

Original Research Article

Serum Bilirubin as a Marker of Oxidative Stress in Patients with Hypertension

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ABSTRACT

In the present study relation between serum bilirubin and hypertension were evaluated. Oxidative stress is found to be one of the causes of hypertension. It can be assessed by serum MDA in 30 patients with hypertension and 30 normotensive healthy adults both showing family history of CAD along with serum bilirubin. Serum Bilirubin is found to be an antioxidant and participates in defence mechanism against oxidative stress.

Key words: Bilirubin, Oxidative stress, Antioxidant, Hypertension, MDA.

INTRODUCTION

Heme oxygenase (HO) is the rate limiting enzyme for the breakdown of heme to generate carbon monoxide, iron, and biliverdin. Biliverdin is rapidly converted to bilirubin by biliverdin reductase. [1] Experimental evidence suggests that the induction of HO-1, the inducible isoform of HO, is an important endogenous mechanism for cytoprotection and the downstream products of heme degradation may mediate the beneficial effects, such as antioxidant, anti-inflammatory properties, etc. Induction of HO-1 has also been demonstrated to lower blood pressure in several animal models. [2,3] The mechanism by which HO-1 induction lowers blood pressure is decreasing vascular resistance by the HO-driven carbon monoxide. Reactive oxygen species (ROS) have been known to be an

important factor in the pathogenesis of hypertension. [4] The increased ROS production in the renal medulla is a key component of angiotensin II-dependent hypertension. [5,6]

Induction of hemeoxygenase has been demonstrated to lower blood pressure in various experimental studies. Bilirubin is a potent antioxidant. [7] We evaluated the levels of serum bilirubin level on the patients of both hypertensive and normotensive subjects.

MATERIALS AND METHODS

The study was carried in the department of Biochemistry and central investigation laboratory in MGM Hospital, Aurangabad. Institutional ethical committee clearance was obtained for the study. Written and informed consent were taken

from the patients for the study. In the present study, we investigated the relationship between serum bilirubin level and the incidence of hypertension in normotensive subjects who had undergone repeated routine health check-ups and hypertensive subjects with family history of CAD in both cases.

Sample Size

Cases- 30 hypertensive patients from MGM College and Hospital, Aurangabad

Controls- 30 normotensive controls

Methods

The blood samples (3-5ml fresh blood) were drawn and collected in a clean, disposable plastic tube from anterior cubital vein under aseptic condition for estimation of serum bilirubin and serum MDA (Malondialdehyde) levels.

Serum bilirubin were assessed by Jendrassik gruff method using fully auto analyser Dimension RxL

Estimation of MDA was done by NouroozZadeh's method [8]

Blood pressure was measured by standard techniques using sphygmomanometer, using 140/90 mmHg for diagnosis of hypertension.

Statistical analysis:

The data were evaluated by SPSS statistical package version 16.0. The results obtained were statistically analyzed by using student t-test. Value of bilirubin was given in mg/dl. MDA levels were given in nmol/ml. Systolic and diastolic blood pressure was measured in mm of Hg. All Values were expressed as mean ± standard. The results were considered significant when $p < 0.05$.

RESULT

The mean age of the patients for this study was (43 ± 5.3) and controls was (41.8 ± 4.8) . The results in this study showed significant decrease in serum bilirubin levels in hypertensive patients as compared to controlled normotensive group ($p = 0.001$)

as shown in figure 1. There was a significant increase in the levels of serum MDA levels in hypertensive subjects as compared to normotensive ($P = 0.0001$) as shown in figure 2.

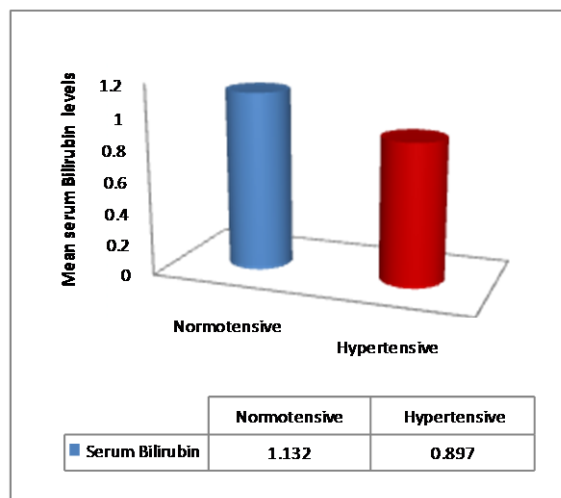


Figure 1: Mean of serum bilirubin levels in Normotensive and Hypertensive subjects.

