

MEDICINA CLINICA



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Original article

Pulmonary hypertension in hemodialysis patients: Prevalence and associated factors*



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ARTICLE INFO

Article history: Received 18 March 2015 Accepted 25 June 2015 Available online 20 May 2016

Keywords: Pulmonary hypertension Hemodialysis Cardiovascular risk Epidemiology

ABSTRACT

Background and objective: Pulmonary hypertension (PH) is a progressive disorder that can be caused by several underlying conditions or an intrinsic alteration of the pulmonary vasculature. Chronic increased pressure in the pulmonary vasculature leads to changes in the architecture of the vessels that can perpetuate PH and produce right ventricular dysfunction. These structural and functional alterations can decrease survival and quality of life of patients on hemodialysis; however, there is a lack of evidence about this problem in this population. The aim of this study is to establish the prevalence of PH in patients on hemodialysis and its association with specific factors related to this patient population.

Material and methods: We included 202 prevalent patients on hemodialysis for at least 6 months and who were clinically stable. We collected demographic data, routine laboratory parameters and data of 2D Doppler-echocardiography. PH was defined as a systolic pulmonary artery pressure (SPAP) estimated by Doppler ultrasound above 35 mmHg. Hydration status was assessed by determining the plasma concentration of N-terminal pro brain natriuretic peptide (Nt-proBNP).

Results: PH prevalence was 37.1% (75 patients). The average SPAP in the entire study population was 32 ± 12 mmHg and in the group with PH it was 45 ± 11 mmHg. We found a direct and statistically significant correlation between the presence of PH and age (p=0.001), time on renal replacement therapy (p=0.04), the presence of systolic dysfunction (p=0.007), diastolic dysfunction (p=0.01), mitral valve disease (p=0.01) and double mitral and aortic disease (p=0.007). Volume overload was closely associated with PH, as demonstrated by the correlation between the SPAP and Nt-proBNP levels (p=0.001).

Conclusion: We conclude that prevalence of PH in hemodialysis patients is high. And one of the most important associated factors is volume overload. More studies are needed to establish the impact of PH on morbidity and mortality of patients and to assess whether a better volume control improves PH.

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Hipertensión pulmonar en pacientes en hemodiálisis: prevalencia y factores asociados

RESUMEN

Palabras clave: Hipertensión pulmonar Hemodiálisis Riesgo cardiovascular Epidemiología Introducción y objetivo: La hipertensión pulmonar (HTP) es un trastorno progresivo que puede deberse a enfermedades subyacentes o a una alteración intrínseca de la vascularización pulmonar. El aumento crónico de la presión en el árbol vascular pulmonar lleva a cambios en la arquitectura de los vasos que perpetúan la propia HTP y producen disfunción ventricular derecha; todo esto podría disminuir la supervivencia y calidad de vida de los pacientes. El objetivo de este estudio es establecer la prevalencia de HTP en los pacientes en hemodiálisis y su asociación con factores propios de este grupo de pacientes.

[†] Please cite this article as: Reque J, Quiroga B, Ruiz C, Villaverde MT, Vega A, Abad S, et al. Hipertensión pulmonar en pacientes en hemodiálisis: prevalencia y factores asociados. Med Clin (Barc). 2016;146:143–147.

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Material y métodos: Incluimos a un total de 202 pacientes prevalentes en hemodiálisis durante al menos 6 meses y estables clínicamente, se recogieron datos demográficos, parámetros analíticos de rutina y los datos de un ecocardiograma doppler-2D. Definimos HTP como una presión sistólica de arteria pulmonar (PSAP) estimada mediante ecografía doppler por encima de 35 mmHg. El estado de hidratación se valoró mediante la determinación de los niveles de fragmento N terminal del péptido natriurético cerebral (Nt-proBNP).

Resultados: La prevalencia de HTP fue del 37,1% (75 pacientes). La media de PSAP en toda la población estudiada fue de 32 ± 12 mmHg y en el grupo con HTP de 45 ± 11 mmHg. Encontramos una correlación directa estadísticamente significativa entre la presencia de HTP y la edad (p=0,001), el tiempo en tratamiento renal sustitutivo (p=0,04), la presencia de disfunción sistólica (p=0,007), disfunción diastólica (p=0,01), valvulopatía mitral (p=0,01) y doble lesión mitral y aórtica (p=0,007). La sobrecarga de volumen se asocia estrechamente con HTP como se demuestra por la correlación entre la PSAP y los niveles de Nt-ProBNP (p=0,001).

