CAROTID ARTERY INTIMA-MEDIA THICKNESS CORRELATES WITH OXIDATIVE STRESS IN HEMODIALYSIS PATIENTS

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The incidence of coronary artery disease (CAD) and death rates remain several-fold higher in end-stage renal disease (ESRD) patients undergoing hemodialysis (HD) when compared to age-matched non-uremic populations [1]. In patients on maintenance HD, half of deaths are attributed to lethal cardiac events, and thus the rate of cardiac mortality is about 5-20 times higher than normal population. Atherosclerosis is accepted as a common mechanism underlying all cardiovascular diseases (CVDs) and atherosclerotic CVD is a significant cause of morbidity and mortality in ESRD patients. Evidence showed that there is an increased incidence and accelerated worsening of atherosclerosis in patients on chronic HD. However, which factor is involved in the facilitation of atherosclerosis in HD patients remains undetermined [2,3]. Traditional cardiovascular and uremia-related risk factors failed to fully explain the accelerated atherosclerosis in HD patients [2-4]. There is now growing evidence that new risk factors such as oxidative stress and inflammation play a significant role in the genesis of atherosclerosis [5-12].

Arterial vessel wall changes and gradual diffuse thickening of the intima can be studied by two-dimensional B-mode ultrasonography. This technique yields information on atherosclerotic wall changes that cannot be obtained by conventional contrast angiography. Assessment of carotid intima-media thickness (CIMT) using high resolution B-mode ultrasonography is a reliable, reproducible, inexpensive, and non-invasive method for detecting and monitoring the progression of atherosclerosis [13].

Increased CIMT is associated with cardiovascular risk factors, prevalent cardiovascular disease, coronary artery calcification on computed tomography, presence and extent of angiographically determined coronary atherosclerosis, and plaque burden on intracoronary ultrasound. Available evidence obtained in several large numbers of prospective cohort studies substantiates that CIMT contains information beyond the classic cardiovascular risk factors and correlates with the presence of coronary atherosclerosis, predicts vascular disease morbidity and mortality risk, and represents an independent risk factor for coronary heart disease events, stroke, and transient cerebral ischemia, thus providing a useful surrogate marker for atherosclerotic disease [14-18]. An increase of 1 standard deviation in CIMT measurement was associated with a 1.36 relative risk for the combined end point of myocardial infarction or stroke. CIMT also can be used as a marker of efficacy of therapies intended to achieve regression of atherosclerosis [19]. It was demonstrated that CIMT is nearly as predictive as all nine risk factors combined (age, sex, previous myocardial infarction and stroke, diabetes mellitus, smoking, systolic blood pressure, diastolic blood pressure, and total and HDL cholesterol levels). This means that CIMT value alone provides a similar risk estimate which is found from the combined total of nine other risk factors [17]. CIMT was shown an independent predictor of 30- and 60-month mortality in HD patients. These findings convincingly suggested that assessment of CIMT is useful in predicting for future mortality in uremic persons [1].

Oxidative stress, defined as an imbalance between oxidants and antioxidants in favor of the former, plays a significant role in the pathogenesis of atherosclerotic vascular disease [14]. It has been accepted that reactive oxygen species (ROS) are involved in the initiation and
progression of atherosclerosis. More recently, ROS have been also implicated in other pathological processes in the vessel wall, including endothelial dysfunction, in the modification of the extracellular matrix, activation of matrix metalloproteinases, and vascular smooth muscle cell (VSMC) migration, growth, and apoptosis [14]. Oxidative stress have been suggested in uremic patients on maintenance HD and could be involved in accelerated atherosclerosis in these patients [6-12]. It has been well documented that even a single session of HD significantly increases lipid peroxides and decreases antioxidants [6].

The impact of traditional risk factors on CIMT has already been well established. CIMT increases with age, sex, hypertension, diabetes mellitus, hyperlipidemia, and many other factors [20]. It has been reported that uremic patients have increased intima-media thickness of the carotid and femoral arteries with atherosclerotic plaques shown in up to 72% of the HD patients and damage of these large arteries is a contributing factor to mortality in ESRD patients [20]. However, the association between CIMT and oxidative stress markers and antioxidants in HD patients requires further investigation.

In our study, we explored correlation between CIMT and oxidative stress markers and antioxidants in ESRD patients. We determined CIMT as an indicator of atherosclerosis; serum thiobarbituric acid reactive substances (TBARS) as an indicator of lipid peroxidation; plasma protein carbonyl content (PCO) as a marker of oxidative protein damage; and serum nitrite/nitrate levels as indicators of reactive nitrogen species (RNS) production. We measured erythrocyte glutathione level (GSH), superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPx) activities; and plasma sulfhydryl (P-SH) and serum vitamin E concentrations as antioxidant markers. We found a significant increase in CIMT and oxidative stress in uremic and HD patients compared to healthy controls. The HD group had the highest CIMT values indicating a higher risk for atherosclerotic diseases. We demonstrated a positive correlation between CIMT and two oxidative stress markers; serum TBARS and nitrite/nitrate levels and a negative correlation between CIMT and three antioxidants; erythrocyte SOD, CAT and P-SH levels when adjusted by certain other factors affecting CIMT [6-8]. We conclude that increased oxidative stress is associated with enhanced atherosclerotic process indicated by higher CIMT values and suggest the use of TBARS and nitrite/nitrate levels as positive determinants, and erythrocyte SOD, CAT and P-SH levels as negative determinants of atherosclerosis as assessed by CIMT in ESRD patients.

References