Journal of Progressive Research in Chemistry (JPRC)
ISSN: 2454-3136

SCITECH
RESEARCH ORGANISATION

Volume 4, Issue 3
May 09, 2017

Journal of Progressive Research in Chemistry
www.scitecresearch.com

Study the level and the fluctuation of Induced nitric oxide synthase in Iraqi patients with Hypertension

Alaa H. Jawad[1], Ali Hammed [1], Hadeel Adil[1], Amir Hasan[1], Zyad Al-Qaisi[2], Amamer Redwan[3], and Emad Yousif[1]

[1] Department of Chemistry, College of Science, Al-Nahrain University, Baghdad, Iraq
[2]Department of Chemistry, College of Science, University of Al-Mustansiriyah, Baghdad, Iraq
[3]Department of Chemistry, Faculty of Science, BaniWalid University, BaniWalid, Libya

Abstract

The known NOS enzymes are generally alluded to as 'dimeric' in their dynamic shape, disregarding the required calmodulins (CaMs) which, entirely, mean they are tetramers (of two NOS) monomers related with two CaMs). This review included 56 subjects coordinated ages and sex separated into two groups; 28 hypertensive subjects and 28 healthy subjects as control group. The accompanying investigation was done: INOS was fundamentally higher in patients contrasted with controls while there were no noteworthy contrasts found in egg whites amongst patient and control gathering. Also, the expansion in iNOS in light of the fact that iNOS creates a lot of NO as a guard component because of cytokines and is an essential consider the reaction of the body to assault by parasites, bacterial contamination, and tumor development. It has been reasoned that is critical nappy on perfect weight, since heftiness considered principle variables for coronary illness and solidifying of the veins. There is a positive connection between oxidation comes about because of hypertension and their advancements. The point of this review was to examine the connection between of some oxidative anxiety markers and cardiovascular infections.

Keywords: Hypertension, Induced nitric oxide synthase(iNOS), Reactive oxygen species (ROS).

Introduction

It has been demonstrated that mechanical extend to vessel divider incites ROS discharge. This recommends the likelihood that hypertension itself makes raises ROS free of renin angiotensin framework movement [1]. What's more, expanded oxidative anxiety causes tissue harm by various components including advancing lipid peroxidation, DNA harm, and protein change [2]. Receptive oxygen species (ROS) are exceedingly responsive intermediates of the oxygen digestion, which are always being created and pulverized. ROS may start from both exogenous and endogenous sources [3]. Exogenous sources incorporate natural agents(like, UV or warmth presentation), ionizing radiation, remedial operators, and tobacco smoke. Endogenous sources incorporate mitochondria, peroxisome and fiery cell activation[3]. At the point when there is an awkwardness between the era of ROS and the cell reinforcement barrier framework so that the last becomes over powered, oxidative anxiety happens [4]. The known NOS chemicals are typically alluded to as 'dimeric'in their dynamic frame, overlooking the required calmodulins (CaMs) which, entirely, mean they are tetramers (of two NOS) monomers related with two CaMs). They contain moderately firmly bound cofactors (6R). catalyze a response of arginine, NADPH, and oxygen to the free radical NO, citrulline and NADP [5-6]. Three very unmistakable isoforms of NOS have been distinguished, results of various qualities, with various confinement, direction, synergist properties and inhibitor affectability, and with 51–57%homology between the human isoforms. These isoforms will be alluded to by the most well-known terminology: nNOS (otherwise called Type I, NOS-I and NOS-1) being the isoform first found (and prevailing) in neuronal tissue, iNOS (otherwise called Type II, NOS-II and

NOS-2) being the isoform which is inducible in an extensive variety of cells and tissues and eNOS (otherwise called Type III, NOS-III and NOS-3) being the isoform first found in vascular endothelial cells. [7] These isoforms have in the past been additionally separated on the premise of their constitutive (eNOS and nNOS) versus inducible (iNOS) expression, and their calcium-reliance (eNOS and nNOS) or –independence (iNOS) [8].

