Is Malondialdehyde a Putative Uremic Toxin?

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Dear Sir, References

Various studies have demonstrated that the lipid per-oxidation (LP) status of chronic renal failure (CRF) patients is significantly increased, irrespective of the dialysis treatment [1–3]. While the actual cause for this increased LP needs further investigation, what alarms us most is the presence of abnormal amounts of malondialdehyde (MDA) in uremic blood. MDA, a secondary breakdown product of fatty acid peroxides, is a highly reactive substance, and even in physiological concentrations can react with erythrocyte membrane phospholipids, cross-linking their polar heads [4]. When modified by MDA, red blood cells (RBC) lose their normal cationic gradient and show reduced deformability in vitro, in addition to a significantly shortened life span in vivo [4, 5]. Further, polymerisation of other membrane components, especially proteins, has been reported in peroxidised RBC membranes [6]. Incidentally, uremic RBC exhibit many of these features. Peroxidised lipids can also damage other proteins, altering their physical properties [7]. Moreover, MDA-altered low-density lipoproteins lead to cholesteryl ester accumulation in human monocyte macrophages, and it has been suggested that modification of native low-density lipoproteins may be a prerequisite for the accumulation of cholesteryl esters within the cells of atherosclerotic reaction [8]. Thus, LP may also contribute to the high incidence of premature atherosclerosis in CRF patients.

The products of LP, especially MDA, can be the most potent candidates for uremic toxicity. No other uremic toxin(s) studied till now had so many established toxic potentialities. Last but not least, the possible contribution of LP to the high incidence of cancer in CRF patients is worth pursuing, especially in view of the fact that oxygen radicals have been implicated as tumor promoters [9].

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