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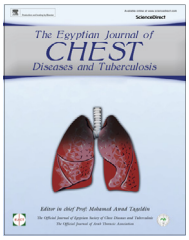

ORIGINAL ARTICLE

Assessment of pulmonary hypertension in patients with liver disease pre and post liver transplantation

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KEYWORDS

Pulmonary hypertension;
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Abstract *Background:* Both hepatopulmonary syndrome and portopulmonary hypertension are associated with chronic liver disease. Liver transplantation is considered a controversial solution.

Aim: The aim of this work is to assess pulmonary hypertension in liver disease patients pre and post liver transplantation. Studying the impact of pulmonary hypertension on hemodynamic of the patients in hospital after liver transplantation.

Patients and methods: Echo cardiographic examination pre and post liver transplantation after at least 3 months was conducted on 20 patients with chronic liver diseases and pulmonary hypertension who underwent liver transplantation to estimate mean PAP and degree of tricuspid regurgitation.

Results: The present study was conducted on 20 patients consisting of 18 males (90%) and two females (10%) with mean age 47.8 ± 8.9. It showed that mean pulmonary arterial pressure improved after liver transplantation 24.65% ± 17.50.The tricuspid regurgitation before operation was mild in 17 patients (85%) and moderate in three patients (15%) and after operation it become normal in 40% and mild in 60% with improvement in 55% and no improvement in 45% of the patients. There was improvement in dyspnea scale after the operation with one grade change in 35%, two grade change in 55% and three grade change in 10% of patients.

Abbreviations: HPS, hepatopulmonary syndrome; PPHTN, portopulmonary hypertension; COPD, chronic obstructive pulmonary disease; ILD, interstitial lung disease; WHO, World Health Organization; PVR, pulmonary vascular resistance; PAP, pulmonary artery pressure; PFT, pulmonary function test

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Conclusion: Liver transplantation was effective in the reduction of pulmonary artery pressure. The degree of pulmonary hypertension affected the functional state according to WHO Classification of pulmonary hypertension patients.

Introduction

Patients with chronic liver disease may show two pulmonary vascular disorders that are considered mutually exclusive: on the one hand, hepatopulmonary syndrome (HPS), which is characterized by pulmonary vascular dilatations and abnormal gas exchange [1], and on the other, portopulmonary hypertension (PPHTN), a process defined by pulmonary hypertension associated with portal hypertension [2].

If severe, both conditions are associated with a high mortality rate. The role of liver transplantation in reversing these vascular disorders is controversial, although complete resolution of HPS and, less frequently, PPHTN, following liver transplantation has been reported [3].

The reported frequency of hepatopulmonary syndrome in patients with liver disease is between 4% and 29%. The differing incidence is primarily due to heterogeneity of the applied diagnostic criteria. This syndrome is a well defined cause of hypoxemia in patients who have liver disease due to abnormal intrapulmonary vascular dilatation, which results in an excess perfusion for a given state of ventilation. This complication is characterized by anatomical shunting and a diffusion–perfusion abnormality [4].

Thus, abnormal pulmonary vascular dilatation plays a central part in the hepatopulmonary syndrome, whereas abnormal vasoconstriction and obliterative vascular remodeling are the key features of portopulmonary hypertension [5].

Aim of the work

Assessment of pulmonary hypertension in liver disease patients pre and post liver transplantation. Studying the impact of pulmonary hypertension on hemodynamic of the patients in hospital after liver transplantation.

Patients and methods

The present study was conducted on 20 patients with chronic liver diseases and pulmonary hypertension who underwent liver transplantation in the Ain Shams University Specialized Hospital and Wadi Elnil Hospital.

All patients were subjected to the following:

(1) Full medical history.
(2) Thorough clinical examination.
(3) Chest X-ray postroanterior view.
(4) ECG before operation.
(5) Echo cardiographic examination pre and post liver transplantation after at least three months to estimate mean PAP and degree of tricuspid regurgitation.
(6) Pulmonary function test pre liver transplantation.
(7) Pelvic-abdominal ultrasound pre liver transplantation to assess portal hypertension.
(8) Recording of those patients who needed hemodynamic support post operative.

We used the American Thoracic Society shortness of breath Scale and World Health Organization functional assessment classification in our study [6].

Inclusion criteria

(1) Chronic liver disease with or without portal hypertension.
(2) Estimated mean pulmonary artery pressure >25 mmHg.
(3) Survived patients after liver transplantation.

Exclusion criteria

- Chronic chest disease e.g. COPD and ILD.
- Cardiac disease e.g. valvular heart disease or congenital heart disease.
- History of pulmonary embolism.
- Connective tissue disease.