Materials and methods:

Fifty six sample subjects comprising of 28 patients and 28 healthy were included in the present study, table 1 shows the means and standard deviation of age, body mass index (BMI),duration of disease albumin levels for the control and patients groups.

The present study comprised of56men divide to two groups [namely control group (28), hypertensive group (28) aged between 22–65 years. These patients were hospitalized at educational laboratories in the Al-yarmouk teaching hospital. They were divided into groups of healthy as control group and hypertensive patients group. Blood sample were collected and centrifuged at [4000 xg] for 5 min after clotting .The resultant serum were separated and stored at [-20] °C until used. Estimation of serum albumin was done using kit provided by BioSystems Company. Serum Induced nitric oxide synthase iNOS is typically quantified from serum samples the as sassay employs the quantitative sandwich enzyme immunoassay technique.

Statistics:

The Statistical Analysis System- SAS (2012) was used to determine of different factors in studied parameters, P-value used to significant compare between means in this study.

Results and Discussion:

Table 1: Characteristics of the Hypertension (HT) and control group (mean ± SD) :

Characteristic	Hypertension group n=28	Control group n=28	P-Value
Age(year)	55.46 ± 8.91	23.82 ± 5.02	<0.01
Body Mass index (Kg/ m2)	33.34 ± 4.68	25.18 ± 2.89	<0.01
Systolic blood pressure(mmHg)	14.60 ± 1.22	11.96 ± 0.66	<0.01
Diastolic blood pressure (mmHg)	9.23 ± 0.85	8.63 ± 0.56	<0.01
iNOS(ng/L)	10.11 ± 7.08	6.42 ± 4.93	<0.01
Albumin(g /L)	4.38 ± 0.27	4.73 ±0.25	<0.01

The study reveal a significant increase of albumin in patients with hypertension as shown in table (1) Albumin is the most prevalent protein in blood and has many important functions including roles in colloid-osmotic homeostasis, binding and transport of smaller molecules and as a storage form of metabolic energy. Aside these well-known functions, albumin was reported to directly influence the immune-system after post-translational modifications like polymerisation or glycation, introducing additional biological implications. As the albumin-induced pathways of enzymatic phosphorylations in RAW 267.4 cells appeared to include NF-kB, JAK/ STAT and ERK (a profile that mirrors classical LPS-activated pathways) [9]. However, the albumin fractions used in this study included only very low levels of endotoxin, as determined by a limulus test. The estimated LPS contamination in both albumin types remained clearly below the threshold concentrations required for activation of RAW 267.4 cells by purified LPS from *Escherichia coli*[10].

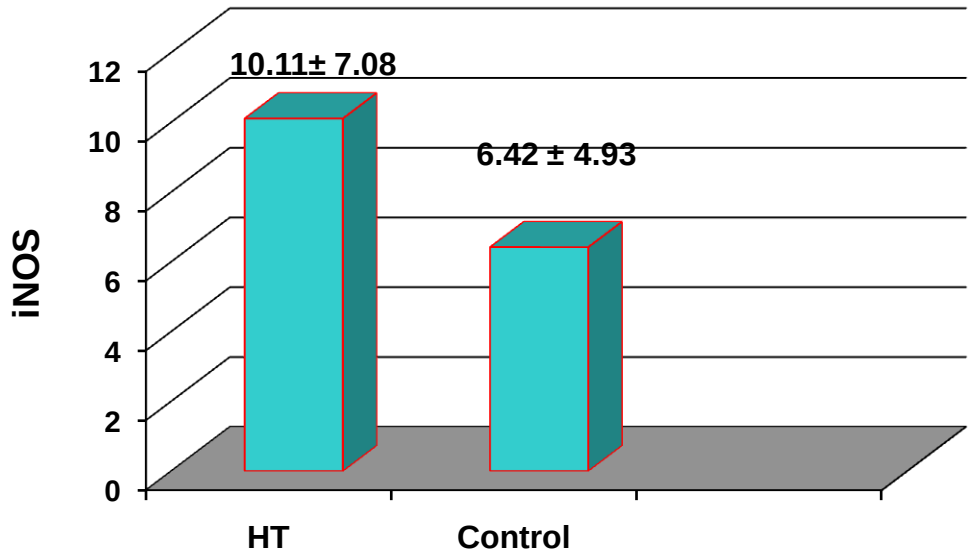

Fig.(1) Mean concentration(IU/ml) of INOSin the studied groups.

