STUDY ON ANTIOXIDANT ACTIVITY IN PLASMA OF DIABETIC PATIENTS WITH AND WITHOUT NEPROPATHY – A Review

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ABSTRACT

Oxidative stress has crucial role in pathogenesis of diabetic nephropathy (DN). Despite satisfactory results from antioxidant therapy in rodent, antioxidant therapy showed conflicting results in combat with DN in diabetic patients .In the present experiment antioxidant activity on plasma membrane with and with out nephropathy.

Keywords: Anti-oxidant Activity, Diabetic Nephropathy, Hypochlorous Acid.

Number of References: 30

INTRODUCTION

Diabetic nephropathy is the common cause of leading to end-stage of renal disease (ESRD). Diabetic nephropathy is a progressive and irreversible renal disease characterized by the accumulation of extra cellular matrix in glomerular mesangium and kidney interstitial tissue that eventually leads to renal failure. In present paper we are go through regarding antioxidant effect in plasma of diabetic patients with and without nephropathy.

Discussion

Several mechanisms are thought to be involved in the pathogenesis of diabetic nephropathy and its complications, all of them originating from hyperglycemia. Some of these pathways are: increasing and activation of intra-renal rennin angiotensin system (RAS), formation of advanced glycation end products (AGEs), polyol pathway activation, aldol reductase activation, activation of protein kinase C (PKC), increase of some cytokines – such as insulin like growth factor-1 (IGF1), transforming growth factor beta (TGF-β)- and the oxidative stress pathway (1-5). There are many evidences that oxidative stress plays a key role in the most pathogenic pathways of diabetic complications. Free radicals such as superoxide can induce cell and tissue injuries throughout lipid peroxidation, activation of nuclear factor of Kappa-Beta, production of peroxynitrite, PKC activation and induction of apoptosis. Furthermore, reactive oxygen species (ROS) and other free radicals can directly induce injury. Oxidative stress activate pathogenic pathways such as RAS, polyol pathway, PKC-B and AGEs (1-8). AgII activate NADPH oxidase that leads to the superoxide ions formation. AGEs can induce ROS production and activate PKC by induction of oxidative stress in mesangial cell. Experimental researches established the role of oxidative stress as a central factor in onset and progression of diabetic nephropathy. Human studies also showed that oxidative stress markers such as 8-oxodG (oxo-2'- deoxyguanosine), 8-iso PGF2 (20) and MDA increased in diabetic patients. Interestingly, oxidative stress has been suggested as a common product of much of mechanisms that are involved in pathogenesis of diabetic nephropathy. In fact, in the tangle web of diabetic nephropathy pathogenesis, oxidative stress activates other pathogenic pathways, other pathways make injury via oxidative stress, and oxidative stress directly leads to injury. Thus, inhibition of oxidative stress may constitute a focal point for multiple therapeutic synergies. At the present DN manages by means of RAS blockers. Drugs such as angiotensin converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs) currently are the main strategy of DN management. However, despite RAS inhibition DN progress to ESRD in a large proportion of diabetic patients in other word in addition to activation of RAS system, other pathways are involved in the

DN pathogenesis and combined therapy must be introduced to block pathways. Based on molecular mechanisms of diabetic nephropathy pathogenesis that mentioned in introduction , and increase of oxidative stress markers in experimental and diabetics patient, there is no doubt that oxidative stress plays a pivotal or central role in the initiation and progression of diabetic complications . Besides epidemiological studies have demonstrated association between inflammatory and oxidative stress markers with cardiovascular and renal outcomes in chronic kidney disease (CKD) and ESRD. Thus combined therapy with antioxidants and anti-inflammatory agent may be leads to satisfactory results.

The most known free radicals involving in the diabetic nephropathy pathogenesis are reactive oxygen species (ROS) such as s superoxide (-O2), hydroxyl (-OH), and peroxyl (-RO2) and non radical species such as hydrogen peroxide (H2 O2) and hypochlorous acid (HClO) and reactive nitrogen species produced from Similar pathways, which include the radicals nitric oxide (-NO) and nitrogen dioxide (-NO2), as well as the nonradical peroxynitrite (ONOO-), nitrous oxide (HNO2), and alkyl peroxynitrates (RONOO). Of these, -O2 , -NO, H2 O2 , and ONOO- have been the most widely investigated in the diabetic kidney . There are a number of enzymatic and no enzymatic sources of ROS in the diabetic kidney, including auto oxidation of glucose, transition metal–catalyzed Fenton reactions, advanced glycation, polyol pathway flux, mitochondrial respiratory chain deficiencies, and xanthine oxidize activity, peroxidase, nitric oxide synthase (NOS) and NADPH oxidase. Human body combat against free radicals by natural defense with antioxidant enzymes and exogenous antioxidants. Reactive oxygen species can be eliminated by a number of enzymatic and no enzymatic antioxidant mechanisms. Super oxide dismutase (SOD) immediately converts •O2 - to H2 O2 , which is then detoxified to water either by catalase in the lysosomes or by glutathione peroxidase (GPX) in the mitochondria, catalase that invert H2 O2 to O2 and H2 O. Another enzyme is glutathione reductase, which regenerates glutathione that is used as a hydrogen donor by GPX during the elimination of H2 O2 . No enzymatic antioxidants include vitamins A, C and E; glutathione; a-lipoic acid; carotenoids; trace elements like copper, zinc and selenium; coenzyme Q10 (CoQ10); and cofactors like folic acid, uric acid, albumin, and vitamins B1, B2, B6 and B12. In diabetic nephropathy, structural injury develops over years before clinical and laboratory abnormalities such as albuminuria, hypertension, or declining glomerular filtration rate appear. Thus, waiting for clinical or laboratory manifestation of DN without initiating treatment may hinder the efforts that prevent progression to ESRD. Since oxidative stress appears to play an important role as an early etiologic factor in diabetic nephropathy and later progression, we suggest antioxidant therapy as one of the most important

treatment strategies for diabetic patients without nephropathy for the prevention and slowing of diabetic nephropathy before reaching to ESRD. Antioxidant supplementation studies have shown conflicting results in endothelial function and renal function outcomes in diabetic patients. Antioxidants per se have demonstrated minimal renoprotection in humans despite positive preclinical research findings. However, the classical antioxidants, such as vitamins E and C, do not appear to be helpful. Some clinical evidences for the effectiveness of antioxidants on the treatment of diabetic nephropathy have not been established and there are several reports that indicated the absence of improvement and even worsening of diabetic nephropathy with antioxidant treatment. According to these studies antioxidant supplementation such as vitamin use, may not be the ideal antioxidant strategy in human diabetic nephropathy. However, some studies that used combined antioxidants therapy or antioxidant with anti-inflammatory agent showed that improvement of albuminuria, HbA1C and MDA in diabetic patients.

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