Pulmonary artery pressure in association with serum parathormone in maintenance hemodialysis patients

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Introduction: There are several potential explanations for the development of PH in patients with stable hemodialysis patients. Hormonal and metabolic derangement associated with end-stage renal failure might lead to pulmonary arterial vasoconstriction and an increase of the pulmonary vascular resistance. The aim of this study was to consider the association of pulmonary artery pressure (PAP) with serum parathormone in end-stage renal disease (ESRD) patients under regular hemodialysis treatment.

Material and methods: This cross-sectional study was conducted on patients with end-stage renal disease undergoing maintenance hemodialysis treatment through an arteriovenous fistula which was created on the hand, and with acetate basis dialysate and polysulfone membranes. For all patients serum intact parathormone (iPTH) was measured. For assessment of pulmonary artery pressure, all patients were subjected to two-dimensional and doppler echocardiographic studies that were done for the patients after their hemodialysis sessions.

Results: The study comprised 102 patients (F=46, M=56) consisting of 73 non diabetic hemodialysis patients (F=33, M=40), and 29 diabetic hemodialysis patients (F=13, M=16). The duration of hemodialysis was 17.8±29 months. The mean ±SD of serum iPTH of total patients was 338±306 pg/ml. The mean ±SD of pulmonary artery systolic pressure (PAP) was 41.5±12.6 mmHg. A significant positive correlation of PAP with the dosage (r=0.36, p=0.001) and duration of hemodialysis (r=0.33, p<0.001) was seen, also a significant positive correlation of pulmonary artery systolic pressure with serum intact parathormone (iPTH) in hemodialysis patients was found.

Conclusions: A significant positive correlation of serum intact parathormone with pulmonary artery pressure, which is a new aspect of uncontrolled secondary hyperparathyroidism implies the need for a better control of poorly controlled hyperparathyroidism disease in hemodialysis patients.

Key words: pulmonary hypertension, pulmonary artery pressure (PAP), hemodialysis, end-stage renal failure, parathormone.

Introduction

Cardiovascular disease (CVD) remains the main cause of morbidity and mortality in patients with end-stage renal disease (ESRD) [1, 2]. Left ventricular hypertrophy (LVH), interstitial myocardial fibrosis, arteriolar wall thickening and coronary artery calcification are hallmarks of this disorder [3, 4]. Although traditional risk factors such as diabetes mellitus, hypertension, dyslipidemia and advanced age, are prevalent in ESRD patients, they may not be sufficient...
by themselves to account for the high prevalence of CVD in patients with this condition [1]. Thus the search for other non-traditional risk factors that may be involved in the pathogenesis of uremic CVD has been an area of intense study [1, 5]. There is growing evidence to suggest that abnormalities in serum parathyroid hormone (PTH) levels are resulting in vascular and visceral calcification leading to an increased risk of cardiovascular morbidity and mortality in these patients [6, 7]. Secondary hyperparathyroidism is often found to be an independent risk factor for uremic calcification. Serum PTH contributes to cardiovascular complications in many ways [6, 8]. It has a permissive role in arteriolar wall thickening, myocardial interstitial fibrosis [9] promoting hyperlipidemia and hypertension [10-12]. It was suggested that the abnormalities in right ventricular function in patients with end-stage renal disease (ESRD) are in largely due to pulmonary hypertension (PH) which may develop secondary to ESRD [13, 14]. There are several potential explanations for the development of PH in patients with ESRD, hormonal and metabolic derangement associated with ESRD might lead to pulmonary arterial vasoconstriction and an increase of the pulmonary vascular resistance [13, 7]. The parathyroid hormone is known to enhance the entry of calcium into many cells, chronic exposure to excess blood levels of PTH is associated with increased calcium content of many tissues [4, 7, 13]. Cardiovascular cells (cardiomyocytes and smooth muscle cells) are target cells for the parathyroid hormone [7, 15]. In addition to the cardiovascular effects of secondary hyperparathyroidism (SHPTH), it has been shown that high serum parathormone is associated with an increased incidence of hypertension [7, 16]. Therefore, it is possible that SHPTH in hemodialysis patients may also have some effects to increase the pulmonary artery pressure. Studies concerning the effect of high serum PTH on the pulmonary artery systolic pressure (PAP) increment are scarce and controversial, we therefore aimed to consider the association of serum parathormone with PAP in ESRD patients who are undergoing regular hemodialysis treatment.