Our results showed a significant difference between hypertension patient and control groups ($p<0.01$). This result was agreed with [11]who found a significant difference in iNOS levels in hypertensive patients. Blood pressure is frequently elevated, blood volume is usually normal or increased and plasma renin and aldosterone are usually low in nephrotic syndrome (NS). These observations challenge the conventional view attributing sodium retention in NS to a hypoalbuminemia-induced intravascular volume contraction. Given the pivotal role of nitric oxide (NO) in regulation of renal sodium (Na) handling, vascular resistance and sympathetic activity, we considered that Na retention and hypertension in NS may be associated with impaired NO system. Urinary excretion of Na and NO metabolites (NOx), as well as immunodetectable endothelial (eNOS), inducible (iNOS) and neuronal (nNOS) NO synthases were determined in rats with puromycinaminonucleoside (PAN)-induced NS, rats with protein overload proteinuria, Nagase rats (NAR) with inherited analbuminemia, iNOS inhibitor (aminoguanidine)-treated rats, prenephrotic PAN-treated and placebo-treated control rats. The NS group showed marked proteinuria, hypoalbuminemia, decreased fractional excretion of Na (FENa), reduced urinary NOx excretion, and severe reduction of iNOS and nNOS protein abundance in the kidney. Similar results were found in rats with protein overload proteinuria in which proteinuria was present without hypoalbuminemia. In contrast, despite extreme hypoalbuminemia, NAR showed normal FENa, increased urinary NOx excretion and upregulations of iNOS and nNOS protein abundance in the kidney. Administration of aminoguanidine for 3 weeks lowered FENa in normal rats to levels approximating those found in the NS group. Animals studied 2 days after PAN administration (wherein proteinuria was absent) showed no abnormality. Thus, chronic PAN-induced NS results in downregulation of kidney iNOS and nNOS, which can contribute to the reduction of FENa by augmenting renal tubular Na reabsorption, and preglomerular vasoconstriction. Findings in the NAR, which had profound hypoalbuminemia without proteinuria, and in rats with protein overload proteinuria, which had proteinuria without hypoalbuminemia, point to proteinuria as the primary mediator of kidney iNOS and nNOS deficiency and impaired Na excretion in PAN-induced NS.[12]

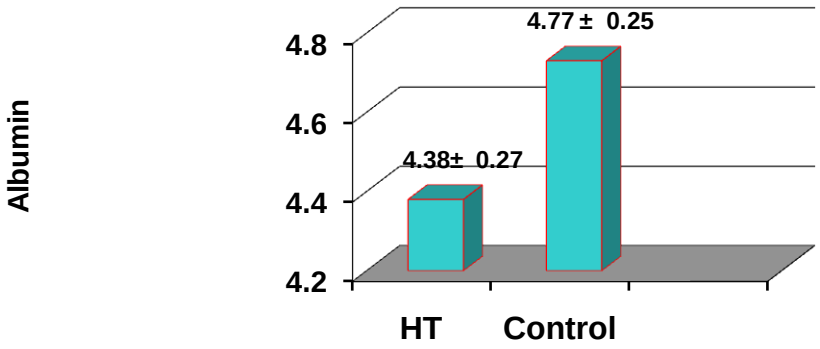

Fig.(2) Mean concentration (g/L) of Albumine in the studied groups.

