Hemodialysis International 2006; **10**:356–359

Doppler echocardiograph evaluation of pulmonary hypertension in patients undergoing hemodialysis

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Abstract

Pulmonary hypertension (PH) has been reported in hemodialysis (HD) patients, but data regarding its incidence and mechanisms are scarce. The aims of this study was to evaluate the prevalence of unexplained PH in long-term HD patients, and to examine some possible etiologic factors for its occurrence. The prevalence of PH was estimated by Doppler echocardiography in a cohort of 86 stable patients on HD via arteriovenous access for more than 12 months. All the patients underwent full clinical evaluation, chest radiography, and a standard 12-lead echocardiograph. Laboratory investigation included a mean of 12 months (serum calcium, phosphorus, parathormone (PTH), alkaline phosphatase, lipids, and hemoglobin). Pulmonary hypertension was defined as pulmonary artery systolic pressure >35 mmHg as determined by Doppler echocardiography using the modified Bernoulli equation. Pulmonary hypertension was detected in 23 patients (26.74%). Of those with PH, left ventricular hypertrophy was seen in 13 patients (56.52%), and valvular calcifications in 6 patients (26.08%). There were no significant differences between both groups with regard to age, sex, duration of dialysis, shunt location, and all the biological parameters of the study. The presence of PH was not related to the level of PTH, or the severity of other metabolic abnormalities. This study demonstrates a high prevalence of PH among patients with ESRD receiving long-term HD via surgical arteriovenous access. The role of the vascular access, anemia, or secondary hyperparathyroidism as the etiology of PH in HD patients did not hold in this study.

Key words: End-stage renal disease, hemodialysis, pulmonary hypertension, doppler echocardiography

INTRODUCTION

Pulmonary hypertension (PH) is a well-known complication of the heart, lung, or systemic disorders, with increased morbidity and mortality regardless of its etiology.[1,2] In patients with end-stage renal disease (ESRD), PH is a relatively new entity with a very poor prognosis.[3–5] Patients with such a disorder may develop right ventricular failure with features of systemic venous congestion, pleural effusion, and ascites.[4,6,7] It can also result in reduced systemic arterial pressure and intradialytic hypotension.[8,9] The aims of this study were to evaluate the prevalence of PH in patients with ESRD who are maintained on long-term hemodialysis (HD) therapy and to examine some possible etiologic factors for its occurrence.

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MATERIALS AND METHODS

Patient selection

This descriptive study consisted of 86 patients (46 women) with ESRD, who were maintained on long-term HD

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therapy via surgically created native A-V access. Patients were consecutively enrolled if they agreed to participate in the study. Exclusion criteria were chronic obstructive lung disease, chest wall or parenchymal lung disease, previous pulmonary embolism, collagen vascular disease, systemic lupus erythematosus, left ventricular ejection fraction $\leq 50\%$, left-to-right shunt, and moderate or severe mitral or aortic valve disease.

Patients with PH underwent further evaluation by a specialist pulmonologist that included computed tomography of the chest, complete pulmonary function tests, measurement of blood gases, and O_2 saturation while breathing room air, and a ventilatory perfusion radioisotope lung scan intended to disclose other causes of PH. None of the patients was excluded from the study after this work-up.

Patient evaluation

The patients' general data (age, sex, comorbidities), and data regarding the kidney disease (etiology of renal failure, duration of HD therapy, and access location [brachial or radial]) were recorded directly from the patients or from their hospital files. All patients underwent full clinical evaluation with special emphasis on detecting any clinical condition that predisposes to PH, chest radiography, and a standard 12-lead echocardiograph. Blood tests included the mean of 12 monthly values preceding the echocardiographic study of hemoglobin, serum calcium, phosphorus, alkaline phosphatase, and complete lipid profile. Intact molecule parathormone (PTH) was measured by radioimmunoassay. Two-dimensional and M-mode, Doppler echocardiography was performed in all patients within 12 hr after completion of dialysis, to avoid overestimation of PAP due to volume overload. In the presence of tricuspid regurgitation, continuous-wave doppler echocardiography was used to estimate the systolic PAP. Systolic right ventricular (or pulmonary artery) pressure was calculated using the modified Bernoulli equation: PAP = 4 × (tricuspid systolic jet)^2 + 10 mmHg (estimated right atrial pressure).[7] Pulmonary hypertension was defined as a systolic PAP35 mmHg. Left ventricular geometry was measured following recommendations of the American Society of Echocardiography.[8,9] The presence of left ventricular hypertrophy (LVH) was defined on the basis of a left ventricular mass index (LVMI) greater than 100 g/m^2 for women and greater than 131 g/m^2 for men.

