Zinc as antiperoxidative agent following iodine-131 induced changes on the antioxidant system and the morphology of red blood cells

To the Editor: In the January/April issue 2006; 9(1): 22-26 of the Hell J Nucl Med, Dani V and Dhawan DK. reported on the antiperoxidative effect of zinc (Zn) in iodine-131 (^{131}I) treated rats, assessed via the antioxidant status of red blood cells by a single measurement, only seven days after radioiodine application [1]. Identical findings have been obtained by the same group before, after 2 days. Concerning the antiperoxidative action, pretreatment with zinc aspartate [2] is significantly more effective than Zn alone in protecting membranes by occupying negatively charged sites with potential iron binding capacity. However, in vivo under certain circumstances even a pro-oxidative action may occur [3]. In the summary, the authors describe that malondialdehyde (MDA) in the red blood lysate was increased, while in the methodology and results section further information on MDA is missing. Other consequences of ^{131}I on red blood cells, such as deformability, cellular shrinkage, intracellular hemoglobin condensation, accompanying potassium loss and hemoglobin oxidation [4, 5], have not been examined. It's a pity that the authors did not provide a time course. The oxidant status of red blood cells under the influence of Zn ranged between the controls and the Zn treated animals. A critical consequence of irradiation is free radical formation which is used in cancer therapeutics to damage cancer cells. Lipid peroxidation, a process initiated by the production of oxygen free radicals, is increased in red cells in the presence of reactive iron species and various heme moieties [6]. For example, enhanced (lipid-) peroxidation is well known and documented after ^{131}I treatment [7, 8]. An increase in red blood cells (by erythropoietin, for example) attempts to enhance the therapeutic efficacy of the same radiation dose via increasing oxidative damage. Determining 8-epi-PGF_{2a} as a measure of in-vivo oxidation injury [9] in patients with ^{131}I treatment shows a significant positive correlation with the content of hemoglobin in the blood (unpublished data). The balance between the irradiation effect at the local therapeutic site (thyroid destruction, for example) and the unwanted effect (at the resting tissue), needs to be considered. Concomitant treatment with Zn may not only protect red blood cells from damage but also reduce even more the desired effect on thyroid tissue. Data on this key issue such as hormone values or others have not been provided and are lacking. Even months after ^{131}I treatment, a great variety of significant changes in local mediators in the salivary glands can be seen [10]. A variety of other damaging mechanisms should also be considered. Radiation-induced oxidation injury will harm platelets much more and much earlier than rather radioresistant red blood cells and will also modify preferentially plasma proteins (fibrinogen, lipoproteins) increasing either their pathogenicity (LDL, VLDL) or decreasing their physiological protective action (HDL).

As long as the effect on the therapeutic target tissue, i.e. the thyroid gland (benefit-risk-ratio), is not assessed in human, the approach to induce uncontrolled radioprotection of red blood cells (and other tissues) by Zn (to an unknown extent), therefore, remains highly questionable.

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Authors' reply

We thank Professor H. Sinzinger and Dr H. Ahmadjadehfar for their comments. We did publish some identical findings pertaining to antioxidant status of red blood cells following single intraperitoneal injection of ^{131}I, however in the article published in the Hell J Nucl Med mentioned above, we have reported changes with regard to antioxidant status as well as to the morphology of red blood cells after seven days of ^{131}I administration and with regard to the protection afforded by zinc supplementation. In the paper published in the Indian journal of Medical Research entitled "Radioprotective role of zinc following single dose radioiodine exposure to red blood cells to rats" 2005; 122: 338-342, we had reported the protective effects of zinc only on the antioxidant status of red blood cells following two days of ^{131}I treatment.

With regard to the second query that malondialdehyde (MDA) levels were discussed in the summary while these were missing in the methodology and result section, we reiterate that the levels of MDA were mentioned and shown to be enhanced following ^{131}I administration, in the results section. Of course MDA levels represent the lipid peroxide levels and are the degradation product of peroxidised lipids, that reacts with thiobarbituric acid (TBA), forming TBA-MDA chromophore which is taken as an index of lipid peroxidation and has also been quoted by Wills (1966) in the same article of ours mentioned above.

As advised by Professor Sinzinger and Dr Alhamjadehfar, other parameters such as, deformability, cellular shrinkage, intracellular haemoglobin condensation, potassium loss and haemoglobin oxidation, are being looked into. Actually the study was to be carried out in different phases in order to cover large number of parameters. Understandably, we have also conducted studies to evaluate the role of zinc on thyroid function, which include, thyroidal ^{131}I uptake and total T_3, T_4 and TSH levels, following single radioiodine application. We agree with the comments made by Prof. H. Sinzinger and Dr H. Alhamjadehfar, that the "the balance between irradiation effect at the local therapeutic site (thyroid distruction for example) and the unwanted effect (at the resting tissue),

needs to be considered". To be in line, we were interested to investigate the effects of zinc both on the thyroid hormones and the uptake and retention of ^{131}I following damage of thyroid tissue by ^{131}I. Our results on this part of the study are under publication in the Hell J Nucl Med. In that article we have shown interesting effects on the uptake values of ^{131}I both at 2 and 24 h following the application of ^{131}I and also following the simultaneous zinc supplementation. Interesting are also results as above on the thyroid biological half-life, indicative of ^{131}I retention. Concomitant treatment with zinc in rats may not only protect red blood cells from damage but also enhance the desired effect on thyroid tissue which may have supporting therapeutic implications. Of course studies in men should follow.

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Forthcoming meetings

18-19 May, 2007
Second Eastern and Middle Europe Conference of Nuclear Medicine
Krakow, Poland
e-mail: mkostkiewicz@szpitaljp2.krakow.pl

2-6 June, 2007
Society of Nuclear Medicine
54th Annual Meeting
Washington, Info: http://www.snm.org

4-7 June, 2007
XVth International Conference on the Use of Computers in Radiation Therapy (ICCR 2007)
Toronto, Canada, Info: http://www.iccr2007.org

14-15 June, 2007
The second International Conference of the European Society for Molecular Imaging
Royal Continental Hotel Convention Center in Naples, Italy
On: molecular basis of cancer, cardiovascular etc.
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26-30 June, 2007
Medicon 2007
Ljubljana, Slovenia
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23-25 July, 2007
Frontline of PET-CT Image Interpretation
Lebanon, New Hampshire
Dartmouth-Hitchcock Medical Center
Info: www.hitchcock.org

6-9 September, 2007
ASNC 2007 12th Annual Scientific Session of the American Society of Nuclear Cardiology
San Diego, California, USA, Info: www.eanm.org

8-11 September, 2007
Molecular Imaging Joint Conference
Providence, Rhode Island, USA
Info: www.ami-imaging.org/

13-17 October, 2007
20th Annual Congress of the European Association of Nuclear Medicine
Copenhagen, Denmark, Info: www.eanm.org

28 October – 3 November, 2007
2007 IEEE Nuclear Science Symposium
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Molecular Nuclear Medicine (IPET-2007)
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