ORIGINAL ARTICLE
KLİNİK ARAŞTIRMA

Portabl pulse oxymetry and contrast echocardiography in hepatopulmonary syndrome diagnosis

Hepatopulmoner sendrom tanısında portabl pulse oksimetre ve kontrast ekokardiyografi

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SUMMARY

Aim: The aim of this study is investigating hepatopulmonary syndrome's (HPS) diagnosis in cirrhosis patients with ortodeoxy symptom by portabl pulse oxymetry and transthoracic echocardiography with contrast enhancement.

Material and Methods: Ninety five (95) patients (67/28 M/F) with the diagnosis of cirrhosis were included into the study. Mean age of the patients was 52,28±12,0. Measurements of portabl pulse oximetry were obtained in a supin position and in a seated position breathing room air. The suitable patients' response to oxygen therapy with nasal cannula was evaluated. The patients with hypoxaemia (Sa,02<%94) in seated position were investigated HPS by transthoracic echocardiography with contrast enhancement.

Results: Eight (8) patients defined HPS had hypoxaemia in seated position with pulse oxymetry and positive contrast echocardiography. Four patients (4) had type I HPS and four patients (4) had type II HPS.

Conclusion: In conclusion, eight of 95(%8,4) patients had HPS. Patients with HPS were old age and were in Child B and C class. In cirrhosis patients with hypoxaemia in seated position, further studies are needed to investigate HPS.

Keywords: Hepatopulmonary syndrome, hypoxaemia, pulse oxymetry, transthoracic contrast echocardiography

ÖZET

Amaç: Bu çalışmanın amacı, ortodeoksi semptomu olan siroz hastalarında hepatopulmoner sendrom (HPS) tanısının portabl pulse oksimetri ve kontrastlı transtorasik ekokardiyografi ile araştırılmasıdır.

Materyal ve Metodlar: Çalışmaya siroz tanılı doksan beş (95) hasta (67/28 E/K) dahil edildi. Hastaların yaş ortalaması 52,28±12,0 idi. Portabl nabız oksimetresi ölçümleri, supin pozisyonunda ve oturma pozisyonunda oda havasını soluyarak elde edildi. Uygun hastaların nazal kanül ile oksijen tedavisine yanıtları değerlendirildi. Oturur pozisyonda hipoksemisi (Sa,02<%94) olan hastalarda kontrastlı transtorasik ekokardiyografi ile HPS incelendi.

Bulgular: HPS olarak tanımlanan sekiz (8) hastada nabız oksimetrisi ve pozitif kontrastlı ekokardiyografi ile oturur pozisyonda hipoksemi vardı. Dört hastada (4) tip I HPS ve dört hastada (4) tip II HPS vardı.

Sonuç: Sonuç olarak 95 (%8,4) hastanın sekizinde HPS vardı. HPS'li hastalar ileri yaştaydı ve Child B ve C sınıfındaydılar. Oturur pozisyonda hipoksemisi olan siroz hastalarında HPS'yi araştırmak için daha ileri çalışmalara ihtiyaç vardır.

Anahtar kelimeler: Hepatopulmoner sendrom, hipoksemi, nabız oksimetrisi, transtorasik kontrast ekokardiyografi

INTRODUCTION

One of the pulmonary complications of cirrhosis, which is related to portal hypertension and important for liver transplantation, is hepatopulmonary syndrome (HPS). Hepatopulmonary syndrome with arterial hypoxemia, intrapulmonary vascular dilatation or shunts is very important especially in the process of identifying transplant candidates and evaluating the efficiency of transplantation (1,2). Intrapulmonary vascular dilatation or shunt is indicated by positive transthoracic contrast echocardiography, especially in patients with hypoxemia in the seated position (Pa,02<80 mmHg and Pa,02<70 mmHg with arterial blood gas or Sa,02 <92% with pulse oximetry). In these patients, the demonstration of extrapulmonary involvement by lung scintigraphy with macroaggreated albumin labeled with technetium 99m and the demonstration of dilated vessels or arteriovenous connections by pulmonary angiography support the diagnosis of HPS. Many studies have investigated the frequency of HPS in cirrhotic patients with hypoxemia, especially with pulse oxymetry sampling. Contrast echocardiography is the gold standard for HPS screening in patients with hypoxemia (3-6).
We aimed to diagnose hepatopulmonary syndrome by pulse oxymetry and transthoracic contrast echocardiography in patients with cirrhosis with orthodeoxy symptom.

MATERIAL AND METHODS

In accordance with the Ethics Committee of Çukurova University Faculty of Medicine (13092006/8) and in accordance with the Principles of the Declaration of Helsinki, 95 patients with cirrhosis who were followed up in Çukurova University Faculty of Medicine Gastroenterology Department were included in this single center cohort study. HCC, lung cancer diagnosis. history of upper and lower GI bleeding, history of COPD, history of right heart failure and previous transplantation were considered exclusion criteria.

