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Serum 4-Hydroxy-2-nonenal and Induced Nitric Oxide Synthase in Hypertension Patient

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ABSTRACT

Hypertension (HT) And related diseases such as chronic kidney disease(CKD) share in that one of the main reasons for them is to increase the oxidative stress, which in turn increases the severity of the disease and exacerbation of symptoms. Reactive molecules produced from oxidative stress, in addition to causing tissue damage by oxidation of biomolecules like DNA, lipids, proteins and sugars; they are lead to the formation of mediators with potent inflammatory effect. The objective of this study was to investigate some markers of oxidative stress in hypertension (HT) and HT with CKD patients in addition to some biochemical parameters related to these diseases. This study involved 84 male subjects aged between (25-65) year equally divided into three groups, first and second one belong to HT and HT with CKD patients respectively from Al-yarmouk Teaching hospital, while the third one for apparently healthy 28 subjects considered as control group. For each subject in the three groups these markers and parameters were evaluated; 4-hydroxy-2-nonenl(4HNE), induced nitric oxide synthase(iNOS), albumin, urea, creatinine ,total serum protein. The results were compared to control; There was a significantly higher ($p<0.01$) in 4HNE, and iNOS levels in both HT and HT with CKD patients, while serum albumin and Total serum protein shows significantly ($p<0.01$) lower levels in both groups. The elevation levels of oxidative stress markers may be due to oxidative damage of tissues that caused by these inflammatory diseases. Was concluded that there was a positive relation between oxidation results from these diseases and their developments and suggest increase need to intake of antioxidants as precaution in front of these disease.

Keywords: Hypertension, antioxidants, 4-Hydroxy-2-nonenal.

INTRODUCTION

Blood pressure is a measure of the force exercised circulation on the walls of the major arteries. hypertension is a chronic medical case which in the blood pressure in the arteries is elevated. Macrophages had been supposed to be the source of the most reactive oxygen species in the vessel's wall, However, it has become clear that all the cells in the vessel wall produce ROS in different quantities and in response to diverse stimuli. Cardiovascular disease is a pathological condition interrelated with cardiac valves, Oxidative stress promotes vascular smooth muscle cell proliferation and hypertrophy and collagen deposition, which leading to thickening in the vascular media and narrowing of the vascular cavity. It has been shown that mechanical stretch to vessel wall induces ROS release. This suggests the possibility that high blood pressure itself causes raises to ROS independent of renin angiotensin system activity . In addition, increased oxidative stress causes tissue damage by different mechanisms including promoting lipid peroxidation, DNA damage, and protein modification. . Reactive oxygen species (ROS) are highly reactive intermediates of the oxygen metabolism, which

are constantly being generated and destroyed. ROS may originate from both exogenous and endogenous sources. Exogenous sources include environmental agents(like, UV or heat exposure), ionizing radiation, therapeutic agents, and tobacco smoke. Endogenous sources include mitochondria, peroxisome and inflammatory cell activation. When there is an imbalance between the generation of ROS and the antioxidant defense system so that the latter becomes overwhelmed, oxidative stress occurs . Oxidants and free radicals are inevitably produced during most physiological and metabolical processes, and the human body has defensive antioxidant mechanisms, these mechanisms vary according to the cell and tissue type and they may act antagonistically or synergistically. Oxidative stress leads to many pathophysiological conditions in the body. including neurodegenerative diseases like Parkinson's disease and Alzheimer's disease, gene mutations and cancers, chronic fatigue syndrome, heart and blood vessel Disturbance, atherosclerosis, heart, congestive heart attack and inflammatory diseases. In physiological conditions, low level ROS play a role in the protection the organism, while high levels of ROS may cause damage to the structures of the cell, nucleic acids, lipids, proteins or DNA damage .4-hydroxy-2-nonenal (4HNE), a high toxicity product of lipid peroxidation, is an inhibitor of mitochondrial respiration. 4HNE It exerts its influence on respiration by inhibiting á-ketoglutaratedehydrogenase(KGDH) . . a study by Teresa S.et al recorded a significant increase in 4HNE values in hypertension patients and Juliane Cruz Campos et al 2015 observed an increase in 4HNE with hypertension and kidney disease Nitric oxide synthases (NOSs) are a family of enzymes catalyzing the production of nitric oxide (NO) from L-arginine. NO is an important cellular signaling molecule. Albumin represents the most abundant protein in the circulatory system with a significant antioxidant activity ,the antioxidant activity of albumin result from its ability to bind bilirubin, homocysteine and lipids .The results of the present study showed that the levels of albumin was significantly decrease ($p<0.01$) in diagnosed hypertension patients which is agree with (Oda E) in hypertension .