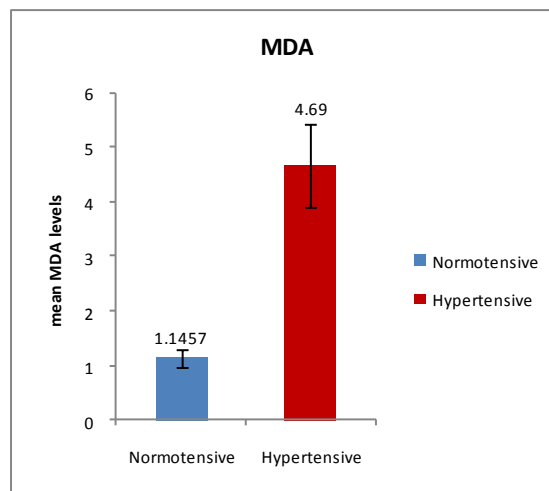


Figure 2: Mean of serum MDA levels in Normotensive and Hypertensive subjects.

Figure 3 shows the mean values of systolic and diastolic blood pressure in cases and controls. The mean of systolic and diastolic blood pressure in cases was 152.44 and 110.64 respectively, which were significantly higher as compared with the control groups. ($P < 0.0001$).

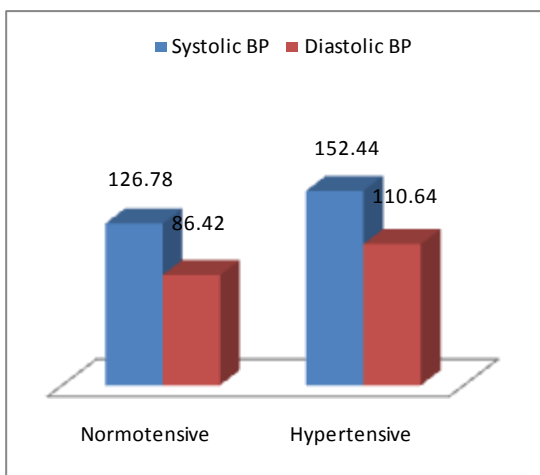


Figure 3: Mean of systolic and diastolic blood pressure in Normotensive and Hypertensive subjects.

DISCUSSION

A serum bilirubin level of 10 $\mu\text{M/L}$ was suggested as a cutpoint for the discrimination of cardiovascular risk but other cut-points have been proposed in other studies. In this study, the serum bilirubin level assigned to discriminate the risk of hypertension was 1.1 mg/dL. Endothelial dysfunction is the initial step in the pathogenesis of atherosclerosis, leading to cardiovascular complications. Oxidative stress also plays an important role in the pathogenesis and development of cardiovascular diseases. Normal endothelial function is maintained by a balance of oxidative stress and nitric oxide (NO). One mechanism of endothelial dysfunction is an increase in oxidative stress, which inactivates NO. [9]

Although bilirubin at a high concentration acts as a cytotoxic metabolite, bilirubin at a low concentration is a potent endogenous antioxidant. [9] Serum bilirubin should be one of the key mediators of the antioxidant system in humans.

Clinical studies have shown that serum concentrations of bilirubin inversely correlate with risk of cardiovascular diseases

and peripheral arterial disease. [10][11] The major mechanism by which HO-1 induction reduces ROS is through the generation of bilirubin, a potent antioxidant. [12] Increased levels of bilirubin can prevent the pressor actions of angiotensin II through the scavenging of superoxide anions in the vasculature [13] and also inhibit NADPH oxidase [14] and protein kinase C activity, both of which mediate angiotensin II-induced vascular injury. [15]

In the cardiovascular system ROS play a physiological role in controlling endothelial function, vascular tone, and cardiac function, and a pathophysiological role in inflammation, hypertrophy, proliferation, apoptosis, migration, fibrosis, angiogenesis, and rarefaction, all of which are important processes contributing to endothelial dysfunction and cardiovascular remodelling in hypertension. A major source for cardiovascular ROS is a family of nonphagocytic nicotinamide adenine dinucleotide phosphate (NADPH) oxidases (Nox1, Nox2, Nox4, and Nox5). Other sources include mitochondrial enzymes, xanthine oxidase, and uncoupled NO synthase (NOS). Biomarkers of excess ROS are increased in patients with hypertension and oxidative damage is important in the molecular mechanisms associated with cardiovascular and renal injury in hypertension. [15]

CONCLUSION

The subjects with higher bilirubin level showed a lower incidence of hypertension than did the subjects with lower bilirubin level. In humans, the effects of mildly increased serum bilirubin levels have been reported to be a decreased risk for the development of coronary artery disease and atherosclerosis.