Diagnostic Criteria of HPS

Chronic Liver Disease,Late positive contrast echocardiography (left atrial microbubble opacification after 3 heart beats after right atrial opacification) Abnormal oxygenation (pulse oximetry) when transitioning from supine to seated position were considered HPS diagnosis.
Cirrhosis was classified according to functional, etiological and clinical stages.

Severity of liver disease was evaluated by Child-Pugh scoring method (Table-1).

Table 1. Modified child-pugh-turcott scoring system

Parameter	Numerical score		
	1	2	3
Ascites	None	Slight	Moderate to severe
Encephalopathy	None	Slight to moderate	Moderate to severe
Bilirubin (mg/dL)	< 2.0	2-3	> 3.0
Albumin (g/dL)	> 3.5	2.8-3.5	< 2.8
Prothrombin time (prolonged in seconds)	1-3 s	4-6 s	> 6.0

Child's Pugh Class A = 5-6 points; Child's Pugh Class B = 7-9 points; Child's Pugh Class C = 10-15 points.

At the end of the scoring, those with 5-6 points were considered as Child-Pugh A, those with 7-9 points as Child-Pugh B and those with 10-15 points as Child-Pugh C (Severe liver disease).

Echocardiographic Criterion

Trans-thoracic contrast-enhanced echocardiography was performed in patients with cirrhosis who could be compatible with HPS. After 10 ml of %3 saline solution was administered from the upper extremity peripheral vein, patients with positive contrast echocardiography were described as having intrapulmonary vascular dilatation. Positive contrast echocardiography was performed 3 heartbeats without right atrial opacification following administration of saline solution. It was considered as the opacification of microbubbles in the left atrium after post-operative period (7). These findings supported the dilated precapillary or capillary or direct arteriovenous connections of microbubbles in intrapulmonary passage. Intra atrial right-to-left shunt supported by opacification in the left atrium in less than 3 cardiac cycles was not observed in any patient.

Abnormal Oxygenation Criterion

Oxygen saturation measurement with portable pulse oximetry was applied to evaluate the oxygenation of the patients in the lying (after 10 minutes) and seated (at the end of 15 minutes) positions.

Working Design

95 cirrhosis patients followed in Çukurova University Faculty of Medicine Gastroenterology Department were included in the study. The functional, clinical stages and etiological classifications of chronic liver diseases of the patients were performed. The oxygenation status of the patients was measured by pulse oximetry. Oxygenation was evaluated with pulse oximetry in 95 patients. SaO2 <94% in sitting position with pulse oximetry (3.4) was considered significant for HPS. Response to oxygen therapy with pulse oximetry in sitting position was evaluated by giving 02 through nasal cannula for 15 minutes in the seated position to patients who were compatible with HPS. Sa02 >97% after 15 minutes of nasal cannula 02 was evaluated as response to treatment. The patient group responding to oxygen was classified as HPS type I. The patient group that did not respond to oxygen was classified as HPS type II.

Augmented transthoracic contrast echocardiography was performed in patients who were hypoxemic in the seated position. In patients with positive contrast echocardiography results, technetium 99m-labeled macroaggregated albumin lung scintigraphy was used to evaluate HPS severity and intrapulmonary shunt, lung HRCT to exclude comorbid disease, and arteriovenous focal arteriovenous connections, spider varicose or diffuse arteries. Pulmonary angiography was performed to show vascular abnormalities. Intracardiac right-to-left shunt was excluded with contrast echocardiography. The dyspnea-orthopnea status of the patients compatible with HPS was evaluated by physical examination, and the acid status by ultrasonography.

Statistical Analysis

Data were analyzed with SPSS (Statistical Packages of Social Sciences, SPSS for Windows Version 25.0, Chicago, IC, USA) package program. Age values were summarized as mean, SD, median, min and max values, and discrete variables such as gender and etiology were summarized as numbers and percentages. Chi-square test was used to compare discrete variables, and Mann-Whitney U test was used to compare continuous variables.

RESULTS

Findings

95 patients with cirrhosis were included in the study. 67 (70.5%) of the patients were male. The mean age of the patients was 52.28±12.0.

