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Letter to Editor

GESDAV

Ischemia modified albumin and nitric oxide in hyperthyroidism

Sir,

It was with great interest, we read an article "Comparative study of ischemia modified albumin (IMA) and nitric oxide (NO) in hyperthyroidism" by Verma *et al*. [1]. They concluded that increased IMA levels may be a consequence of and cause for decreased NO levels in hyperthyroidism.

The concept of IMA as oxidative stress marker has been the major topic of research interest. However, there have been very few reports on the status of IMA in thyroid dysfunction [1-3]. Though IMA has been proposed as a novel indicator of endothelial damage in diabetes [4], to the best of our knowledge, this study by Verma *et al*. [1] is the first report simultaneously studying IMA and NO in hyperthyroidism. Therefore, this article is timely and provides important information in support of earlier only report on IMA in hyperthyroidism [2]. However, we have few important issues in mind. To address:

- Firstly, it has been clearly stated in the results section that hyperthyroid patients showed significantly lower body mass index (BMI) than in their control counterparts ($P < 0.001$). This appears to be an important aspect in the light of the recent report showing low BMI as an important risk factor for impaired endothelium-dependent vasodilation through increased oxidative stress, leading to the reduced bioavailability of NO [5]. Considering this evidence, the significant decrease in BMI found in their study may possibly influence the results and final conclusions drawn. There is also no mention on the association of BMI with either of IMA and NO. Therefore, to strengthen the study conclusions, independent factor analysis and/or partial correlation analysis would have been performed to nullify or control the role of decreased BMI, if any, on the observed results.
- Secondly, measurement of IMA by albumin cobalt binding assay applies the ability of normal albumin binding to cobalt. In case of modified albumin, the capacity of albumin binding to cobalt decreases, leaving more unbound/free cobalt to develop color indicating IMA value in absorbance units. Therefore, it is very much possible that alterations in albumin concentrations may affect IMA values. Given the previous evidence of decreased serum albumin levels in hyperthyroidism [6], and the interference of albumin level with the IMA estimation, it is important to provide IMA values corrected for albumin interference [7]. Thirdly, it has been reported [8] that hyperthyroidism increases plasma free fatty acids (FFA) and change in FFA level may influence binding of cobalt to serum albumin and IMA result [9]. In light of this previous evidence, it appears important to address the IMA values in relation to albumin and FFA levels in hyperthyroidism.
- Finally, although better discussed the consequence or causal association between IMA and NO, authors would have also discussed their finding of decreased NO in the context of increased asymmetric dimethylarginine (ADMA) levels with supportive direct evidence. However, there is no information, either direct or indirect, in support of this. If not direct information on ADMA, oxidative damage marker such as malondialdehyde (MDA) would have been helpful in indirectly explaining decreased NO due to increase in ADMA levels. This is supported by the previous evidence of correlation between MDA and ADMA levels. Furthermore, it has been reported that increased oxidative stress decreases the activity of dimethylarginine dimethylaminohydrolase, leading to accumulation of endogenous ADMA [10,11].

We hope that the issues described here would carry scientific importance.

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