol+Mg=76%; high vol-Mg=67% and low volume+Mg=94%) – females are proposed to be more sensitive to cisplatin-induced nephrotoxicity. Has this been considered? The authors should address this.

8. The authors should discuss how they decided on the low and high volume protocols. Were there differences in osmolarity in these two protocols?

9. One important consideration the authors should address is whether Mg supplementation will also protect the tumors from cisplatin-mediated killing – this could be discussed in the discussion section. Hopefully, the authors are considering long-term studies that would be able to answer the question concerning the effects of Mg on guarding against cisplatin-induced tumor killing.

Minor essential revisions:

1. Why did the authors choose a historical prospective design rather than a randomized prospective design (if they knew they would be testing three treatment strategies)? Please clarify that this wasn’t a retrospective study. Did the subjects agree to participate in research testing the effects of hydration volume and Mg on kidney injury induced by cisplatin or were they consented to receive cisplatin for the treatment of their lung cancer (according to the current regimen used by the hospital)?

2. Standard abbreviations for creatinine and creatinine clearance should be considered (e.g. sCr or Cr for creatinine and CrCl or ClCr for creatinine clearance.

3. Is the data shown in Figure 1 the same as the data shown in Table 4 – if they are the same, why show both sets of data?

4. Why not combine Table 4 into Table 2 – simply add pre and post Cr values (above and below each other) to keep the data together in a single table?

5. Out of curiosity – why wasn’t serum Mg data available for patients…isn’t that part of standard of care for cisplatin patients?

6. Several grammatical and spelling errors should be corrected (e.g. abstract should be re-written to improve clarity; line 72 nephrotoxic damage; line 75 shortening; lines 168 and 171 higher (instead of increased); line 203 Second in our study; and throughout manuscript the use of respectively requires an ‘and’ between the p values (e.g. p< 0.05, p<0.01, respectively – should be p<0.05 and p<0.01, respectively).

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

Quality of written English: Needs some language corrections before being published
**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