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Review article

Antioxidants Status in Haemodialysis Patients

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ABSTRACT

People with advanced chronic renal failure (CRF) who have progressed to end stage renal disease (ESRD) usually require dialysis. The aim of treatment by dialysis is to replace all the lost functions of the natural kidneys, as far as possible using artificial means. The process of separating solutes using semi permeable membrane in vitro and termed the word Dialysis. It is more efficient in terms of rapidly removing wastes. The patients blood is pumped through an artificial kidney machine. Importantly, major antioxidant trials have observed a neutral effect of vitamin E, a lipid-soluble reactive species scavenger, on cardiovascular outcomes. In a biologic system, free radical attack takes place in the presence of an unbalanced ratio between free radicals and antioxidants. OS is likely to be involved in the development of complications due to hemodialysis. Though there is evidence for production of oxygen free radicals during hemodialysis, reports on net oxidative imbalance due to a single dialysis session are conflicting. Vitamin E, being associated with lipoproteins, is not cleared during dialysis. So, a decrease in the level is mostly because of consumption in its attempt to reduce the effect of oxygen free radicals generated during hemodialysis.

1. Introduction

At the end of 2003, the dialysis population worldwide consisted of 1.3 million patients and the number is increasing five times faster than the world population [1]. The growth is driven by an aging population,increased incidence of diseases involving renal failure, particularly diabetes mellitus and hypertension, improved technology and better access to treatment. In Europe, dialysis alone takes up about 2% of health care budgets, with only small proportion of the population needing treatment [2]. At the end of 2003, over 300 800 people in the world were living with kidney transplants [3]. Around 10% of population has chronic kidney disease (CKD) with diabetic and hypertensive nephropathy being the leading underlying aetiologies [3]. Kidney failure requiring dialysis or transplantation is the most visible outcome of CKD, but also associated cardiovascular disease (CVD) constitutes a serious societal burden. Indeed, patients with CKD are more likely to die of CVD than to develop end stage renal disease (ESRD) [4]. In the 1970s it became evident that haemodialysis (HD) patients have increased mortality due to CVD [5]. Several studies in mainly high-risk populations have ever since demonstrated worse outcome in people with impaired renal function or with kidney damage [6-9]. Despite that, renal dysfunction still remains underappreciated as CVD risk factor. This may be due to the complex and partly unknown mechanisms by which impaired renal function has impact on CVD risk.In the kidney a fluid that resembles plasma is filtered through the glomerular capillaries into the renal tubules (glomerlar filtration). This glomerular filtrate passes down the tubules, its volume is reduced and its composition altered by the processes of tubular reabsorption (removal of water and solutes from the tubular fluid) and tubular secretion (secretion of solutes into the tubular fluid) to form the urine that enters the renal pelvis [10].Homeostatic regulatory mechanisms minimize or prevent changes in the composition of the ECF by changing the amount of water and various specific solutes in the urine [11]. Maintainance of body composition the kidney regulates the volume of fluid in the body, its osmolality, electrolyte content and concentration of and its acidity. It achieves this regulation by varying the amounts of water and ions excreted in the urine. Electrolytes regulated by changes in urinary excretion include Na+, K+, Cl-,Ca2+, Mg2+ and phosphate [12].

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2.Discussion

Dialysis: The aim of treatment by dialysis is to replace all the lost functions of the natural kidneys, as far as possible using artificial means. The process of separating solutes using semi permeable membrane in vitro and termed the word "Dialysis". Dialysis should be instituted when ever early signs of uremia (anorexia, nausea, vomiting and occasionally pericarditis) are present or if fluid overload, electrolyte disorders or acidosis cannot be otherwise controlled. No specific value of creatinine or urea is regarded as critical. People with advanced chronic renal failure (CRF) who have progressed to end stage renal disease (ESRD) usually require dialysis. Hemodialysis requires having a fistula created in the forearm several months before it can be started. The need for dialysis is indicated by various findings in blood analysis, such as a high creatinine level and high levels of blood urea nitrogen, and by a glomerular filtration rate that is, at most, 15 and usually les than 10. Pericarditis (inflammation of the sac that surrounds the heart) is associated with end-stage renal disease (ESRD) and indicates the need for dialysis.

Peritoneal Dialysis is also effective and is of particular value when hemodialysis is difficult due to problems with vascular access, hypotension or active haemorrhage. Peritoneal dialysis is probably less efficacious than hemodialysis in hypercatabolic patients, in patients with recent abdominal disease. Peritoneal dialysis cleans the blood without it being removed. Dialysate is injected into the peritoneal space in the abdomen through a two-way catheter (the Tenckhoff catheter). The membrane that lines the abdomen (the peritoneum) allows waste and fluid to pass from the blood into the dialysate, which is pumped out. Peritoneal dialysate, made up mostly of salts and sugar (glucose), encourages ultrafiltration through the peritoneum.

Haemodialysis : It is more efficient in terms of rapidly removing wastes. The patients blood is pumped through an artificial kidney machine. The blood is separated from a balanced salt solution by a cellophane like membrane and small molecules can diffuse across the membrane. Excess fluid can be removed by applying pressure to the blood and filtering it .

Start of maintenance of haemodialysis: The preparation of patients with ESRD for replacement therapy should begin with providing vascular access will be in advance of its need. The Cimino-Brescia arterio-venous fistula in the furred arms is the access of choice for most patients. The standard dialysis schedule is 4 — 5 hours, three times per week depending on residual function, age, body weight and fluid weight status. The initial 4-5 dialysis treatments should be considerably shorter (2-3 h) to prevent the development of the so called dialysis disequilibrium.

