Reviewer’s report

Title: Hypothyroidism attenuates protein tyrosine nitration, oxidative stress and renal damage induced by ischemia and reperfusion: effect unrelated to antioxidant enzymes activity

Version: 1 Date: 21 July 2005

Reviewer: Prabal K Chatterjee

Reviewer’s report:

General

This study by Tenorio-Velázquez and collagues investigated whether surgically-induced hypothyroidism could protect rats against renal ischemia-reperfusion (I-R) injury (unilateral renal artery clamping for 60 min followed by reperfusion for 24 h) 15 days after thyroidectomy. Hypothyroidism reduced the degree of renal dysfunction and injury caused by I-R. Evidence of nitrosative and oxidative stress of the kidney was also reduced. Intriguingly, levels of antioxidant enzymes (SOD, CAT, GPx) were unaffected by both hypothyroidism or I-R. The authors conclude that rats subjected to hypothyroidism demonstrate increased resistance to renal dysfunction and injury and oxidative and nitrosative stress caused by I-R and that activities of the antioxidant enzymes are unaffected.

Overall, the manuscript is well written and presented and the study follows on from the initial findings of Mark Paller in 1986. However, this referee has the following points, shown in the sections below, which the authors are invited to consider:

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

(1) There is now good evidence that hypothyroidism can contribute to the development of acute renal failure by causing rhabdomyolysis (see Sekine N, et al., Intern Med. 1993 32:269-71).
   (i) Could the authors comment on the lack of any renal dysfunction or injury in their thyroidectomised rats prior to I-R?
   (ii) In view of this potential complication of hypothyroidism, what is the clinical relevance of this study? If there is any, the authors should describe this in their Introduction or Discussion.

(2) There is also some evidence that renal I-R can modulate the protein expression and activity of antioxidant enzymes, especially after 90 min ischemia (see Dobashi K, et al. Mol Cell Biochem. 2000 205:1-11). There is some suggestion in the data that CAT and GPx levels were modulated by I-R. Could a significant effect be hidden by the small number of samples used for the determination of CAT and GPx (n=5 or 7)? If further analysis were performed and group sizes matched (n=16) would a significant effect become apparent? The authors should consider this in light of their claim that antioxidant enzyme activities were unaffected by renal I-R in their model.

(3) A more robust method of assessment of histological evidence of renal injury is required, e.g. a commonly-used scoring system based on loss of nuclei from tubules could also be used (see Chatterjee PK, Kidney Int. 2000 58:658-73). Measurement of glomerular size is inadequate – even in Figure 1 the glomeruli look similar in size in most of the images.

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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. Grammatical and typographical errors are present throughout the manuscript from Abstract (glutathione peroxide?) to References ('membrana' in Ref 41?). There are too many to list here but they all need to be corrected.

2. What was the species of rat used in this study?

3. How were total protein levels measured?

4. Bobadilla (ref 42) described how hypothyroidism can protect the heart against I-R injury, not Chavez (ref 41) as stated at the end of the Discussion.


Discretionary Revisions (which the author can choose to ignore)

1. Page numbering would have been helpful (not present on my PDF version).

2. It would be interesting to see if thyroxine levels change in thyroidectomised rats after I-R.

**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:** Needs some language corrections before being published

**Statistical review:** No

**Declaration of competing interests:**

I declare that I have no competing interests