The collected data were revised, coded, tabulated and statistically analyzed using SPSS 15 version.

Results

The present study was conducted on 20 patients consisting of 18 males (90%) and two females (10%) with mean age 47.8 ± 8.9 having chronic liver disease and pulmonary hypertension who underwent liver transplantation in the Ain Shams University Specialized Hospital and Wadi Elnil Hospital.

Table 1 shows that mean pulmonary arterial pressure improved after liver transplantation (Fig. 1).

Table 2 shows that tricuspid regurgitation before operation was mild in 17 patients (85%) and moderate in three patients (15%) and after operation it become normal in 40% and mild in 60% with improvement in 55% and no improvement in 45% of the patients (Fig. 2).

Table 3 shows that there was improvement in post operative functional state as regards the WHO Classification with one class change in 35% of cases, two class change in 35%, three class change in 25% and no change in 5% of patients.

Table 4 shows that there was improvement in dyspnea scale after the operation with one grade change in 35%, two grade change in 55% and three grade change in 10% of patients (Fig. 3).

Table 5 shows a highly significant statistical difference between mean pulmonary arterial pressure, tricuspid regurgita-

Table 1 Description of mean pulmonary arterial pressure before and after operation and the resulting change due to operation among the studied patients.

	Mean	±SD	Minimum	Maximum
Mean pulmonary arterial pressure before transplantation	37.35	4.21	32.00	49.00
Mean pulmonary arterial pressure after 3 months at least	27.95	6.67	12.00	35.00
Mean pulmonary arterial pressure change	9.40	7.34	2.00	33.00
Mean pulmonary arterial pressure percent of change	24.65	17.50	6.25	73.33

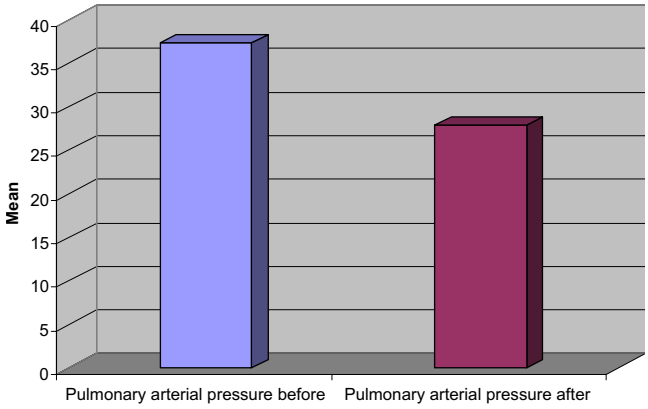

Figure 1 Description of mean pulmonary arterial pressure before and after operation and the resulting change due to operation among study patients.

Table 2 Description of tricuspid regurgitation before and after operation and the resulting change due to operation among study patients.

	Number of patients	%
TR before transplantation		
Mild	17	85.0
Moderate	3	15.0
TR after at least 3 months		
Normal	8	40.0
Mild	12	60.0
Change in TR		
No improvement	9	45.0
Improvement	11	55.0

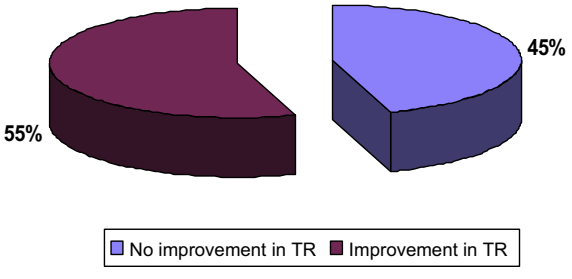

Figure 2 Improvement in TR after operation

tion, functional classification of pulmonary hypertension and dyspnea scale before and after liver transplantation.

Table 3 Description of functional state according to WHO classification before and after operation and the resulting change due to operation among study patients.

	No.	%
WHO classification before		
Class 1	0	.0
Class 2	6	30.0
Class 3	9	45.0
Class 4	5	25.0
WHO classification after 3 months		
Class 1	17	85.0
Class 2	3	15.0
Class 3	0	.0
Class 4	0	.0
WHO change in classification		
No change	1	5.0
One class change	7	35.0
Two class change	7	35.0
Three class change	5	25.0

Table 4 Description of degree of dyspnea scale (American Thoracic Society) before and after operation and the resulting change due to operation among study patients.