Material and methods

This is a cross-sectional study conducted on patients with end-stage renal disease undergoing maintenance hemodialysis treatment through an arteriovenous fistula which was created on the hand, and with acetate basis dialysate and polysulfone membranes. The study was carried out in the hemodialysis section of Hajer Medical Educational & Therapeutic Center of Shahrekord University of Medical Sciences in Shahrekord of Iran. Blood samples were collected after an overnight fast. In all patients serum intact parathormone (iPTH) was determined by the radio-immuno assay (RIA) method using DSL-8000 kits of the USA (normal range of values is 10-65 pg/ml). The patients were under hemodialysis (HD) for two or three times per week. Exclusion criteria were past history of chronic obstructive lung disease (COPD), multiple lung infections, cigarette smoking, history of cough, allergy, asthma, using drugs affects pulmonary function or structure, chest wall or parenchymal lung disease, previous pulmonary embolism, systemic lupus erythmatosous, left-to-right shunt, and significant mitral or aortic valve disease and also any other past history of lung disease and also any lung abnormality on the chest x-ray. According to the severity of secondary hyperparathyroidism, each patient being treated for secondary hyperparathyroidism (SHPTH) was given oral active vitamin D3 (Rocaltrol), calcium carbonate capsule, and Rena-Gel tablets at various doses. After their hemodialysis session, the patients were subjected to two-dimensional and doppler echocardiographic studies. Systolic right ventricular (or pulmonary artery) pressure was calculated using the Bernoulli equation $p = 4 v^2$, where $p$ is the pressure drop [mmHg] and $v$ is the velocity of blood flow [m/sec], the pressure in the RV can be calculated by RV pressure = RA pressure + (4 x [TR jet velocity]) [17, 18]. All echocardiographic studies were done by a single cardiologist. Pulmonary hypertension (PH) was defined as a systolic PAP greater than or equal to 35 mmHg [14, 17, 18]. Duration and doses of hemodialysis treatment were calculated from patient’s records and the duration of each hemodialysis session was four hours. For 3 years before the study, the polysulfone membranes had been used in our hemodialysis center. For the statistical analysis descriptive data are expressed as mean ±SD. A comparison between groups was considered using the students’ t test. For correlations the partial correlation test was used. All statistical analysis was performed using the SPSS (version 11.5.00). The statistical analysis was considered significant when p<0.05.

Results

The total patients were 102 (F=46, M=56) under hemodialysis due to end-stage renal disease (ESRD) consisting of 73 non diabetic hemodialysis patients (F=33, M=40), and 29 diabetic hemodialysis patients (F=13, M=16). Table I shows the mean ±SD of age, the length of the time patients had been on hemodialysis, dialysis dosage and serum values of iPTH. The mean ±SD of age of total patients were 51±17.6 years. The length of the time patients had been on hemodialysis were 17.8±29 months. Mean ±SD of serum iPTH of total patients were 338±306 pg/ml. Mean ±SD of iPTH of diabetic group and nondiabetic group were 272±237 pg/ml and 364±227 pg/ml respectively. Mean ±SD of pulmonary artery systolic pressure (PAP) of total HD patients, diabetic HD group and non diabetic hemodialysis were...
In this study, significant positive correlations of PAP with hemodialysis duration and dosage were seen, also a significant positive correlation of pulmonary artery systolic pressure with serum intact parathormone was found, too. Studies regarding the prevalence and the predictors of pulmonary hypertension (PH) in patients with end-stage renal failure undergoing regular hemodialysis are quite scarce. Yigla et al. in a study on 58 patients with ESRD receiving long-term hemodialysis and on control groups of 5 patients receiving peritoneal dialysis (PD) and 12 predialysis patients, found a 39.7% of pulmonary hypertension in patients who were under hemodialysis, (mean ±SD =44±7 mmHg; range, 37 to 65 mmHg) [14]. Amin et al. in a study on 51 patients (28 men and 23 women) with end-stage renal disease, who were receiving regular hemodialysis PH was detected in 15 patients (29%), this study showed women had a higher prevalence of PH (48% vs 14%), moreover in this study there were no significant differences between patients with PH and those without PH with regard to age, duration of dialysis, serum calcium, phosphorus, alkaline phosphatase, parathyroid hormone (PTH) or the prevalence of an abnormal (99m)Tc diphosphate lung scan result (60% vs 73%, respectively). They showed that 29% of patients with ESRD receiving regular hemodialysis have PH and the presence of PH was not related to the level of PTH or the severity of other metabolic abnormalities, also there was no relation

### Table I. Mean ±SD, minimum and maximum of age, duration, dose and also laboratory results of all patients and non-diabetic and diabetic groups