Statistical analysis

All data are expressed as mean ± SD. The characteristics of the 2 groups were compared by a 2-tailed unpaired t test (continuous variables) or a chi-square test (categorical variables). Significant differences were defined as $p < 0.05$. Statistical analysis was performed using the SPSS 10.0 for Windows (SPSS, Inc., Chicago, IL, U.S.A.).

RESULTS

Patient characteristics for the 86 patients receiving HD are presented in Table 1. The mean duration of HD therapy before the echocardiographic study was 88.20 ± 42.22 months. The common etiologies of renal failure were unknown, glomerulonephritis, and arterial hypertension.

PAP values are presented in Table 2. Pulmonary hypertension was observed in 23 patients receiving HD (26.74%). Data on the 23 patients with PH were compared with the 63 patients without PH (Table 3). The mean duration of HD therapy was not significantly shorter in the PH group (84.52 ± 43.36 vs. 89.54 ± 42.06 months, p = 0.55). There were no significant differences between both groups, with regard to age (p = 0.37), sex (p = 0.69), serum calcium (89.65 ± 6.63 vs. 88 ± 7.27 mg/L, p = 0.30), phosphorus (51.55 ± 18.15 vs. 51.75 ± 16.85 mg/L, p = 0.87), alkaline phosphatase (452.08 ± 391.19 vs. 570.71 ± 620.03 IU/L, p = 0.70), PTH (285.62 ± 201.13 vs. 512.38 ± 605.81 pg/mL, p = 0.38), cholesterol (1.45 ± 0.3 vs. 1.63 ± 0.4 g/L, p = 0.08), and triglycerides (1.58 ± 0.87 vs. 1.53 ± 0.61 g/L, p = 0.53).

The hemoglobin levels were not significantly lower in the PH group (8.89 ± 1.4 vs. 8.51 ± 1.43 g/dL, p = 0.36).

Table 1 Data on 86 patients with ESRD receiving hemodialysis via surgical A-V access

Variables	Data
Age (years)	
Mean ± SD	45.42 ± 14.36
Range	18 to 84
Sex	
Male/female (N)	40/46
Male/female ratio	0.87
Duration of dialysis, (months)	
Mean ± SD	88.20 ± 42.22
Range	14 to 204
Etiology of renal failure (N)	
Glomerulonephritis	29
Hypertension	9
Diabetes mellitus	5
Polycystic kidney	1
Chronic pyelonephritis	6
Unknown	36

ESRD = end-stage renal disease.

Table 2 Distribution of systolic PAP among HD patients with PH

Systolic PAP values (mmHg)	N	%
Total patients	23	26.74
SPAP > 35 mmHg	17	19.8
SPAP > 45 mmHg	6	7

HD = hemodialysis.

Other variables, such as cigarette smoking (p = 0.50), systolic (124.34 ± 18.04 vs. 124.76 ± 17.214 mmHg, p = 0.82), or diastolic arterial pressure (74.78 ± 6.65 vs. 73.25 ± 10.51 mmHg, p = 0.44), LVMI (151.4 ± 47.5 vs. 140.5 ± 45.2 g/m^2, p = 0.24), LVH (p = 0.81), valvular calcifications (p = 0.57), and the anatomic location of the dialysis vascular access, did not differ significantly.

DISCUSSION

Pulmonary hypertension is a new entity in ESRD patients receiving maintenance HD. Data regarding its incidence and mechanisms are scarce. In this study, we assessed the prevalence of PH in 86 patients with ESRD receiving regular HD. Patients with significant left ventricular systolic dysfunction, valvular heart disease, pulmonary parenchymal or vascular disease, or intracardiac shunts were not included in the study because of the independent association between these conditions and PH. The prevalence of PH as defined by Doppler echocardiographic assessment of tricuspid valve was 26.74%. Age, sex, and duration of dialysis were not different in patients with and without PH.

