Study of Paraoxonase 1 And Fibrinogen As An Inflammatory Marker in Essential Hypertension

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ABSTRACT
Introduction- Worldwide, hypertension (HTN) is estimated to cause 7.5 million deaths, about 12.8% of total of all annual deaths. It is one of the most important risk factors for cardiovascular diseases and other clinical outcomes. In India prevalence of HTN varies from 17% to 20%, in all the states with marginal rural-urban difference. Essential hypertension accounts for more than 90% of cases of hypertension.

Aim & objective: The present study was carried out with the objective to find out correlation between inflammatory marker like fibrinogen and paraoxonase 1 in hypertension.

Methods: The study was carried out on 90 hypertensive patients and 90 normotensive controls. Cases with diabetes mellitus, thyroid disease, chronic kidney disease, smoking, autoimmune diseases and any other chronic diseases are excluded. The study was approved by Institutional ethical committee. Informed consent was obtained from all cases. Serum PON 1 was estimated by ELISA method using commercial kit procured from Aviscera Bioscience and plasma fibrinogen was estimated by tyrosine method (LAMPERT).

Result: Plasma fibrinogen was increased and antioxidant enzyme (PON 1) was decreased in primary hypertension in comparison to normal controls (P< 0.001). There was a negative correlation between plasma fibrinogen and serum PONI (r = - 0.971).

Conclusion: Fibrinogen, involved in the process of inflammation is increased in primary hypertension. PON 1 is an antioxidant enzyme present on the surface of HDL also significantly decreased which is responsible for prevention of HTN and it’s complications.

Keywords: Primary hypertension, serum paraoxonase 1, plasma fibrinogen.

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I. Introduction
Worldwide, hypertension (HTN) is estimated to cause 7.5 million deaths, about 12.8% of total of all annual deaths (1). In India prevalence of HTN varies from 17% to 20%, in all the states with marginal rural-urban difference. Essential hypertension accounts for more than 90% of cases of hypertension (2). It is one of the most important risk factors for cardiovascular diseases and other clinical outcomes. In addition, hypertension is associated to target-organ damage such as left ventricular hypertrophy, microalbuminuria and subclinical vascular impairment as endothelial dysfunction which is an early marker of atherosclerosis. The role of inflammation in HTN has been increasingly recognized as evidence of inflammatory markers and mediators (3,4). Many factors including reduced blood flow due to elevated viscosity of plasma have been implicated in the pathogenesis of hypertension (5). Fibrinogen, a plasma protein, contributes more than other proteins to plasma viscosity in healthy subjects (6). This contribution is greatly increased in disease states (7), particularly in hypertension (8).

Serum Paraoxonase (PON 1) is an Arylesterase synthesized in the liver and is an HDL associated enzyme which is responsible for the antioxidant properties of the high density lipoproteins (HDL) (9,10). It protects low density lipoproteins (LDL) from oxidative stress by destroying biologically active phospholipids (11). Human serum PON1 activity was shown to be inversely related to the risk of cardiovascular diseases (12). Various studies showing low PON1 activities in atherosclerotics, hypercholserolemics and hypertensive patients (12).
II. Materials And Methods

The study was carried out on 90 hypertensive patients and 90 normotensive controls who attended the outpatient department of medicine of M.K.C.G. Medical College and Hospital Berhampur, INDIA. Cases with diabetes mellitus, thyroid disease, chronic kidney disease, smoking, autoimmune diseases and any other chronic diseases were excluded. The study was approved by Institutional ethical committee. Informed consents were obtained from all cases. Serum PON 1 was estimated using commercially available ELISA kit marketed by Aviscera Bioscience Catalog number: SK00141-01. Plasma fibrinogen was measured by tyrosine method (LEMPERT).

III. Result

Table -1: Demographic And Clinical Data Of Cases And Controls

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Cases (N=90) Mean±SD</th>
<th>Controls (N=90) Mean±SD</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGE (years)</td>
<td>51.74±10.13</td>
<td>52.60±9.94</td>
<td>0.563</td>
</tr>
<tr>
<td>Systolic BP in mm of Hg</td>
<td>147.98±2.445</td>
<td>115.44±3.672</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Diastolic BP in mm of Hg</td>
<td>96.78±3.765</td>
<td>78.62±3.996</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

The demographic and clinical data of cases and controls were shown in table 1. The mean age of cases were 51.74±10.13. Mean systolic and diastolic BP were 147.98±2.445 and 96.78±3.765 in cases. It was statistically significant when compared to controls (P<0.01).