<table>
<thead>
<tr>
<th>Total HD patients N=102</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Mean ±SD</th>
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<tr>
<td>Age [years]</td>
<td>14</td>
<td>84</td>
<td>51±17.6</td>
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<tr>
<td>DiH* [months]</td>
<td>1</td>
<td>145</td>
<td>17.8±29</td>
</tr>
<tr>
<td>Dialysis dose sessions</td>
<td>12</td>
<td>1740</td>
<td>199±349</td>
</tr>
<tr>
<td>iPTH [pg/ml]</td>
<td>5</td>
<td>1980</td>
<td>338±306</td>
</tr>
<tr>
<td>PASP [mmHg]</td>
<td>20</td>
<td>80</td>
<td>41.5±12.6</td>
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<tr>
<td>Non diabetics N=73</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Age [years]</td>
<td>14</td>
<td>84</td>
<td>48.3±18</td>
</tr>
<tr>
<td>DiH* [months]</td>
<td>1</td>
<td>145</td>
<td>18.8±31</td>
</tr>
<tr>
<td>Dialysis dose sessions</td>
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<td>1740</td>
<td>208±375</td>
</tr>
<tr>
<td>iPTH [pg/ml]</td>
<td>10</td>
<td>1980</td>
<td>364±227</td>
</tr>
<tr>
<td>PASP [mmHg]</td>
<td>20</td>
<td>80</td>
<td>40±118</td>
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<tr>
<td>Diabetics N=29</td>
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<tr>
<td>Age [years]</td>
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<td>79</td>
<td>58±15</td>
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<tr>
<td>DiH* [months]</td>
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<tr>
<td>Dialysis dose sessions</td>
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<td>272±237</td>
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<tr>
<td>PASP [mmHg]</td>
<td>30</td>
<td>65</td>
<td>45±9.8</td>
</tr>
</tbody>
</table>

*duration of the hemodialysis treatment

![Figure 1](image.png)

A significant positive correlation of pulmonary artery pressure with serum parathormone in hemodialysis patients

41.5±12.6, 45±9.8 and 40±18 mmHg respectively. In this study no significant difference of serum iPTH between diabetics and nondiabetic hemodialysis patients was found (p NS). A significant positive correlation of PAP with dosage (r=0.36, p=0.001) and duration of hemodialysis (r=0.35, p<0.001) (data adjusted for ages of patients for two above correlations) were seen. A significant positive correlation of pulmonary artery systolic pressure with serum intact parathormone (iPTH) in hemodialysis patients was found (r=0.20, p=0.040; Figure 1) (data adjusted for ages of patients).
between PH and the presence or the severity of pulmonary artery calcification. They also found that PH is detected more frequently in women. Their study does not support a role for secondary hyperparathyroidism as one of the etiologies of PH in patients with ESRD [19]. Yigla also in an another study evaluated the role of pulmonary calcification in the pathogenesis of PH in patients with ESRD who receiving chronic HD therapy by an A-V access. To consider the correlation between pulmonary calcification expressed by lung uptake of 99mTc-MDP and PH, selected 36 men and 13 women with a mean age of 61.7±13.2 years receiving HD therapy for 38.2±43 months. Yigla concluded that pulmonary calcification has no role in the pathogenesis of PH among ESRD patients undergoing hemodialysis therapy [20]. Our study is in agreement with previous two studies in which ESRD patients under regular hemodialysis had pulmonary hypertension. In contrast to the Amin’s study, only our female diabetic hemodialysis patients had PAP more than male diabetic patients. In contrast to the above mentioned studies we could show a significant positive correlation of serum iPTH with pulmonary artery pressure. The influence of high serum parathormone hormone concentration on pulmonary pressure may be through an increasing calcium content of the smooth muscle cells of the artery [4, 7, 13]. Previously we shown that high serum parathormone is associated with increased incidence of systemic hypertension in stable hemodialysis patients [7]. Indeed, the parathyroid hormone is known to enhance the entry of calcium into many cells, chronic exposure to excess blood levels of PTH is associated with increased calcium content of many tissues [4, 7, 13].

Conclusions
In conclusion, a positive association of high serum parathormone and pulmonary artery pressure is very important because pulmonary hypertension is a disease with poor prognosis and implies the need for a better control of secondary hyperparathyroidism in hemodialysis patients through controlling of hyperphosphatemia.

Acknowledgements
We would like to thank Dr. B. Amra, Pulmonologist, and Associate professor of Isfahan University of Medical Sciences for his very useful comments and from Dr. F. Roghani cardiologist of our hospital for cardiac graphies.

References