In a recently published study, Yigla et al.,[2] evaluated the incidence of PH in 58 HD patients using Doppler echocardiography. Almost 40% of patients had systolic PAP above 35 mmHg, and their cardiac output was significantly higher compared with HD patients without PH. Because the study population had no obvious cause for PH, they assumed that some factors, such as the size or the location of A-V fistulae, are involved in the mechanism that increases cardiac output and contributes to the pathogenesis of PH. In our study, cardiac output did not differ between patients with and without PH, and the effect of shunt location was not statistically significant. The other suggested mechanism of PH is increased pulmonary flow due to anemia and fluid overload.[10] In our patients, the findings indicate that the relation between anemia and PH could not be assessed.

In patients with ESRD, chronic exposure to excess blood level of PTH is associated with the increased calcium content of many tissues. Therefore, it is possible that the state of hyperparathyroidism in these patients is responsible for the development of PH secondary to pulmonary artery calcifications. This notion is supported by a study[11] of 2 subgroups of a dog model of ESRD: one

Table 3 Clinical and laboratory data of patients with and without PH

	PH+ (N = 23)	PH − (N = 63)	p
Age (years)	48.21 ± 15.5	44.39 ± 13.9	0.37
Sex (male/female), N(%)	12 (52.2)/11 (47.8)	28 (44.4)/35 (55.6)	0.69
Cigarette smoking, N(%)	2 (8.7)	10 (15.8)	0.50
Duration of dialysis (months)	84.52 ± 43.36	89.54 ± 42.06	0.55
Shunt location (brachial/radial), N(%)	22 (95.6)/1 (4.4)	53 (84.1)/10 (15.9)	0.27
Systolic AP (mmHg)	124.34 ± 18.04	124.76 ± 17.21	0.82
Diastolic AP (mmHg)	74.78 ± 6.65	73.25 ± 10.51	0.44
Valvular calcifications, N(%)	6 (26)	13 (20.6)	0.57
LVMI (g/m^2)	151.4 ± 47.5	140.5 ± 45.2	0.24
LVH, N(%)	13 (56.5)	33 (52.4)	0.81
Cardiac output (L/min)	5.76 ± 1.3	6.03 ± 0.9	0.22
Serum calcium (mg/L)	89.65 ± 6.63	88 ± 7.27	0.30
Serum phosphorus (mg/L)	51.55 ± 18.15	51.75 ± 16.85	0.87
Calcium–phosphate product (mg^2/L^2)	4620.68 ± 1669.41	5640.86 ± 9596.27	0.68
Alkaline phosphate (IU/L)	452.08 ± 391.19	570.71 ± 620.03	0.70
PTH (pg/mL)	285.62 ± 201.13	512.38 ± 605.81	0.38
Total cholesterol (g/L)	1.45 ± 0.3	1.63 ± 0.4	0.08
Triglycerides (g/L)	1.58 ± 0.87	1.53 ± 0.61	0.53
Hemoglobin (g/dL)	8.89 ± 1.4	8.51 ± 1.43	0.36

LVH = left ventricular hypertrophy; LVMI = left ventricular mass index; PH = pulmonary hypertension; PTH = parathormone.

with an intact parathyroid and the other parathyroidectomized. This study showed increased PTH activity, lung calcium content, and PAP values in the dogs with intact parathyroid glands, thus suggesting a link between PH and hyperparathyroidism. In our patients, investigations of the parathyroid gland activity revealed no difference between those with and without PH, with regard to values of PTH, calcium, phosphorus, and alkaline phosphatase.

STUDY LIMITATIONS

1. The exclusion criteria used in our protocol resulted in a small study group, as the majority of HD patients had concomitant cardiac or pulmonary disease. As the number of eligible patients in any center is limited, further studies including a multicenter approach are required.
2. PAP was noninvasively measured by Doppler echocardiography without obtaining direct invasive measurements. However, measurements of PAP by the applied Doppler echocardiographic method were reported to have an excellent correlation with measurements obtained by invasive methods.[12]
3. Pulmonary functions tests were not performed; therefore, the relations among respiratory function and PH were not evaluated.

CONCLUSION

This study demonstrated that 26.74% of patients with ESRD receiving regular HD have PH. The findings do not support a role of anemia or shunt location as the etiology of PH in these patients. The presence of PH was not related to the level of PTH, or the severity of other metabolic abnormalities.

Manuscript received September 2005; revised April 2006.

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