

Role of Pulse Oximetry in Detecting Mild to Moderate Hepatopulmonary Syndrome in Children

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ABSTRACT

Background:

Hepatopulmonary syndrome (HPS) refers to arterial hypoxemia caused by pulmonary vasodilation, which is a consequence of portal hypertension. HPS is associated with increased morbidity and mortality; thus, it is important to diagnose this entity as soon as possible for treatment to be administered.

Materials and Methods:

In a cross-sectional study, 40 children (6 months to 14 years old) with chronic liver disease were enrolled. In all patients, measurements of Oxygen saturation (SaO₂) were performed with a pulse oximeter in the supine position (SPO₂) and then in the upright position (ΔSPO₂). Children were divided into three groups: i) those with both SPO₂>96% and ΔSPO₂>4%; ii) children with either SPO₂>96% or ΔSPO₂> 4%; and iii) those with neither of these signs. Then, contrast-enhanced echocardiography (CEE) and arterial blood gas (ABG) were performed. Finally, the prevalence of mild to moderate HPS was calculated in the three groups.

Results:

There were 30 patients who had neither of the two signs, of which 9 had HPS. Ten patients had one of the two signs, in whom 4 had HPS. None of the patients had both signs. The sensitivity of the pulse oximetry was 30%, specificity was 77%, positive predictive value was 38% and negative predictive value was 70%.

Conclusion:

There is a significant prevalence of HPS in cirrhotic patients which effects prognosis. Based on our study results, we have determined that pulse oximetry could not be a reliable screening procedure in mild to moderate HPS. It is recommended to use gold standard tests (echocardiography and arterial blood gasometry) for the screening and diagnosis of HPS in children.

Keywords: Hepatopulmonary Syndrome; Intrapulmonary shunt; Contrast echocardiography; Arterial oxygen saturation; Pulse oximetry

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INTRODUCTION

Hepatopulmonary Syndrome (HPS) is defined as a triad of chronic liver diseases and/or portal hypertension, gas exchange defects (increased alveolar-arterial PO₂ difference regardless of the presence of arterial hypoxemia), and intrapulmonary vascular dilatation(1). Patients of all ages can be affected; however there is a frequency of 4% to 32% among patients with chronic liver disease(2). HPS is responsible for an increase in morbidity and mortality among patients awaiting liver transplantation (LT). Early diagnosis would increase recognition of LT

candidates and thus decrease mortality(3-4).

HPS is classically identified by arterial blood oxygen reduction on arterial blood gas (ABG) analysis and the presence of intrapulmonary shunting using contrast-enhanced echocardiography (CEE). In addition, when a diagnosis of HPS is confirmed, knowledge of the degree of hypoxemia is important for optimum management. Oxygenation defect in HPS is characterized by an abnormal alveolar-arterial oxygen gradient ($A-a PO_2 \geq 15$ mmHg) and the degree of severity has been classified from mild ($PaO_2 \geq 80$ mmHg) to severe ($PaO_2 < 50$ mmHg)(1).

Even though platypnea and orthodeoxia are not pathognomonic for HPS, these phenomena are particularly suggestive of this diagnosis in the setting of liver dysfunction(5) Orthodeoxia is defined as a decrease in the partial pressure of oxygen (PaO_2) of at least 5% or 4 mmHg in an upright position. Since early diagnosis can considerably decrease mortality, identifying patients with orthodeoxia in chronic liver disease by non-invasive tests is important.

Because performing ABG for children with HPS is invasive and challenging, children prefer pulse oximetry. However, information regarding the utility of pulse oximetry screening for HPS in children is scarce. In adults, oxygen saturation of $<96\%$ measured by pulse oximetry identifies hypoxemia, with a sensitivity of up to 100% and specificity of about 88%(6).

As most HPS syndromes have mild to moderate hypoxemia, it is important to diagnose the syndrome in its early phases. In this study, we evaluate the accuracy of pulse oximetry as a screening test for mild to moderate HPS syndrome in children.