	No.	%
Dyspnea scale before		
Moderate	3	15.0
Severe	15	75.0
Very severe	2	10.0
Dyspnea scale after 3 months of operation		
None	3	15.0
Mild	11	55.0
Moderate	5	25.0
Severe	1	5.0
Very severe	0	.0
Dyspnea scale change		
No change	0	.0
One Grade change	7	35.0
Two Grade change	11	55.0
Three Grade change	2	10.0

There were four patients (20% of patients) who showed post operative hemodynamic instability necessitating inotropic/vasopressor support.

There was no significant relation between the presence or absence of pre-operative portal hypertension and the pre-operative mean pulmonary hypertension or the need of post operative hemodynamic support.

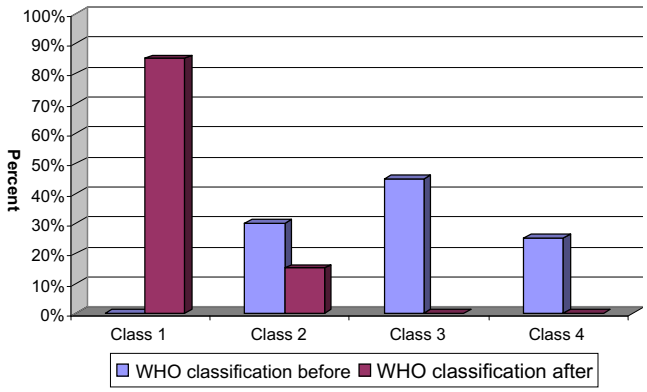

Figure 3 Description – according to WHO classification – of the resulting change due to operation among study patients.

Discussion

This is a preliminary study on the impact of liver transplantation on PAP, as liver transplantation surgery was recently used in Egypt, so there were lack of statistical data to compare with.

In the present study, the estimated mean PAP was 37.35 ± 4.21 mmHg preoperatively which decreased to 27.95 ± 6.67 mmHg in the postoperative follow up for 3 months with the pressure percentage of change being 24.65 ± 17.50%.

These results matched with the study by Martınez Palli et al. [7] who found that seven of 33 PPHTN patients undergoing liver transplantation in their series (3 with MPAP >45 mmHg) showed dramatically improved pulmonary pressures at 18 months.

These results also matched the study by Bozbas et al. [8] who studied 114 adult liver transplantation patients, 24 (21.1%) of them had PPHTN on Doppler echocardiography examination. The results showed that the mean systolic PAP was 46.6 ± 7.6 mmHg preoperatively which decreased to 37.8 ± 15.5 mmHg in the postoperative follow up.

Our result also matched a case report of a 38 years old male patient who had liver cirrhosis and hepatitis c virus (Schott et al. [9]) and his mean pulmonary artery pressure was 45 mmHg that decreased to 30 mmHg after one year of liver transplantation.

On the other hand the current results contradict with two case reports by Martinez-Palli et al. [10] who documented on the increase in preexisting pulmonary hypertension after liver transplantation and Albert et al. [11] who studied a 32 years old female patient who underwent liver transplantation at the Cleveland Clinic Foundation with increase of PPHTN after 4 years but it was only in one patient.

In the present study there were nine mild cases (45%), nine moderate (45%) cases and two severe cases (10%) of pulmonary hypertension according to the estimated mean pulmonary artery pressure (Marius et al. [12]).

Our results agree with the results of a study by Saner et al. (2006) among 74 consecutive patients that underwent LT between February 2004 and November 2005. The total incidence of PPHTN was 31% and most of them had mild to moderate PHTN (16 mild = 69.5%, 5 moderate = 21.7%, and 2 severe = 8.8%). Also, Strakel et al. [13] found that most of the patients of PHTN among liver transplant patients were mild PHTN 31 of 38 patients (81.5%).

In the present study, there was an improvement in severity of tricuspid regurgitation after liver transplantation. These results matched a case report done by Roland Schott et al. [9] who found that the tricuspid regurgitation completely disappeared after 2 years of liver transplantation.

On the other side these results did not match with Albert et al. [11] who found an increase in the severity of tricuspid regurgitation after 4 years of liver transplantation but that was a case report of one patient and after a long period of operation in contrast to our study which was on 20 patients and after 3 months to 1 year after operation.

In the present study the post-operative functional state according to the WHO Classification improved by one class in 35% of patients, two classes in 35% of patients, and three classes in 25% of patients while no improvement in 5% of patients.

These results agreed with a case report by Roland Schott et al. [9], however, this case report used The New York Heart Association Classification instead of WHO Classification, which revealed improvement of dyspnea from grade III to grade I.

However, these results did not agree with a case report Albert et al. [11] that revealed deterioration of dyspnea from grade I to grade III–IV after liver transplantation as mean pulmonary artery pressure was 45 and did not improve.