Dialysis and Antioxidants: Importantly, major antioxidant trials have observed a neutral effect of vitamin E, a lipid-soluble reactive species scavenger, on cardiovascular outcomes [13]. In patients with mild to moderate CKD at high cardiovascular risk, one study showed vitamin E at dose 400 IU/day has shown no effect on cardiovascular outcomes [14]. Exceptionally, the Secondary Prevention with Antioxidants of Cardiovascular disease in ESRD (SPACE) trial reported a benefit of 800 IU/day vitamin E on major cardiovascular outcomes [15]. Treatment of HD patients with the thiol-containing antioxidant N-acetylcysteine significantly decreased cardiovascular events compared with the placebo group [16]. However,neither of the studies showed effect of treatment on overall mortality in HD patients. Apparently, there is a need to further elucidate the mechanisms by which reactive species may lead to vascular injury.

Effects of Free Radicals on Biological System: Free radicals do not only exert disadvantageous effects, but are also formed deliberately in the body for useful purposes and have important physiological functions. One of the well defined roles of free radicals is when activated phagocytic cells produce superoxide anion radicals and hydrogen peroxide as one mechanism to kill bacteria and fungi and to inactivate viruses. In a biologic system, free radical attack takes place in the presence of an unbalanced ratio between free radicals and antioxidants.

Antioxidants Status in Haemodialysis: Antioxidants are the substances that protect the tissues from free radical attack by preventing free radical formation, by blocking chain reaction or by repairing the oxidatively damaged bio-molecules. There are a number of antioxidants present in the body and derived from the diet. Based on the location, they can be divided into intracellular and extra cellular antioxidants. Intracellular enzymatic antioxidants are Superoxide Dismutase (SOD), Catalase and Glutathione Main non-enzymatic cellular antioxidant is reduced glutathione (GSH). Glutathione reductase (GR), Antioxidant enzymes such as catalase, superoxide dismutase and glutathione peroxidase maintain a reducing tone within cells. Catalase is a common enzyme found in nearly all living organisms .An enzyme found in the blood and in most living cells that catalyzes the decomposition of hydrogen peroxide into water and oxygen.It is a tetramer of four polypeptide chains, each over 500 amino acids long [17]. It contains four porphyrin heme (iron) groups that allow it to react with the hydrogen peroxide. The optimum pH for catalase is approximately 7 [18], while the optimum temperature varies by species [19]. Glutathione is found in two forms, a monomer that is a single molecule of the protein, and is the active form of glutathuine; and second a dimmer that is two of the single molecules joined together. The monomer is sometimes called reduced glutathione, while the dimmer is also called oxidized glutathione. The monomer is the active form of glutathione. Oxidized glutathione is broken down to the single molecule by an enzyme called glutathione reductase. Glutathione peroxidase (GPx) is a selenium-containing enzyme whose blood level is a good indicator of the selenium status of the animal; occurs in a plasma form, an enzyme with specificity for phospholipids, and an intracellular form. Glutathione reductase (GR) is a flavin enzyme involved in the defense of the erythrocyte against hemolysis. A partial deficiency occurs relatively frequently but is due to a deficiency of riboflavin. In mammalian tissues, there are at least three district superoxide dismutase isoenzymes, including one managanese from (Mn-SOD) present in the mitochondrial matrix and two copper and zinc forms (Cu, Zn-SOD), one of which is in the cytosol and the other in various extracellular fluids. Superoxide dismutases play a key role in catalyzing the dismutation of O_2.- to O_2 and H_2O_2. Catalase or GSH-Px must then remove the hydrogen

peroxide formed. In the presence of transition metals, H_2O_2can be reduced (in the metal-catalyzed Haber-Weiss sreaction) to the extremely reactive ·OH. In many tissues, catalase activity, largely localized to peroxisomes, is very low and frequently not available for decomposition of H_2O_2.

Several extracellular antioxidants such as proteins (Transferrin, lactoferrin, albumin, ceruloplasmin), and urate prevent free radical reaction in the body sequestering transition metal ions by chelation in plasma. Albumin, bilirubin, and urate may also scavenge free radicals directly. Furthermore, plasma has a considerable peroxyl radical scavenging ability, which is mainly determined by its content of ascorbic acid.Some antioxidants are located both intra and extracellularly, such as alpha tocopherol, which is the major lipid soluble antioxidant, present in cellular membrane and plasma lipoproteins. It is an effective chain-breaking antioxidant that protects polyunsaturated lipids from peroxidation by scavenging peroxyl radicals. The effect of free radicals is immediately counteracted by chain breaking antioxidant mainly vitamin E, C and thiols. Reports on plasma vitaminE levels in dialysis patients are highly variable with some reporting low levels [20] and some arguing against them [21-23]. Vitamin C is another important antioxidant especially due to its ability to regenerate vitamin E from the vitamin E radical [24-27]. Dialysis has been shown to decrease plasma vitamin C levels [20, 28].

3.Conclusion: OS is implicated as one of the important contributors to the increased prevalence, morbidity and mortality of cardiovascular diseases in these patients. OS is a potential mediator of cardiovascular, neurological and several other complications of CKD. OS is likely to be involved in the development of complications due to hemodialysis. Though there is evidence for production of oxygen free radicals during hemodialysis, reports on net oxidative imbalance due to a single dialysis session are conflicting. Vitamin E prevents lipid per oxidation by being preferentially oxidized instead of fatty acids and gets consumed in this process. Vitamin E, being associated with lipoproteins, is not cleared during dialysis. So, a decrease in the level is mostly because of consumption in its attempt to reduce the effect of oxygen free radicals generated during hemodialysis.

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