The chronic liver disease etiologies of the patients included in the study were examined. (Table 2)

Table 2. Etiology of cirrhosis

Etiology	Number	Percent
Unknownn	18	18,9
HBV	44	46,3
HCV	18	18,9
Alcohol	9	9,5
Autoimmune	2	2,1
Others (Metabolic..)	4	4,2
Total	95	100,0

The distribution of patients included in the study according to Child-Pugh scoring was analyzed (Table 3)

Table 3. Distribution of patients according to Child-Pugh scoring

Child-Pugh scoring	Number (n)	Percent (%)
Child A	14	14,7
Child B	41	43,2
Child C	40	42,1
Total	95	100,0

In 95 cirrhosis patients included in the study, hypoxemia in the seated position and 8 (8.42%) patients were diagnosed with HPS according to the results of positive contrast echocardiography (Table 4,5). 4 of 8 HPS patients were considered as HPS type I responding (50%) to oxygen therapy and 4 as HPS type II unresponsive to oxygen therapy (50%).

Table 4. Frequency of HPS

HPS	Number (n)	Percent (%)
HPS not detected	87	91,6
Type 1 HPS	4	4,2
Type 2 HPS	4	4,2
Total	95	100,0

Table 5. Evaluation of patients with orthodeoxia by contrast echocardiography

Positive contrast echocardiography	Number (n)	Percent (%)	Valid Percentage (%)	Cumulative Percentage (%)
negative	11	11,6	57,9	57,9
grade 1	4	4,2	21,1	78,9
grade 2	1	1,1	5,3	84,2
grade 3	3	3,2	15,8	100,0
Total	19	20,0	100,0	
Others	76	80,0		
Total	95	100,0		

The etiology of the underlying cirrhosis was HCV in 3 of 8 patients diagnosed with HPS (37.5%), HBV (25%) in 2, and the etiology of the underlying cirrhosis in 3 (37.5%). 3 of the patients were female (27.5%) and 5 were male (62.5%). 6 of 8 patients who were diagnosed with HPS had a Child score of C (75%) and 2 had a Child score of B (Ascites was present in 7) (87.5%) of 8 HPS patients and no acid was detected in 1 HPS patient (12.5%). We detected HPS in 8 patients with pulse oximetry (Sa 02 as ≤94%). In patients diagnosed with HPS, lung HRCT was performed to exclude comorbidities and no comorbidity was detected in the patients. MAA lung scintigraphy and pulmonary angiography were performed in 3 patients to show intrapulmonary vascular dilatation or shunt, but no significant results were obtained.

The mean age of HPS patients with cirrhosis (58.75±11.63) and Child Pugh score were significantly higher than the mean age of the other 87 patients with cirrhosis (51.68±11.9) and Child Pugh score (with 99% confidence interval)($P < 0.001$).

DISCUSSION

Hepatopulmonary Syndrome is a pulmonary complication of cirrhosis and its frequency is 4-29% in patients with cirrhosis (7-9). The average incidence is 15% (10,11). The causes of HPS are not fully known, but are considered to

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result from an imbalance between vasoconstrictors and vasodilators and/or hepatic factors that stimulate and inhibit vascular cell growth (5-7). It is defined as an arterial oxygenation defect caused by intrapulmonary vascular dilatations (IPVD) associated with liver disease (4-6). Its vascular component typically includes diffuse or localized dilated pulmonary capillaries, and less commonly pleural and pulmonary arteriovenous connections. Shortly, HPS is defined a clinical triad that includes arterial deoxygenation ,IPVD and liver disorder.

In our study, of 8 patients who were diagnosed with HPS in 95 cirrhosis patients, 6 were Child C and 2 were Child score B class. Similar findings were shown in a study which was conducted with 98 cirrhosis patients, 9 of 33 HPS patients were in Child B and 24 in Child C, and 66% of 98 cirrhosis patients included in the study were male and 34% were female (12). Likewise, in a study by Amir Houshang Muhammed Alizadeh friends, age and Child C classification were significantly associated with HPS (13). With portable pulse oximetry, we detected 8 patients (8.42%) with a Sa02 <94 in 95 cirrhosis patients in seated position and positive results with contrast echocardiography. Peter Deibert et al. found the frequency of HPS to be 5.4% with contrast echocardiography in patients with Sa02≤93 in the seated position (13). As a result of the same study, they recommend pulse oximetry and HPS examination with portable pulse oximetry in patients with severe hypoxemia. HPS was investigated by transthoracic contrast echocardiography in patients with hypoxemia in the seated position. Positive contrast echocardiography results were obtained in 8 (42%) of 19 eligible hypoxemic patients. Similar results were obtained with a positive contrast echo of 47% in 53 hypoxemic cirrhosis patients performed by Hopkins et al.(14).

CONCLUSION

In our study, the frequency of hepatopulmonary syndrome was found to be 8.4% in patients with cirrhosis. HPS has been investigated to identify candidates suitable for liver transplantation and to predict post-transplant survival and mortality. Oxygenation status was investigated with an easy-to-use noninvasive pulse oximeter, and HPS was diagnosed by transthoracic contrast echocardiography, a noninvasive method, in suitable patients. Larger case studies are needed for HPS screening in patients with cirrhosis.

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