MATERIALS AND METHODS

A 55-year-old rancher, and current resident of ZaThis was a cross-sectional study conducted on 40 children diagnosed with chronic liver disease and/or portal hypertension in Ghaem Hospital, Mashhad, Iran.

The study protocol was approved by the Institutional Ethics Committee of the Mashhad University of Medical Sciences and written informed consent was obtained from the parents of the children.

Patient selection

Enrolled children were between the ages of 6 months and 14 years with clinical and pathological (biopsy) evidence of chronic liver disease.

Patients with congenital heart diseases, acute and

chronic lung diseases, and symptoms of any other concomitant severe diseases were excluded from the study. Demographic, clinical, and laboratory data were recorded. All patients underwent ABG and CEE which served as the gold standard diagnoses for HPS. Children with severe HPS (three cases) were excluded.

Echocardiographic (CEE) criteria

After confirmation of normal cardiac anatomy for identifying evidence of intrapulmonary vascular dilations (IPVD), CEE was performed by one operator. Ten millilitres of an agitated normal saline solution was rapidly injected via an upper extremity peripheral vein while patients were in the supine position. The time of contrast appearance in the right ventricle and in the left ventricle was recorded. After three to six heart beats, the identification of contrast in the left atrium by CEE was considered as evidence for IPVD(1).

Arterial blood gas (ABG) analyses and abnormal oxygenation

In order to ascertain oxygenation status, we performed ABG from the right radial artery with patients situated in the supine position and breathing room air. PaO_2 , $PaCO_2$, and pH were reported. According to the standard formula using a respiratory quotient of 0.8, () abnormal oxygenation was defined as $P(A-a) O_2$ of ≥ 15 mmHg.

Diagnostic criteria for HPS

According to the diagnostic criteria for HPS as proposed by Rodriguez-Roisin et al.,(1) both the presence of IPVD and $P(A-a) O_2 \geq 15$ mmHg confirmed the diagnosis of HPS in all patients. Patients were classified according to severity of hypoxemia as following: mild HPS with $PaO_2 \geq 80$ mmHg and moderate HPS as $60 \leq PaO_2 < 80$ mmHg.

Pulse oximetry and patient classification

In all patients, data from pulse oximetry were obtained at ambient temperature and O_2 pressure initially with patients in the supine position (test 1). A second reading was taken after 10 minutes with patients in the upright position (test 2). Then, we calculated the gradient of these two tests and the ΔSPO_2 of $>4\%$ was defined as orthodeoxia. The $SPO_2 < 96\%$ threshold was used as identification for hypoxemia. The pulse oximeter was placed on the same finger for each test.

Patients were divided based on the pulse oximetry results into three groups: i) those with one of two signs ($SPO_2 > 96\%$ or $\Delta SPO_2 > 4\%$); ii) those who had neither sign; iii) children with both signs ($SPO_2 > 96\%$ or $\Delta SPO_2 > 4\%$). However in this study since none of the patients presented with both signs, there were only two groups assessed.

Other clinical assessments

Similarly, biochemical evidences such as CBC, PT, PTT, and liver function tests, as well as nutrition and consciousness status were assessed in order to classify children by the Child-Pugh classification and the Paediatric End Stage Liver Disease (PELD Score).

Statistical analysis

Statistical analyses were performed using SPSS 11.5 for Windows. Data was compared using the independent sample t-test. For non-normally distributed data, we used the Mann-Whitney U test. Sensitivity, specificity, positive and negative predictive values of pulse oximetry in the diagnosis of mild to moderate HPS were evaluated.

Results were reported as mean \pm SD unless otherwise specified. $p < 0.05$ was considered to be statistically significant.

RESULTS

A total of 40 patients diagnosed with chronic liver disease were evaluated in this study. Patients' mean age was 7.61 ± 3.79 years. Demographic and para-clinical aspects were assessed to evaluate the severity of chronic liver disease by the Child-Pugh classification (Table 1).

For definitive diagnosis of HPS, all patients underwent ABG and CEE. Using the gold standard test, 13 (32%) of our patients had mild to moderate HPS.

