ORIGINAL ARTICLE

Influence of ascites on pulmonary function in patients with portal hypertension*

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Background: Oxygen deficiency in patients with portal hypertension may be secondary to changes in respiratory mechanics due to ascites.

Objectives: To evaluate pulmonary function in patients with portal hypertension before and after reduction of the ascites.

Method: Fifteen patients with portal hypertension and ascites were submitted to pulmonary function tests, including spirometry and arterial blood gas analysis, before and after reduction of ascites. The analyzed parameters were: forced vital capacity (FVC); forced expiratory volume in one second (FEV_1); forced expiratory flow between 25% and 75% of forced vital capacity ($FEF_{25-75\%}$); expiratory reserve volume (ERV); FEV_1/FVC ratio; arterial oxygen tension (PaO_2); arterial carbon dioxide tension ($PaCO_2$) and arterial oxygen saturation (SaO_2).

Results: Reduction of ascites through treatment with diuretics, with or without paracentesis, resulted in marked improvement in pulmonary volume.

Conclusion: We concluded that, in patients with portal hypertension and ascites, there is a decrease in pulmonary volume in comparison to predicted values, and that this condition improves significantly after successful treatment of ascites. Similarly, we observed an increase in arterial oxygen pressure and arterial oxygen saturation after ascites reduction.

Key words: **Ascites/therapy. Hypertension, portal. Respiratory function tests.**

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Abbreviations used in this paper:

TLC	– Total lung capacity
FVC	– Forced vital capacity
COPD	– Chronic obstructive pulmonary disease
RLD	– Restrictive lung disease
$FEF_{25-75\%}$	– Forced expiratory flow between 25% and 75% of forced vital capacity
ISCMSP	– Irmandade da Santa Casa de Misericórdia de São Paulo
$PaCO_2$	– Arterial carbon dioxide tension
PaO_2	– Arterial oxygen tension
SaO_2	– Arterial oxygen saturation
FV	– Flow volume
FEV_1	– Forced expiratory volume in one second
V/Q	– Ventilation/perfusion ratio
RV	– Residual volume
ERV	– Expiratory reserve volume

INTRODUCTION

Hepatic cirrhosis is the main cause of portal hypertension and ascites. Ascites is found in 50% of cirrhotic patients by approximately 10 years after they have been diagnosed with compensated cirrhosis.[1-3]

Various changes can be detected by pulmonary function tests in patients diagnosed with chronic hepatic diseases, mainly in those diagnosed with cirrhosis. These changes, which characterize the "hepatopulmonary syndrome" result in hypoxemia and affect one-third of all patients diagnosed with cirrhosis.[4]

In patients diagnosed with cirrhosis, inadequate oxygenation is caused by various physiopathological mechanisms, such as inadequate vascular tonus, pulmonary vasodilation, altered ventilation/perfusion (V/Q) ratio, more arterial-venous shunts, and changes in the diffusion/perfusion ratio.[4-9]

In addition to the expected changes in cirrhotic patients, we can observe restrictive and obstructive changes in pulmonary function tests when there is ascites.[10] The hypoxemia and decreased pulmonary volume seen in such cases improves after the ascites has been reduced.[11-15]

The increased intra-abdominal volume and pressure caused by the ascites results in decreased lung expansion, and consequent hypoventilation, mainly in the lung bases. Together with the interstitial edema seen in cirrhotic patients, alveolar collapse and microatelectasis may also occur, a situation which could explain the changes in spirometry and blood gas analysis [10].

Therefore, ascites, especially when severe and when combined with cirrhosis, impairs pulmonary function in patients with portal hypertension. The nature and degree of this impairment varies depending upon the etiology of the ascites. This study evaluates and quantifies the effect that reducing ascitic fluid has on the pulmonary function of patients diagnosed with portal hypertension.

METHODS

Using spirometry and blood gas analysis, we evaluated pulmonary function in adult male and female patients diagnosed with portal hypertension and ascites and admitted to the Central Hospital and to the Hospital São Luiz Gonzaga between March 1996 and October 2000. Both institutions operate under the auspices of the Irmandade Santa Casa de Misericórdia de São Paulo (ISCMSP).

All patients were admitted to the study group after having the proposed treatment fully explained and agreeing to be submitted to spirometry and blood gas analysis.

Exclusion criteria included: history of prior heart and lung diseases, unstable hemodynamics, neoplasias, renal insufficiency with serum creatinine values > 3.5 mg/dL, gastrointestinal hemorrhage, encephalopathy, bacterial peritonitis, and difficulty to cooperate during the spirometric exam. Smokers were included in the group only when they presented no clinical or radiograph signs of prior pulmonary impairment.

In all of the patients studied, chest radiographs were normal, although decreased lung expansion (due to abdomen volume increase) was observed.

In the cirrhotic patients studied, severity of the cirrhosis was determined by using the Child-Pugh classification system (Chart 1).

All patients presented with moderate to severe ascites, which was characterized by physical examination and tomography. Large volume ascites was diagnosed by simple abdomen examination. Ascites with increased abdominal wall tension was diagnosed through palpation. Ascites causing respiratory distress, especially when in supine position was confirmed through sonograms evidencing large volume ascites.

All patients were submitted to pulmonary function tests before and after treatment for ascites. The clinical treatment prescribed included rest, salt restriction (2 g/day) and diuretics. The chosen diuretic was spironolactone, combined with furosemide in some cases. Patients were not submitted to pulmonary physiotherapy.