In the present study, there was an improvement in dyspnea scale according to the American Thoracic Society after the operation with one grade improvement in 35% of patients, two grades improvement in 55% of patients and three grades improvement in 10%.

These results agreed with the case report by Roland Schott et al., (1998) [9] who found improvement of dyspnea from grade III to grade I.

Table 5 Statistical comparison between different indicators before and after operation.

	Mean	±SD	P^*	Sig.
Mean pulmonary arterial pressure before	37.35	4.209	.0001	HS
Mean pulmonary arterial pressure after	27.95	6.669		
TR before	1.15	.366	.0001	HS
TR after	.60	.503		
WHO classification before	2.95	.759	.0001	HS
WHO classification after	1.15	.366		
Dyspnea scale before	3.05	.686	.0001	HS
Dyspnea scale after	1.20	.768		

* Paired *t* test.

In this study the patient had a mean pulmonary artery pressure of 44.50 ± 3.42 mmHg and developed hemodynamic instability after the operation.

These results agreed with the study by Le Pavec et al. [14] of the French National Center for PAH between 1984 and 2004 and revealed that mean pulmonary artery pressure greater than 35 mmHg and/or PVR greater than 250 dyn/s/cm^5 have an increased risk of hemodynamic instability and cardiopulmonary death after liver transplantation.

These results were in concordance with a study by Krowka et al. (2000) [15] who found that mean PAP greater than 35 mmHg is associated with an increased post-operative liver transplantation mortality.

Also these results matched a database published by Krowka et al. [16] from 10 liver transplant centers from 1996 to 2001, 13 (36%) of 36 patients who underwent liver transplantation developed hemodynamic instability and died in the hospital.

In the present study there was no difference in hospital stay between patients who needed post operative hemodynamic support (higher pulmonary hypertension) and who did not.

This result agreed with Strakel et al. [13] who found that the duration of ventilation and intensive care unit stay was unaffected by the degree of PPHTN.

But these results did not match the study by Bozbas et al. [17] who found a longer length of post operative hospitalization among patients with PHTN compared to those without preoperative PHTN.

In our study there was nonstatistical difference in pulmonary artery pressure between those patients who had portal hypertension and those who did not.

Robalino and Moodie [18] studied the clinical, laboratory and hemodynamic profile of patients with primary pulmonary hypertension and associated portal hypertension, seven new cases and 71 previously reported cases were analyzed. Liver cirrhosis was the most frequent cause of hypertension (82%) and a surgical portosystemic shunt was present in 29%. Almost invariably, portal hypertension either preceded or was diagnosed concurrently with pulmonary hypertension, favoring the hypothesis that in portal hypertension, the pulmonary vasculature may be exposed to vasoactive substances normally metabolized or produced by the diseased liver, possibly inducing vasoconstriction or direct toxic damage to the pulmonary arteries. Clinically, exertional dyspnea was the most frequent presenting symptom (81%); other symptoms, such as syncope, chest pain and fatigue, were present in less than 33%. An accentuated pulmonary component of the second heart sound (82%) and a systolic murmur (69%) were the most common physical findings. At least 75% of these patients had evidence of pulmonary hypertension on electrocardiography (right ventricular hypertrophy) or roentgenography (cardiomegaly or dilated main pulmonary arteries, or both). All these results nearly matched with our results.

Still there are not enough researches to state that liver transplantation is a recommended solution for PPHTN, Delcroix [19] stated that in the moderate-to-severe stages, liver transplantation is not widely recommended, and is even regarded as a contraindication due to its negative peri- and post-operative impact. As a consequence, screening by repeated transthoracic echocardiography is highly recommended in liver transplant candidates. Therapy with prostacyclin analogues may partially relieve this pulmonary hypertension.

In our study we found a significant reduction in pulmonary artery pressure after liver transplantation with improvement in morbidity such as dyspnea, performance, etc., however, most of our cases were mild to moderate and our follow up period was limited to 3 months only.

Recommendations

More studies on a larger scale and prolonged time are needed to assess the impact of liver transplantation on PHTN and to detect morbidity and mortality in liver transplant patients.

The use of pulmonary catheterization in assessing PHTN and comparing its results with the echo results may become more informative.

Also more studies are needed to compare between surgery (liver transplantation) and medical treatment by different pulmonary vasodilators in patients with pulmonary hypertension associated with chronic liver disease who are not candidates for surgery.

Limitation

The heart rate of the patients during echocardiographic examination was not identical before and after operation and this might have affected the mean PAP measurement. PFT and CXR were not done after operation. Also, the small number of patients used was a limitation.

Conflict of interest

No conflict of interest in this study.

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