According to the study protocol, pulse oximetry results showed that 10 patients had one of the two signs (group 1) whereas 30 patients had no signs (group 2). No patient had both signs concomitantly.

In group 1, there were 4 out of 13 definitive mild to moderate HPS patients and 9 were in group 2. There was no statistically significant difference between the two groups in terms of para-clinical results.

The severity grading of HPS in each group is shown in Table 2 based on oxygenation abnormalities, as has been proposed by Rodriguez-Roisin et al.¹

There was a significant difference in mean SpO_2 characterized by pulse oximetry compared to ABG

Table 1: Demographic and para-clinic data in 40 patients with chronic liver disease.

Variable	Value
Mean age in years (range)	7.61(0.9-14)
Gender (female)	21(52.5%)
Child-Pugh class A (mild)	23(57.5%)
Child-Pugh class B (moderate)	10(25%)
Child-Pugh class C (severe)	7(17.5%)
PT	14.20 \pm 3.88*
INR	1.38 \pm 0.51*
Albumin (g/dl)	4.11 \pm 0.85*
Total bilirubin (mg/dl)	3.40(1.05)**
Direct bilirubin (mg/dl)	0.97 \pm 0.40*
Hb (g/dl)	11.40 \pm 2.09*
WBC (cell/mm ³)	7.65 \pm 4.20*
PLT (103 cells/mm ³)	194.09(29.24)**
PELD score	18 \pm 6*

*Mean \pm SD

**Mean (Std. error of mean)

Table 2: Severity grading of HPS.

	Mild	Moderate
Group 1*	1	3
Group 2	5	6

*Group 1: With one of two signs obtained by pulse oximetry ($SPO_2 > 96\%$ or $\Delta SPO_2 > 4\%$)

Group 2: No signs.

Table 3: Mean SPO2 measured by pulse oximetry and SaO2 obtained from ABG.

	SPO2 (%)	SaO2 (%)	P-value**
Group 1*	87.60 \pm 8.22	92.55 \pm 5.39	<0.001
Group 2	97.96 \pm 1.09	92.84 \pm 10.76	<0.001
Total	95.38 \pm 6.09	92.77 \pm 9.79	<0.001

*Group 1: One of two signs obtained by pulse oximetry ($SPO_2 > 96\%$ or $\Delta SPO_2 > 4\%$).

Group 2: No signs.

**t-test

Table 4: Accuracy indices of pulse oximetry testing for diagnosis of HPS.

Indices	Percent 95%	Confidence interval (CI)
Sensitivity	30%	(10%-61%)
Sensitivity	77%	(57%-90%)
Positive predictive value	38%	(29%-47%)
Negative predictive value	70%	(60%-78%)

analyses. This difference was seen in each group as shown in Table 3. The accuracy indices of pulse oximetry testing for diagnosis of mild to moderate HPS are shown in Table 4.

raw lamb liver. According to the literature there are only 10 reports of pentastomiasis from Iran(16,17). As mentioned in our reported case the infection usually has subclinical manifestations. Our patient presented with chronic abdominal pain for a 3-year duration. According to the literature, there are 2 types of infections in humans, nasopharyngeal pentastomiasis which presents as a severe illness with symptoms of thoracic pain and upper respiratory tract bleeding. This type is termed Halzoun syndrome which has been described previously by Schacher et al.(18) Visceral pentastomiasis, the usual and most common form of the disease, infects internal organs such as the esophagus, stomach, ileum, colon, appendix, rectum, mesentery, gallbladder, lungs, pleura, omentum, bladder, adrenal glands, heart (pericardium), lymph nodes, and skin, however the liver is the most commonly affected site(10).

Our case was a rare form of visceral pentastomiasis. In the current report, abdominal pain with evidence of small bowel obstruction noted on CT scan, in addition to multiple intra-abdominal masses were odd presentations of a parasitic infection which caused the patient to undergo surgery due to suspicion of malignancy.

According to the literature, humans are usually tolerant to pentastomiasis and treatment is not necessary unless symptoms are present. In our case the patient was treated with medical therapy after definitive diagnosis, with subsequent symptom resolution.

