Perioprative management of Portopulmonary Hypertension & Hepatopulmonary Syndrome in Liver Transplantation

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Abstract

Key Words: Portopulmonary hypertension, hepatopulmonary syndromes, integrated approach.

Portopulmonary hypertension and hepatopulmonary syndromes are distinct clinical and pathophysiological entities occur in substantial proportion of candidates for liver transplant .These disorders are notoriously under diagnosed and have substantial impact on survival and liver transplant success rates

Integrated preoperative diagnosis, effective therapeutic approaches and wise anesthetic decisions make liver transplantation feasible &safe.

LIST OF ABBREVIATIONS

ALK1	Activin like kinase 1 gene
BMPR2	Bone morphogenetic protein receptor type 2 gene
CO	Carbon monoxide
CEE	Contrast esophageal echocardiography
CETEE	Contrast enhanced transeosophageal ecocardiography
COPD	Chronic obstructive pulmonary disease
CT	Computed tomography
ET-1	Endothelin -1
eNOS	Endothelial nitric oxide
FIO2	Fraction of inspired O2
HPS	Hepatopulmonary pulmonary syndrome
HRCT	High resolution computed tomography
INOS	Inducible nitric oxide synthatase
IPVD	Intrapulmonary vascular dilatation
L-NAME	L- nitro-argenine methyl ester
LT	Liver transplantation
MAPK	Mitogen-activated protein kinase
mPAP	Mean pulmonary arterial pressure
NO	Nitric oxide
OLT	Orthtopic liver transplantation

PAH	Pulmonary artery hypertension
PA-aO2	Alveolar-arterial O2 pressure
PAOP	Pulmonary artery occlusion pressure
PELD	Pediatric end stage liver disease
PPVA	Porto-pulmonary venous anastmosis
PVR	Pulmonary vascular resistance
Q	perfusion
RAP	Right atrial pressure
RHC	Right heart catheterization
RVSP	Right ventricular systolic pressure
AO2	Alveolar O2
SLE	Systemic lupus erthromatosis
SVR	Systemic venous resistance
TNF-alpha	Tumor necrotic factor alpha
TC-MAA	Technicieum macro aggregated albumin
TRV	Tricuspid regurge velocity
VA,Q	Alveolar ventilation perfusion matching

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INTRODUCTION

For better understanding the complicated and often mystifying language of modern medicine and owing to the success of liver transplantation (LT), there has been increasing recognition of the importance of pulmonary vascular complications of hepatic disease state. Such vascular complications include hepatopulmonary syndrome (HPS) and portopulmonary hypertension (POPH).

More importantly, since the late 1980s, experience has taught that such complications influence survival and candidacy for LT. Currently, LT is the only effective treatment for improving outcome in patients with HPS, a life-threatening condition whose prevalence can approach 20% in some series of patients awaiting LT. (1)

POPH, occurring in the setting of liver disorders, another dramatic pulmonary–hepatic vascular condition, has prevalence in the order of 5% in hepatic patients submitted to LT. From a pathophysiological point of view, hepatopulmonary syndrome is almost exactly the opposite of portopulmonary hypertension. (2)

Unlike in HPS, in the moderate-to-severe stages of POPH, LT is not widely recommended, even being regarded a contraindication due to its negative perioperative and postoperative impact. As a consequence of its high mortality rates if getting transplantation without proper management, difficult pharmacological vasodilators strategies become mandatory before proceeding to LT. (3)

Prostanoids like epoprostenol, treprostinil and iloprost have showed a nice reduction in pulmonary hypertension in session of liver transplantation in front of POPH also endothelin receptors blocker as bonsentan and ambrisentan showed the same promising results .Sildenafil also was effective either a mono or combined therapy in bridging to safe transplantation . [4]

Notwithstanding, it is now evident that knowledge and proper understanding of diagnosis and management of these two distinct entities are rudimentary, such that underdiagnosis, undertreatment and inconsistent management are common worldwide. [5].

Major objectives of orientation with liver induced lung injury

1) Increase awareness of both HPS and POPH in the medical community in order to minimize the growing impact of their morbidity and mortality.

