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Pulmonary Hypertension in Hemodialysis Patients: The Missed Diagnosis

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Abstract

Chronic Kidney Disease (CKD) is a common health problem worldwide. Cardiovascular disease is the most common cause of morbidity and mortality in CKD. Pulmonary Hypertension (PHT) is a missed cardiovascular complication of CKD, especially in End-Stage Renal Disease (ESRD). The prevalence of PHT in patients with ESRD ranges from 27% to 58%. Patients with advanced CKD have a prevalence of PHT that is lesser than that in patients with ESRD, ranging from 8% to 39%. PHT is an independent predictor of increased morbidity/mortality in patients with CKD and hemodialysis.

Abbreviations

CKD: Chronic Kidney Disease; PHT: Pulmonary Hypertension; PAP: Pulmonary Arterial Pressure; ESRD: End Stage Renal Disease; HD: Hemodialysis; CO: Cardiac Output

Introduction

Pulmonary Hypertension (PHT) is characterized by increased Pulmonary Artery Pressure (PAP) and resistance. The disease results from many diverse mechanisms among which the most common are cardiac, pulmonary, and systemic diseases. Pulmonary Hypertension (PH) is a progressive, fatal pulmonary circulatory disease that accompanies many conditions (including left to right side shunt) with compensatory elevated cardiac output [1,2]. The vast majority of PHT in the population of End-Stage Renal Disease (ESRD) patients receiving Hemodialysis (HD) therapy through a surgical Arterio-Venous (A-V) access is secondary to heart conditions [1-3]. A distinct clinical syndrome, in which PHT occurs shortly after the A-V access formation, sometimes even before starting HD therapy, mainly among patients with significantly (A-V access mediated) increased Cardiac Output (CO), and may regress after reduction of CO by temporary A-V access closure or after reversing the uremia by successful kidney transplantation. PH also complicates chronic Hemodialysis (HD) therapy immediately after the creation of an Arteriovenous (AV) access, even before starting HD therapy. It tends to regress after temporary AV access closure and after successful kidney transplantation. Affected patients have significantly higher cardiac output [3-6].

Discussion

There are several potential explanations for the development of PHT in patients with ESRD. Hormonal and metabolic derangement associated with ESRD might lead to vasoconstriction of pulmonary vessels and increased pulmonary vascular resistance. However, the fact that only about half of the uremic patients developed PHT suggests that mechanisms other than uremia may be involved in this disorder. These may include underlying concomitant diseases such as diabetes mellitus or systemic hypertension.

The hormonal mechanism mainly involves in the pathogenesis of PHT is the nitric oxide-endothelin axis. The well known ESRD-related endothelial dysfunction that restricts the ability of the pulmonary vessels to accommodate the A-V access-mediated elevated CO. The laboratory hallmark of this syndrome is reduced basal and stimulatory Nitric Oxide (NO) levels (Vasodilatation) and elevated blood levels of endothelin (Vasoconstriction). It appears that patients with End-Stage Renal Disease (ESRD) acquire endothelial dysfunction that reduces the ability of their pulmonary vessels to accommodate the AV access-mediated elevated cardiac output, exacerbating the PHT [7,8]. Other metabolic factor in the pathogenesis of PHT is the increased multiplication of calcium

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phosphor in the blood of HD patients due to hyperphosphatemia and deposition in the pulmonary vasculature [9].

Results

Doppler echocardiographic screening of ESRD patients scheduled for HD therapy for the occurrence of PHT is indicated before few months after a-V fistula creation. Early diagnosis enables timely intervention, currently limited to changing dialysis modality or referring for kidney transplantation. An echocardiographic diagnosis of PHT is made when the systolic Pulmonary Arterial Pressure (PAP) exceeds normal values (30 mmHg) after completion of HD session. In mild PH, PAP values range up to 45 mmHg, in moderate PHT, PAP is between 45 mmHg and 65 mmHg, and in severe PHT, PAP values are greater than 65 mmHg. Systolic PAP equals cardiac output times Pulmonary Vascular Resistance (PVR), (i.e., PAP = cardiac output × PVR). Increased cardiac output by itself does not cause PH because of the enormous capacity of the pulmonary circulation to accommodate the increase in blood flow. Therefore development of PHT requires pathologic, marked elevation of pulmonary vascular resistance.

Conclusion

Reversibility of PHT following kidney transplantation is encouraging, and patients with significant PHT should be particularly encouraged to seek a transplant. Surgical reduction of oversized AV accesses should be considered in patients with PH and extremely high cardiac output who demonstrate reduction of both cardiac output and PHT following temporary closure of their AV access in the echo laboratory. Different metabolic, hormonal and genetic factors are involved [10]. Peritoneal dialysis is a reasonable alternative in some patients. However, the efficacy of current medical therapeutics for PHT, such as prostanoids, ET-1 blocker, and specific phosphodiesterase inhibitors, has not been studied in this syndrome.

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