Conclusión: Concluimos que la prevalencia de HTP en los pacientes en hemodiálisis es alta y uno de los factores asociados más importante es la hipervolemia. Son necesarios más estudios para establecer el impacto de la HTP sobre la morbimortalidad de los pacientes y valorar si un mejor control de la volemia lleva a mejoría de la HTP.

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Introduction

Pulmonary hypertension (PH) is a progressive and sometimes fatal disorder that may be due to underlying cardiopulmonary disorders, an intrinsic alteration of the pulmonary vascular tree or a combination of both factors. Regardless of its etiology, sustained increase in pressure in the pulmonary vasculature produces alterations in the architecture of the vessels and varying degrees of right ventricular dysfunction, which translates into medium- and long-term negative impact on patient survival. 2

The exploration of choice for the diagnosis of PH is right heart catheterization (RHC), where PH is defined when the mean pulmonary artery pressure is above 25 mmHg at rest, values between 8 and 20 mmHg are considered normal and controversy still exists when pressure is between 21 and 24 mmHg.³

In clinical practice the use of Doppler transthoracic echocardiography for the diagnosis of this entity⁴ is recommended because of its high correlation with RHC,⁵ its cost-effectiveness and for being a non-invasive test that is more accessible than the RHC. Although it is also possible to estimate the mean pulmonary arterial pressure by echocardiography, what has been reported by consensus and has demonstrated greater precision is the pulmonary artery systolic pressure (PASP).⁶

Although theoretically the predisposing factors for the development of PH are highly prevalent among patients in haemodialysis (HD) and in addition this complication can play an important role in the evolution of its course, it is a subject that has not been studied much until now.

The aim of this study is to analyze the prevalence of PH in patients in HD, their possible association with other clinical and analytical factors and other factors that are specific to renal replacement therapy.

Materials and methods

Initially we recruited 286 patients in HD who were aged over 18 years and had undergone renal replacement therapy for at least 6 months; they were clinically stable, i.e. no changes in vascular access in the last 3 months and had not been admitted into hospital or A&E during the month prior to recruitment. In total 84 patients were excluded, 25 of them because they did not have a recent echocardiogram, 45 because they had not done a PSAP estimation and 14 because they did not meet the criteria of clinical stability. Finally 202 patients were included in the study.

Data on the affiliation and history of comorbidities were collected; the cardiovascular history collected was: cardiac (heart weakness, angina and acute myocardial infarction), stroke and peripheral vascular events. Likewise, routine analytic parameters were collected, as well as inflammatory markers (C-reactive protein determined by turbidimetry) and concomitant treatments. To assess the hydration status, we determined the N-terminal fragment of brain natriuretic peptide (NT-proBNP) by electrochemiluminescence immunoassay ECLIA using the analyser Roche/Hitachi Cobas E601. High-sensitive cardiac troponin T were also determined using the same method and analyser.

Data from a doppler-2D echocardiogram was gathered from the year prior to inclusion. By protocol, all echocardiograms for patients in HD are conducted on interdialysis day. The calculation of the PSAP through echocardiography is based on the modified Bernoulli equation⁷:

$$PSAP = 4 \times (VRT)^2 + PAD$$

where VRT is the maximum speed of the tricuspid insufficiency jet and PAD is the pressure in the right atrium that is estimated by the diameter of the superior vena cava according to recommendations by the American Society of Echocardiography.⁸ The upper limit of normality is usually set between 30 and 35 mmHg based on a large population-based study.⁹ The echocardiographic data collected, in addition to the PSAP were: systolic dysfunction, defined as a left ventricle ejection fraction lower than 55% and diastolic dysfunction defined according to echocardiographic parameters of the *American Heart Association* guidelines.^{10,11} PH is defined as a PSAP above 35 mmHg.

The study was approved by the hospital's ethics committee.

Statistical analysis

Data were analyzed using the software SPSS v20.0 (IBM, Munich, Germany), the normal distribution variables were expressed as mean and standard deviation and the non-parametric as median and interquartile range. We determined the differences between groups by performing the Student T, Chi-square and Mann–Whitney–U tests accordingly. To analyze the variables related to PH, we performed a logistic regression, including, in the multivariate model, those that were initially significant in the univariate analysis. The correlation between PSAP and Nt-proBNP was established by a Pearson analysis. Statistical significance was established as the value $p \leq 0.05$.

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