History of the study

In this study found positive correlation between obesity and disease, this finding was agree with (Ahmed A. *et al 2013*)[1] and (Shugar L *et al 2008)*[2] who found a significant increase in BMI in hypertensive patients .Obese patients are more ready to be hypertensive than lean patients, and weight gain is typically associated with increases in arterial pressure. Findings of the present study in hypertension patient is also found by (Kamelija Z. *et al 2015*)[3] ,(Ethan J. et al2013)[4] , and (Teresa Sousa *et al 2012*)[5].

There is significantly elevated ($p<0.01$) in diagnosed hypertension patient and oxidative stress and this agree with (Mariso P. *et al* 2014)[6]. The accumulation of 4-HNE-adducts is very high in the intimal aorta, mainly in older patients with high atherosclerosis grade. These data were expected since oxidized LDL and lipids accumulate in the intima in the early lesions and in the lipid core of advanced atherosclerotic lesions(Negre-Salvayre A et al 2010)[7].

These data confirm that 4-HNE is a main marker of oxidative stress and LDL oxidation which could contribute to the evolution of the lesions via its ability to modify proteins and generate cell dysfunction also found by (Subbotin V.M et al 2012)[8].

The recently found effect of 4-HNE suggests a role for this aldehyde in the development of vasa vasorum and micro capillaries in atherosclerotic plaque also found by(Mulligan-Kehoe M.J. 2014)[9].

It has been demonstrated that increased intracellular generation of ROS plays an important role in chronic inflammatory responses to arterial diseases , so this causes damage to the membrane polyunsaturated fatty acids leading to the generation of 4HNE cause elevation in 4HNE in these patients and this also found by(Antonio Ayala et al 2014)[10].

The results show a significant difference between hypertension patient and control group ($p<0.01$). these results were agreed with (Caroline J. Smith *et al2011*)[11] who found a significant difference in iNOS levels in hypertensive patient. Also (Y Álvarez *et al2009*)[12] found an elevation in NO synthesis might be associated with elevations of vascular resistance and, thus with hypertension.

The increased in iNOS in hypertensive subjects as compared to the control group which may be due to the increased generation of ROS in certain type of white blood cells which contribute in reduction bioavailability of nitric oxide and thus to the endothelial dysfunction and this agree with(Marian Valko et al 2007)[13].

(Rubbo H et al 1995)[14] found that NO can then react with superoxide anion, produce highly reactive peroxynitrite, and cause oxidative damage to cellular components. The results of the present study showed that the levels of albumin was significantly decrease (p<0.01) in diagnosed hypertension and hypertension with kidney patients which is agreed with (Oda E et al 2012)[15] in hypertension and (Vandana M. et al 2005)[16] in hypertension with kidney disease.

(Liu M., Chan C. P et al 2012)[17] found that Plasma albumin levels are known to be decreased in inflammatory conditions, including infection, trauma, and surgery. In this study found increase in level of urea with hypertension and this also found by(Rakhee Y. et al2014)[18] in hypertension and with (Noor ul Amin *et al2014)*[19] in hypertension with kidney disease.

(Harvey R. et al 2011)[20] found In the heart failure and hypertension the blood flow decrease so less blood is delivered to the kidney; consequently, less urea is filtered.
(Hasan E et al 2010)[21] found that a reduction in renal blood flow leads to a decrease of glomular filtration, this is lead to a decrease distal tubular flow rate which lead to increase of urea reabsorption and decreased secretion which may be the reason for elevated serum urea concentration.

(Lisa M. Walker.*et al* 2001)[22] Found that urea level increase with increase oxidative stress (4HNE) in hypertension. There is a relation between creatinine which is antioxidant and hypertension and this also found by (Isra'a H. AL – Hamdani et al 2010)[23].

The elevation of serum creatinine concentration may be attributed to the decrease in creatinine clearance due to the decrease in the GFR and this agree with(Pragna P et al 2015)[24]. There is a negative correlation between oxidative stress(4HNE) and creatinine in hypertension patient and control group was observed in this study which agreed with (Hiroyuki Kobori.*et al2008*)[25] who found a negative correlation between 4HNE and creatinine.

The results showed a significant in TSP levels in patients groups when compared to control group and this agree with(Koenig W.et al1991) and(Marisol Peña S. et al2014)[26]. There is a positive correlation between 4HNE and Protein in hypertension patients group) was observed in this study and this agreed with (Carlos K. et al 2008)[27,28,29].

CONCLUSIONS

Oxidative stress in its markers and parameters is the main chemical manifestation of hypertension and cardiovascular diseases and related diseases in patients of this study. This conclusion was obvious in high significant difference between serum 4HNE, iNOS and albumin in patients of both HT and HT with CKD. urea, creatinine, protein field in achieve this results.

The association between albumine and 4Hydroxy-2-nonenal(4HNE) leads to conclude that low serum levels of albumine is very risky due to high probability of its oxidation which is exacerbate the diseases of underlying study. Also the association between 4HNE and iNOS leads to conclude the deep effect of cells from membrane to the nucleus by oxidative species.

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