Dysregulation of Superoxide Dismutase in Chronic Kidney Disease

See Akiyama et al., *Nephron Clin Pract* 2005;99:c107–c114

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Chronic kidney disease (CKD) is commonly reported to be associated with oxidative stress but there is still controversy on the mechanism. Numerous sources of radical oxygen species (ROS) have been identified in CKD patients, especially in hemodialysis (HD) patients. Macrophage activation, which produces ROS, is due in these patients to: accumulation of uremic toxins; dialysis membrane bio-incompatibility; influx of endotoxins from the dialysate, and immunologic and metabolic disorders such as diabetes and dyslipidemia [1]. Phagocyte myeloperoxidase-mediated events have also been associated with the production of oxidized low-density lipoprotein [2]; advanced oxidation protein products and advanced glycation end products, which are considered potent mediators of inflammation [3]. Moreover, treatment of anemia with high levels of iron may induce oxidative stress [4]. The massive generation of ROS is all the more damaging given that CKD patients have a weaker antioxidant system due to a diet low in antioxidant vitamins and oligo-elements [5] and due to loss of antioxidants during HD sessions [6].

The superoxide dismutase (SOD) is the front line of defence against superoxide anions (O_2^-) and detoxifies O_2^- into hydrogen peroxide (H_2O_2). SOD is a metalloenzyme existing in three different isoforms [7]: the cytoplasmic copper-zinc SOD (Cu/Zn-SOD); the mitochondrial manganese SOD (Mn-SOD) and the extracellular SOD

found in interstitial fluid, plasma, lymph and synovial fluid.

Few studies have looked at SOD activity and its expression in CKD patients; the present study by Akiyama et al. [8] published in this issue of *Nephron Clinical Practice* is one of them. The authors found a significant increase in SOD activity in leucocytes in CKD patients, but this increase affects only Cu/Zn-SOD. Moreover, Cu/Zn-SOD mRNA expression in leucocytes was also significantly higher as compared to controls. This latter result is in line with an earlier study [9], in which an increase in SOD expression in white blood cells in CKD patients was also found. However, this increase in SOD activity is in contrast to the results of several studies, in which a decrease in erythrocyte SOD activity in CKD patients was observed [5, 10, 11]. Furthermore, we must be careful when comparing these different studies, since different sources of cells were used. Knowing that erythrocytes in CKD patients could have a shorter life span because of anemia, it is possible that this shorter life span could explain the difference in SOD levels between these studies. This discrepancy raises the question as to the ideal blood element in which to evaluate SOD activity in CKD patients.

The role of SOD and its different isoforms in the antioxidant defence mechanism in CKD patients is currently unclear. In light of the importance of myeloperoxidase

and chlorinated stress in CKD patients [3, 11, 12], as well as in the general population [13], it seems of capital importance to evaluate simultaneously SOD activity and chlorinated stress markers to determine to what extent chlorination occurs in consequence to SOD dysregulation. Whether or not the induction of Cu/Zn-SOD expres-

sion and activity in leucocytes is sufficient to protect CKD patients against oxidative stress cannot be determined in the study by Akiyama et al. [8], since the authors did not measure chlorinated stress markers. Therefore, the place of SOD activation as a therapeutic strategy remains elusive.

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