

The Correlation Between the Plasma Level of Endothelin-1 and Pulmonary Artery Pressure in Patients on Hemodialysis Due to End-Stage Renal Disease

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Received: January 2, 2014; Revised: March 7, 2014; Accepted: June 3, 2014

Background: Chronic kidney disease, especially in patients with underlying pulmonary arterial hypertension (PAH), severely deteriorates the patients' quality of life. Early diagnosis would help to improve the outcome.

Objectives: This study was performed to assess the association between the plasma level of endothelin-1 and the measured PAH in the patients on hemodialysis due to end-stage renal disease.

Patients and Methods: In a descriptive, analytic, cross-sectional study, 40 patients were recruited. The pulmonary artery pressure (PAP) was measured via echocardiography and its association with plasma endothelin-1 as well as CRP levels was assessed.

Results: There was a significant association between PAP and endothelin-1 ($r=0.93$; $P<0.0001$) as well as PAP and CRP ($r=0.893$; $P<0.0001$).

Conclusions: The study demonstrated that in patients with underlying kidney disease, pulmonary artery pressure is strongly associated with endothelin-1 levels as well as CRP.

Keywords: Endothelin-1; Chronic Kidney Disease; Artery; Pressure

1. Background

Pulmonary arterial hypertension (PAH) is an uncommon disease due to vasoconstriction of the pulmonary arteries and would end in increased resistance of the pulmonary vasculature, failure of the right ventricle, and finally, death (1). The increased thickness of the endothelium in the pulmonary vascular system as a result of hypertrophy and hyperproliferation would finally result in pulmonary vascular system remodeling, which would be clinically presented as a progressive disorder. The molecular mechanisms and pathologic basis of this disease entity are made clearer by a number of studies (1-3). The endothelins are a group of polypeptides that are the main controllers for the tonicity of the vascular system. Among them, endothelin-1 is a very important and influential vasoconstrictor that can increase the activity level of pulmonary vascular smooth muscle. It has been demonstrated that in patients with idiopathic pulmonary fibrosis, increased plasma levels of endothelin-1 are associated with higher pulmonary artery pressure (PAP) and possibly higher pulmonary vascular resistance (4, 5). The endothelin-1 level has an inverse correlation with the blood flow through the lung vascular bed. In addition, its increased plasma levels in PAH are associated with disease severity and prognosis. Patients with underlying

chronic kidney disease leading to end-stage renal disease (ESRD) usually need renal replacement therapy, which is performed mainly through hemodialysis (HD). In addition, there are a considerable number of these patients with underlying PAH, which cause a great reduction in their quality of life and its early diagnosis would help to improve their life quality.

2. Objectives

This study aimed to assess the association between the plasma level of endothelin-1 and the measured PAP in patients on HD due to ESRD. In addition, the plasma C reactive protein (CRP) was measured to assess the association between this inflammatory protein and the PAP.

3. Patients and Methods

In a descriptive, analytic, cross-sectional study, all the patients on HD in Shahid Modarres Hospital were enrolled in the study. The study was performed after obtaining Institutional Review Board approval for ethical considerations. The patients were included in the study after signing a written informed consent. After power analysis, the study sample size was calculated and 40

patients were selected. A checklist was prepared for data collection. All the echocardiographic measurements were done by the same cardiologist using the same echocardiography machine. The endothelin-1 measurements were performed by the same method. The data were presented as mean \pm SD and P value < 0.05 was considered statistically significant.

4. Results

In the study, the mean of body mass index among 40 participants was 25 ± 4.5 kg/m². The mean of patients' age was 54 ± 13 years and the mean of PAP was 50 ± 21 mmHg. The mean of plasma endothelin-1 level was 2.58 ± 0.77 . There was a statistically significant association between endothelin-1 levels and the PAP ($r = 0.93$; $P < 0.0001$) as well as between plasma CRP levels and PAP ($r = 0.893$; $P < 0.0001$).

5. Discussion

The results of our study demonstrated the association of PAP with the plasma endothelin-1 as well as CRP levels. PAH is a disease with elevated levels of endothelin-1 (6). The activity of endothelin-1 is mediated by two different receptors, namely, ETA and ETB. ETA is inside the smooth muscle cells of the pulmonary vascular bed while ETB is located inside the smooth muscle cells of the pulmonary vascular system as well as inside the endothelial cells (7, 8). In addition, the role of endothelin has been demonstrated in patients with congenital heart disease where PAH deteriorates the clinical course of their underlying cardiac disease (9). Furthermore, endothelin-1 receptor antagonists have been shown to reduce the morbidity and mortality in patients with PAH (10). It seems that the endothelin receptor mediates a potent vasoconstrictive response through G-protein-coupled phospholipase C activation that ends in 1,4,5-inositol triphosphate formation and leads to increased level of intracellular Calcium ion (8, 11). The endothelin receptor seems to express its effects on the endothelial cells, which would mediate pulmonary artery dilatation, through nitric oxide and prostacyclin production. Although some evidence has shown that the endothelin receptor could possibly exert its vasoconstrictive effects in hypoxic conditions, its mechanism is not fully elucidated (12-15). Finally, our study demonstrated that in patients with underlying kidney disease, there is a frank association between PAP and the plasma level of endothelin-1 as plasma level of CRP levels.

Acknowledgements

The authors would like to acknowledge all the kind efforts of Physicians, nurses and other colleagues, Cardiology and Nephrology Wards, Shahid Modarres Hospital, Tehran, Iran

Authors' Contributions

ST took part in study design, clinical stages, and manuscript preparation. HA took part in study design, clinical stages, and manuscript preparation. MK took part in study design and clinical stages. MS took part in study design, clinical stages, and manuscript preparation. AD took part in data analysis and manuscript preparation.

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