Increased urinary albumin excretion is a known risk factor for cardiovascular events and clinical nephropathy in patients with diabetes. Whether the presence of microalbuminuria predicts long-term development of chronic renal failure (CRF) in patients without diabetes but with primary hypertension remains to be documented. Renal dysfunction is a common finding in patients with hypertension and is associated with an increased risk for cardiovascular events (CVEs)as well as with progression to ESRD. It has been pointed out that cardiovascular risk progressively increases as renal function declines and that it is already significantly elevated in the earliest stages of renal damage. Identifying the precursors of overt kidney disease is therefore of utmost importance for limiting the burden of cardiovascular and renal morbidity. Increased albumin excretion rate (AER) has been related to unfavorable cardiovascular outcomes in the general populationand in patients with diabetes and in high-risk patients[13,14]. Furthermore, the Losartan Intervention For Endpoint reduction in hypertension (LIFE) study confirmed the predictive power of microalbuminuria and its changes over time[15] in a large cohort of carefully monitored patients during a 5-year follow-up; however, the renal predictive value of albuminuria is thus far limited to high-risk patients with or without diabetes [16] and to the general population[16]. Some studies have suggested that the presence of microalbuminuria increases the relative risk of an adverse cardiovascular event similarly to the presence of hypercholesterolemia[17]. The prence of micoalbuminuria may need to be viewed in the same light as other risk factors such as blood pressure, cholesterol and blood glucose. [18] To better understand the natural history of hypertensive renal disease, especially in the early stage when intervention may prevent or delay sequelae[19].Albumin contains a free sulfhydryl group, this forms a disulfide with several compounds like cysteine, homocysteine, or glutathione, Albumin is able to scavenge hydroxyl radicals [20,21], the decrease in albumin in patient is agreed with results of Go *et al.*In Hypertension [15]who suggested that result is may be due to its function as antioxidant activity so the non-oxidized albumin is decrease in addition to negative acute phase protein, so inflammation is considered the principle cause of a decrease in the serum albumin.

There is also negative correlation between iNOS and albumin in patient and control group

Conclusion:

The effect of oxidative stress, leads to high blood pressure and thus chronic kidney disease.

All Data obtained, ethically approved experiments by Al-Nahrain University.

Acknowledgements

The authors would like to thank Al-Nahrain University for the financial supports and research facilities.

References:

[1] Yasunobu, H., Hiroshi, S.(2013). Hypertension and Oxidative Stress,*The Journal of CengageLearning*,6, 302.
[2] Hassan, F.,Alshanon, A.,Jawad, A.(2015).Antitumor Effect of 1-[(4-Chloro-Benzylidene)-Amino]-5-Phenyl-1HPyrrole-2-Thiol in Different Type of Cell Lines,*Australian Journal of Basic and Applied Sciences*, 9(35), 44.
[3] Shiv, K.(2011). Free Radicals and Antioxidants Human and Food System,*Advances in Applied Science Research*, 2, 129.

