One Man's Meat and Another's Poison: Adding Glucose in Dialysis Fluid

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Oxidative stress plays a significant role in the development of inflammation in patients undergoing hemodialysis (HD) [1]. Morena et al. [2] nominated the term 'oxidative stress complex syndrome', just as the well-recognized malnutrition-inflammation atherosclerosis' (MIA) syndrome, to emphasize its important association with long-term complications in HD population. The HD procedure itself is claimed to increase the production of reactive oxygen species (ROS), originated mainly from uremic toxins, membrane biocompatibility, non-sterile dialysate and water. Therapeutic potentials provided from variant antioxidants, such as vitamin C [3], vitamin E [4], folic acid [5], and natural products [6], have been postulated with heartening results in HD patients. Serial studies from Dolegowska's group have focused on the role of glucose and the protective effects of erythrocytes on oxidative stress in the HD population [7–10]. In this issue [11], they demonstrated further that glucose present in dialysate could conserve erythrocyte membrane integrity and limit possible hemolysis induced by the HD process. Such observations may bring high clinical implications and deserve further discussions.

First, although substantial evidence [1, 2] has indicated adverse effects of glucose on oxidative stress, endothelial dysfunction and atherosclerosis, adding glucose in dialysate for HD is beneficial in preventing hypoglycemia during therapy, especially for diabetic patients who received insulin injection or oral hypoglycemic agents. It

also provides the main substrate for energetic metabolism in erythrocytes [12]. Meanwhile, glucose also brings about erythrocyte deformability via metabolic sorbitol accumulation within the erythrocytes and glycosylation of various intracellular proteins [13]. Of course, most of these observations were identified under an unphysiologically high glucose level for a long period of time. We can say that conflicting reports do exist which makes the impact of adding glucose in dialysis fluid undetermined.

Second, is the biological basis soundly enough to stand for the effective circulating scavenger system of erythrocyte to clean away ROS produced during HD therapy? According to findings by the group of Dolegowska [7, 8] and others [14], the hexose monophosphate (HMP) cycle may not be impaired in erythrocytes of HD patients. The HMP pathway can provide reducing equivalents and actively increase antioxidant glutathione (GSH) synthesis during HD therapy. Therefore, the risk of hemolysis induced by HD can be reduced by adding glucose in dialysis fluid [11]. However, superoxide production during hypoglycemic status is primarily by NADPH oxidase [15]. And it is the GSH level and rate of ROS elimination that determine oxidative damage [14] and the risk of hemolysis during HD [16]. The work of Dolegowska et al. [11] would be grander if they performed a mechanism study.

Third, can we enhance the anti-oxidant response through other HD facilities independent of glucose-add-

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ing in HD dialysate? The quality and integrity of serum albumin is a neglected but important factor to withstand oxidative stress from uremic toxins and the HD process [17, 18]. Advanced water treatment may be useful to reduce HD-induced erythrocyte impairment in HD patients [19]. Studies on the impact of water quality [20] and its relationship with oxidative stress complex syndrome are expected.

Finally, the work by Dolegowska et al. [11] implicated that physiological concentration of glucose added in HD

fluid is beneficial, at least for preservation of erythrocyte integrity and prevention of hemolysis during HD process. Could this concept be extended to peritoneal dialysis (PD) therapy in patients who are exposed to a higher level of glucose intraperitoneally and have to bear treatment for a longer duration? Case series of uremic patients with underlying defects in erythrocyte survival, such as those of glucose-6-phosphate dehydrogenase (G-6-PD) deficiency, may be one kind of model to study this doubt.

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