To summarize, this was the eleventh report of pentastomiasis from Iran. We have presented a rare case of pentastomiasis infection with symptoms of high fever, abdominal pain, lower GI bleeding, and significant weight loss with involvement of the small intestine and intra-abdominal lymph nodes, but with normal WBC and eosinophil counts on CBC. Also, identification of the larva on the histologic examination was a rare

event with academic and practical significance. Since there are a lack of documented noninvasive diagnostic methods for the detection of parasitic infections, emphasis should be placed on diagnosing these infections particularly in endemic areas. Conclusively, pentastomiasis should be considered in the differential diagnosis of odd abdominal symptoms, notably in patients with histories of consuming uncooked food in endemic areas. However, the definitive diagnosis is the pathology report.

DISCUSSION

This cross-sectional study was conducted to determine the accuracy of pulse oximetry in detection of mild to moderate HPS in children with chronic liver disease. According to the data, 32% of the study patients had mild to moderate HPS based on established diagnostic criteria. This approximated other studies that used similar criteria(8-9). In this study the mean level of SpO₂ was higher than SaO₂. These results demonstrated that pulse oximetry overestimated the level of SpO₂. This overestimation was consistently seen in both groups.

Of note, there were more false negative results with pulse oximetry compared to the gold standard test for the detection of HPS. The sensitivity of pulse oximetry in our study was 30% (95% CI: 10%-61%) with a negative predictive value of 70% (95% CI: 60%-78%). These results have shown that the diagnostic utility of pulse oximetry in the detection of HPS was limited. In cirrhotic patients that are clinically suspect, the gold standard test for HPS must be performed.

Another result of this study was the poor positive predictive value, despite the high specificity of pulse oximetry. One explanation was the low prevalence of HPS in this study which affected the positive predictive value. As 32% of our patients were diagnosed with HPS therefore, positive predictive values were low.

Similarly, Abrams et al. have noted that pulse

oximetry generally overestimated arterial saturation and liver disease did not influence the accuracy of pulse oximetry. These researchers have mentioned that pulse oximetry could be a useful screening tool to identify arterial hypoxemia in cirrhotic patients, however a higher threshold for obtaining an ABG must be used (6).

In a recent study conducted to assess the utility of pulse oximetry for screening HPS in adults, pulse oximetry reliably predicted the presence and severity of hypoxemia in patients with HPS. In this study, 120 patients with chronic liver disease were prospectively enrolled and underwent pulse oximetry, contrast echocardiography, and ABG. The results showed that with a threshold value of <96%, pulse oximetry had a sensitivity of 100% and a specificity of 88% for detecting patients that had partial oxygen pressures of <70 mmHg. In addition, they have explained that the specificity of this test to detect a PO_2 value of <60 mmHg would be increased to 93% if a threshold value of detection of less than 94% is used. Higher pulse oximetry threshold shave dependably recognized HPS patients with less severe hypoxemia, albeit with lower specificity (10).

In our study, we used A-a O_2 gradient for detecting hypoxemia in children with chronic liver disease; therefore, the sensitivity of pulse oximetry in the current study was not comparable with the study by Arguedas et al. (10).

Deibert et al. have shown that the presence of both SpO_2 <92% and ΔSpO_2 >4% in pulse oximetry

is a reliable non-invasive sign of HPS. In line with Abrams et al. regarding a study in adults, due to an overestimation of arterial oxygenation, pulse oximetry may fail to identify milder cases of HPS that only have a A-a O_2 gradient, but no hypoxemia. Rodríguez-Roisin et al. have suggested that pulse oximetry is useful in the

follow-up of patients with moderate to severe HPS, particularly children before liver transplantation, but it is insufficient to replace the information obtained by ABG (1). According to Krowka, an ABG should be considered as the confirmatory study to assess the severity of hypoxemia in liver disease (12). Additional studies can demonstrate the accuracy of this test in severe cases.

Although pulse oximetry is a simple, acceptable and widely available technique, gold standard tests (CEE and ABG) for screening and diagnosis of mild to moderate HPS are still necessary.

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