A mild increase within physiological range of serum bilirubin concentration was

negatively correlated with the increased incidence of hypertension.

REFERENCES

1. Chin H J, Song Y R, Kim H S, Park M, Yoon H J, Na K Y. The Bilirubin Level is Negatively Correlated with the Incidence of Hypertension in Normotensive Korean Population. *J Korean Med Sci* 2009; 24 (Suppl 1): S50-6,ISSN 1011-8934, DOI: 10.3346/jkms.2009.24.S1.S50
2. Kirkby K A, Adin C A. Products of heme oxygenase and their potential therapeutic applications. *Am J Physiol Renal Physiol* 2006; 290: F563-71.
3. Goodman AI, Quan S, Yang L, Synghal A, Abraham NG. Functional expression of human heme oxygenase-1 gene in renal structure of spontaneously hypertensive rats. *Exp Biol Med* 2003; 228: 454-8.
4. Sabaawy HE, Zhang F, Nguyen X, ElHosseiny A, Nasjletti A, Schwartzman M, Dennery P, Kappas A, Abraham NG. Human heme oxygenase-1 gene transfer lowers blood pressure and promotes growth in spontaneously hypertensive rats. *Hypertension* 2001; 38: 210-5.
5. Ndisang JF, Zhao W, Wang R. Selective regulation of blood pressure by heme oxygenase-1 in hypertension. *Hypertension* 2002; 40: 315-21.
6. Botros FT, Schwartzman ML, Stier CT Jr, Goodman AI, Abraham NG. Increase in heme oxygenase-1 levels ameliorates renovascular hypertension. *Kidney Int* 2005; 68: 2745- 55.
7. Ward N C, Hodgson J M, Puddey I B, Mori T A, Beilin L J, Croft K D. Oxidative Stress in human hypertension: association with antihypertensive treatment, gender, nutrition and lifestyle. *Free Radical Biology and Medicine* 2004; 36 (2):226–232
8. Nourooz-zadeh J, Tajaddini Sarmadi J, Carthy MCS, et al. Elevated levels of authentic plasma hydroperoxides in NIDDM. *Diabetes* 1995; 44(9): 1054-1058.
9. Montezano A C, Touyz R M. Molecular Mechanisms of Hypertension-Reactive Oxygen Species and Antioxidants: A Basic Science Update for the Clinician. *Can J Cardiol.* 2012 May; 28(3): 288-95
10. Kitiyakara C, Wilcox CS. Antioxidants for hypertension. *Curr Opin Nephrol Hypertens.* 1998;7:531–538.
11. Reckelhoff JF, Romero JC. Role of oxidative stress in angiotensin-induced hypertension. *Am J Physiol RegulIntegr Comp Physiol.* 2003; 284:R893–R912.
12. Stocker R, Yamamoto Y, McDonagh AF, Glazer AN, Ames BN. Bilirubin is an antioxidant of possible physiological importance. *Science.* 1989;235:1043–1046.
13. Pflueger A, Croatt AJ, Peterson TE, Smith LA, d'Uscio LV, Katusic ZS, Nath KA. The hyperbilirubinemic Gunn rats is resistant to the pressor effects of angiotensin II. *Am J Physiol Renal Physiol.*2005; 288: F552–F558.
14. Lanone S, Bloc S, Foresti R, Almolki A, Taille C, Callebort J, Conti M, Goven D, Aubier M, Dureuil B, El-Benna J, Motterlini R, Boczkowski J. Bilirubin decreases nos2 expression via inhibition of NAD (P)H oxidase: implications for

protection against endotoxic shock in rats. FASEB J. 2005;19:1890–1892.
15. Novotny L, Vitek L. Inverse relationship between serum bilirubin

and atherosclerosis in Men: A meta-analysis of published studies. Exp Biol Med (Maywood) 2003; 228: 568–571.

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