2) Improving diagnosis and management of HPS and POPH through a major concerted effort by medical team deal with liver transplant especially for anesthesiologist in perioperative management in liver transplantation.

Identification approach to HPS &PPOH

The two pulmonary vascular consequences of portal hypertension and liver cirrhosis are hepatopulmonary syndrome (HPS) and portopulmonary hypertension (POPH). HPS is primarily a gas exchange problem characterized by arterial hypoxemia. While POPH is primarily a hemodynamic problem which can result in right heart failure and death, (HPS) and (POPH) are distinct clinical and pathophysiollogical entities that may accompany liver disease. Although characterized by markedly different clinical and physiological features [6]

Definition of hepatopulmonary syndrome.

hepatopulmonary syndrome is characterized by a defect in arterial-oxygenation, induced by pulmonary vascular dilatation in the setting of liver disease; patients of all ages can be affected , more seen in middle-aged patients with minimal sex difference, it can also occur in children The most common hepatic disorder leading to HPS is liver cirrhosis, irrespective of etiology although HPS has also been observed in many other chronic and even acute hepatic conditions [7]

Definition of portopulmonary hypertension.

Portopulmonary hypertension (POPH) is diagnosed when pulmonary arterial hypertension (PAH) exists in a patient with portal hypertension, in the absence of alternative causes of the PAH. POPH is likely best defined as pulmonary artery hypertension (PAH) associated with portal hypertension, whether or not that portal hypertension is secondary to underlying liver disease. [8]

HPS and POPH may occur within the same patient either the HPS preceded the onset of pulmonary hypertension or manifest simultaneously with POPH, with only a few reported cases documented to have pulmonary hypertension prior to developing HPS. [9]

In several instances pulmonary hypertension follows liver transplantation, for which HPS was an indication for liver transplantation in addition that cure of HPS worsen the POPH [10]

Epidemiology and prevalence of POPH

The first retrospective autopsy studies showed that the prevalence of POPH ranged from 0.25% to 0.73% in populations with portal hypertension or cirrhosis [11]

Recent work using hemodynamic studies have estimated the prevalence of POPH to be between 2% and 5% [12].

Its prevalence in patients with cirrhosis and refractory ascites has been documented at 16.1%, while its prevalence in patients with cirrhosis without refractory ascites has been in the range of 0.25% to 4%. [13]

In addition, the prevalence in patients undergoing LT is likely higher, with a prevalence of 8.5% [14].

PAH helps to reclassify POPH as a form of secondary PAH. Conversely, the prevalence of portal hypertension in patients with PAH is approximately 10%.Identification of POPH is made an average of 4 to 7 years after the diagnosis of portal hypertension However, it These studies demonstrated the relationship between portal hypertension and is not

unheard for the diagnosis of POPH to be made before the diagnosis of portal hypertension [15].

The mean age of presentation for POPH is in the fifth decade of life, as compared with the fourth decade for idiopathic PAH.A review from 1998 showed the average age of patients with POPH to be 13-49 years. The sex ratio was 1.1:1 (male: female). [16]

Epidemiology and prevalence of HPS

Hepatopulmonary syndrome (HPS) is a pulmonary vascular disorder, complicating hepatic diseases, most frequently liver cirrhosis and even though it is an indication for liver transplant, it is responsible for an increased morbidity and mortality among patients awaiting liver transplantation. [17]

Interestingly, the relationship between hepatopulmonary syndrome and liver cirrhosis dates back to 1884 when Fluckiger first described based on an observation of a woman with cyanosis, clubbing and cirrhosis. However, the term "Hepatopulmonary syndrome" was coined later on by Kennedy and Knudson in 1977. [18]

This term was proceeded with An autopsy study in patients with liver cirrhosis and cyanosis, reported in 1966 by (Berthelot et al) first suggested that marked pulmonary vascular dilatation may play a role in this condition. [19]

The prevalence of HPS in the setting of cirrhosis ranges between 4%-30%.Transplant hospitalization mortality was 16% in patients with HPS and 36% in patients with Portopulmonary hypertension. [20]