[4] Ahmad, A.,Singhal, U.,Mohd, M., Islam, N.,Rivisi, I.(2013).The Role of the Endogenous Antioxidant Enzymes and Malondialdehyde in Essential Hypertension, *Journal of Clinical and Diagnostic Research*, 7,987.
[5] Jawad, A., Ibrahim, A., Hammed, A., Al-Qaisi, Z.,Redwan, A.,Yousif, E.(2017).4-Hydroxy-2-nonenal Statues in Hypertension Patients.*Preprints*, 2017030037 (doi: 10.20944/preprints201703.0037.v1).
[6] Marletta, M. A.(1994).Nitric oxide synthase: aspects concerning structure andcatalysis,*Cell* (Cambridge, Mass.)**,**78, 927.
[7] Nathan, C.,Xie, Q. W.(1994). Nitric oxide synthases : roles, tolls, and controls,*Cell (Cambridge, Mass.)*, 78, 915.
[8] Ibrahim, A.,Fadhil, D.,Jawad, A.,Thabit, J.,Alqadery, R.,Yousif, E., Al-Amiery, A. (2016).Ginkgo Biloba for Reducing Hyperlipideamia: Case Study. *Preprints*, 2016110134 (doi: 10.20944/preprints201611.0134.v1).
[9] Hassan, F.,Hameed, A.,Alshanon, A., Bashar, M.,Hasniza, Z.,Nany, H.,Yousef, E.(2015). Antitumor Activity for Gold(III) Complex by High Content Screening Technique (HCS) and Cell Viability Assay,*Asian Journal of Biochemistry*, 10(6), 252.
[10] Yoshioka, T.,yamamoto k.,kobashi, H.,Tomita, m.,Tsuji, T.(1994).Receptor-mediated endocytosis of chemicallymodified albumins by sinusoidal endothelial cells and Kupffer cellsin rat and human liver,*Liver*, 14,129.
[11] Hassan, F.,Hairunisa, N., Mohammed, S.,Yousif, E.(2017). A Study on Antitumor Effect of 1,3,4-Thiadiazole Derivatives in Prostate and Breast Cancer Cell Lines (*In Vitro),Preprints*, 2017030053 (doi: 10.20944/preprints201703.0053.v1).
[12] Jawad, A., Ibrahim, A.,Alsayed, R.,Hallab, Z., Al-Qaisi, Z., Al-Amery, A.,Yousif, E.(2016). Study the Impact of Glucose-6-phosphatase Activity in Type 2 Diabetic Patients and Non Diabetic Counterparts, Preprints, 2016100137 (doi: 10.20944/preprints201610.0137.v1).
[13] Jawad, A.,Al-Qaisi, Z., Ibrahim, A.,Hallab, Z.,Graisa, A.,Al-Amiery, A.,Yousif, E.(2016). Effect of Anti Diabetic Drugs on Lipid Profile in Patients with Type 2 Diabetes Mellitus,*Preprints*.**2016**, 2016110071 (doi: 10.20944/preprints201611.0071.v1).
[14] Coresh, J.,Astor, B.,Sarnak, M. J.(2004).Evidence for increased cardiovascular disease risk in patients with chronic kidney disease,*CurrOpinNephrolHypertens*, 13: 73.
[15] Go, A. S.,Chertow, G.M, Fan, D., McCulloch,CE.,Hsu, CY.(2004).Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization.*N. Engl. J. Med*, 351: 1296.
[16] Tonelli, M.,Wiebe, N.,Culleton, B., House, A.,Rabbat, C.,Fok, M.,McAlister, F.,Garg, AX.(2006). Chronic kidney disease and mortality risk: A systematic review,*J Am SocNephrol*, 17: 2034–2047.
[17] Mohammed, S., Ibrahim, A.,Hasan, A.,Yousif, E.(2016). Research Investigation on the Effect of Phytosterols on Lipid Profile,*Journal of Pharmaceutical and Medicinal*, 2(2), 60.
[18] Romundstad, S., Holmen, J.,Kvenild, K.,Hallan, H.,Ellekjaer, H.(2003).Microalbuminuria and all-cause mortality in 2,089 apparently healthy individuals: A 4.4-year follow-up study, The Nord-Trøndelag Health Study (HUNT), *Norway. Am J Kidney Dis*, 42, 466.
[19] Hassan, F., Abdul Hameed, A.,Alshanon, A., Abdullah, B.,ZamanHuri, H.,Hairunisa, N.,Yousif, E.(2015).Antitumor Activity for Gold (III) Complex by High Content Screening Technique (HCS) and Cell Viability Assay,*Asian Journal of Biochemistry*, 10 (6), 252.
[20] Marjolaine, R., Philippe, R.,Nihar, R.,Evelyne, T., Emmanuel , B.(2008).The antioxidant properties of serum albumin;Review,*FEBS Letters*, 582, 1783.
[21] Giancarlo, A., Luca G,Marica O.,Giangiacomo, B., Luca, R.(2006).Mass spectrometric characterization of covalent modification of human serum albumin by 4-hydroxy-trans-2-nonenal,*J. Mass Spectrom*, 41, 1149.