Table – 2: Biochemical Parameters In Cases And Controls

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Cases (N=90) Mean±SD</th>
<th>Control (N=90) Mean±SD</th>
<th>t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>PON1 (ng/ml)</td>
<td>25.62±2.0628</td>
<td>41.06±2.47</td>
<td>45.52</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fibrinogen (mg/dl)</td>
<td>345.91±38.63</td>
<td>164.05±14.62</td>
<td>41.76</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

The mean serum values for PON1 in cases (25.62±2.06) and controls (41.06±2.47) were compared which shows statistically significant value (P <0.001). The Mean ± SD for plasma fibrinogen in mg/dl were (345.91±38.63) for hypertensive patients and (164.05±14.62) for healthy controls respectively. A statistical significant difference was found with a P value of <0.001.

Table- 3: Correlation Of Serum PON 1 And Plasma Fibrinogen

<table>
<thead>
<tr>
<th>Parameters</th>
<th>SERUM PON1</th>
</tr>
</thead>
<tbody>
<tr>
<td>FIBRINOGEN (mg/dl)</td>
<td>-0.971</td>
</tr>
</tbody>
</table>

This table shows that serum PON 1 is negatively correlated with plasma fibrinogen (r = -0.971).
This is the bar diagram showing mean PON 1 level in cases and controls. Mean PON 1 level in cases is 25.62 ng/ml and in controls is 41.06 ng/ml.

Graph 2: Plasma Fibrinogen Level In Cases And Controls

This is the bar diagram showing mean plasma fibrinogen level in cases and controls. Mean fibrinogen level in cases is 345.9153 mg/dl whereas in controls is 164.0508 mg/dl.

Graph- 3: Correlation Between Serum PON 1 And Fibrinogen

IV. Discussion

High blood pressure is ranked as the third most important risk factor for attributable burden of disease in south Asia (2010) (13). Hypertension exerts a substantial public health burden on cardiovascular health status and healthcare systems in India (14).

Paraoxonase 1 in Hypertension:

Paraoxonases are a family of three enzymes called PON 1, PON 2 and PON 3. They have multifactorial roles in various biochemical pathways such as protection against oxidative damage and lipid peroxidation. Uzun et al, (2004) reported that the PON 1 levels were dependent on the difference in the blood pressure levels (2). Saruhan et al, (2007) suggested the serum PON1 levels remained unchanged with age and gender in Turkish population(2). Dildar Konukoglu et al, (2009) also showed decrease in PON1 activities in hypertensive cases as compared to normotensive controls (2). Arun Kumar (2014) showed in his study that oxidative modifications due to HTN causes changes in serum PON 1 activity there by accelerating the atherogenic process. The analysis demonstrated that enzyme activities and concentrations were significantly lowered in hypertensive patients(2).
Possible mechanisms by which serum PON1 activity is decreased in hypertension are due to:
1. Oxidative stress in hypertension causes decrease in total antioxidant capacity which reflects serum PON1 activity. Antioxidants and free radicals could conceivably protect PON1 through augmentation of the overall antioxidant capacity.
2. Hypertension are also associated with lower serum levels of HDL concentrations hence could explain alterations in PON1 activities.

**Fibrinogen in Hypertension:**
Fibrinogen is another inflammatory marker involved in the etiopathogenesis of hypertension. Our study showed increased fibrinogen levels in hypertensive cases as compared to normotensive controls. Letcher et al. (1981) and Mehrrota TN et al. (1987) showed that fibrinogen level was significantly increased in hypertensive cases as compared to normotensive control (15).Vaziri ND et al, (1993) and Tabak et al. (2009) demonstrated that plasma fibrinogen level was insignificantly increased in hypertensive patients (16,17). Smah Saif Alden Osman et al, (2013) demonstrated that, the plasma fibrinogen level was significantly higher in hypertensive patients than in control group (18). Fibrinogen is a major determinant of blood viscosity, and it is involved in haemostasis and thrombosis pathway. It has been identified as a major independent risk factor for cardiovascular diseases.

**V. Conclusion**
The level of serum PON 1 is significantly lower in patients as compared to controls. The inflammatory marker like fibrinogen level is higher in hypertensive patients. PON 1 level is correlated negatively with the inflammatory marker i.e fibrinogen. Antioxidant rich diet and antioxidant therapy may increase serum PON1 level and may decrease inflammatory process of hypertension. Regular exercise, yoga and pranayama may also increase serum HDL level that also reflects serum PON1 level.

**References**

* Dr Diptimayee jena, Dr Nirupama Devi et al. “Study of Paraoxonase 1 And Fibrinogen As An Inflammatory Marker in Essential Hypertension.” IOSR Journal of Dental and Medical Sciences (IOSR-JDMS), vol. 16, no. 10, 2017, pp.26-29