Therapeutic paracentesis was performed in patients diagnosed with ascites and presenting signs and symptoms of respiratory distress or abdominal discomfort, as well as in patients who were not responding well to the clinical treatment with diuretics (good response = continuous weight loss of ± 500g/day).

A mean volume of 6.5 L of ascitic fluid was removed from each patient, with a parenteral replacement of 1 plasma unit (300 mL) for every 2 liters of drained fluid. Patients were submitted to spirometry on the day following paracentesis.

Spirometric tests were performed in the Pulmonary Function Tests Laboratory of the ISCMSP using the MedGraphics Breeze Cardiorespiratory Diagnostic Software, system 1070 (Medical Graphics, St. Paul, MN, USA), a 2.15 Koko spirometer (PDS Instrumentation, Louisville, CO, USA) and a model 113 pH/blood gas analyzer (Instrumentation Laboratory, Lexington, MA, USA).

The methodology used in the test and the parameters analyzed are in accordance with the guidelines set forth by the Brazilian Consensus on Spirometry (routine determined by the Pulmonary Function Tests Laboratory in the Santa Casa de São Paulo).

The parameters analyzed were forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), forced expiratory flow between 25% and 75% of forced vital capacity ($FEF_{25-75\%}$), expiratory reserve volume (ERV) and the FEV_1 to FVC ratio.

Slow vital capacity (SVC) was used to evaluate volume and lung capacity. The adopted predictive values were those suggested by Crapo.[16]

The volume-time curves (forced spirometry) were produced according to the acceptability and reproducibility criteria established by the American Thoracic Society. Of a total of 8 curves, the best of 3 acceptable curves was chosen. The predictive values were those suggested by Knudson.[17]

The flow-volume curves were also submitted to the acceptability and reproducibility criteria of the ATS and the best of 3 acceptable curves was also chosen. An envelope curve was also created.

In patients who were submitted to arterial blood gas tests, the parameters analyzed were arterial oxygen tension (PaO_2), arterial carbon dioxide tension ($PaCO_2$), and arterial oxygen saturation (SaO_2).

Results from the studied variables were analyzed using the paired Student's *t*-test. Values of $p < 0.050$ (5%) were considered statistically significant.

RESULTS

Of the 15 patients with portal hypertension and ascites analyzed, 9 (60%) were male and 6 (40%) were female. Ages ranged from 31 to 67 (mean, 51 ± 9.5). The most common diagnosis was alcoholic liver cirrhosis, which was found in 5 (33.3%) of the patients studied. Portal hypertension combined with hepatitis B, hepatitis C or schistosomiasis was diagnosed in 9 (60%) of the patients (Table 1), a history of prior alcoholism was reported in 10 (67%), and 5 (33.3%) were smokers.

According to the Child-Pugh classification system, which was applied in 13 of the patients, our study group was mainly composed of class B patients (11 patients; 84.6%). Only 2 patients (15.4%; patients 1 and 3, who were diagnosed with schistosomiasis) belonged to class C. None scored low enough to be considered class A.

Twelve patients were submitted to therapeutic paracentesis, and, on average, 6.5 L of ascitic fluid were removed. Average weight loss within the group was 6.9 kg. Three patients had excellent response to the clinical treatment, with substantial reduction of abdominal volume and an average weight loss of 6.4 kg. They were submitted to a second battery of spirometric tests without the need for therapeutic paracentesis. Spirometric results can be seen in Table 2.

Prior to paracentesis or clinical therapy, FVC values were lower than the predicted mean values. After treatment, these numbers improved. This was also true of FEV_1 values. There were no statistically significant differences in FEV_1/FVC ratios after treatment. The $FEF_{25-75\%}$ values were also lower than the predictive mean before paracentesis or clinical treatment and increased after treatment, although the increase was not statistically significant. There was, however, a statistically significant improvement in ERV values after treatment. Table 3 summarizes the main variables analyzed and their significance.

Six patients were submitted to blood gas tests. Prior to paracentesis, mean $PaO_2 = 68 \pm 17$ mmHg, mean $PaCO_2 = 32 \pm 17$ mmHg; and mean $SaO_2 = 92 \pm 6\%$. After paracentesis, mean $PaO_2 = 76 \pm 17$ mmHg, mean $PaCO_2 = 29 \pm 5$ mmHg and mean $SaO_2 = 94 \pm 4\%$. The increases in PaO_2 and SaO_2 attained a level of statistical significance (Table 3).

DISCUSSION

Even though the number of patients studied was small, we observed a higher prevalence of male patients diagnosed with alcoholic liver cirrhosis. This is in accordance with data found in the literature.[1,2,18]

According to various studies,[4,9,19,20] the pulmonary changes seen in cirrhotic patients are closely related to the degree of hepatic involvement. This is important for the interpretation of the results in our study, since most of our patients were cirrhotic (60%), suffering from moderate to severe forms of the disease (Child-Pugh scores of B or C in 13 patients; 86.66%). These patients could present with pulmonary manifestations due to the baseline disease, as well as with other symptoms caused by the ascites-induced increase in intra-abdominal pressure.

We observed a higher prevalence of chronic obstructive pulmonary disease (COPD; 8 patients; 53.32%), whereas other authors have reported a higher prevalence of restrictive lung disease (RLD).[10,14,21-,23]

According to Yao et al.,[10] ascites causes elevation of the diaphragm, with lung volume reduction and increased intrathoracic pressure. This, together with the pulmonary edema found in cirrhotic patients, may result in pulmonary tissue compression and the attendant microatelectasis, which are responsible for the hypoxemia and restrictive pattern observed in the pulmonary function tests. Similarly to our study, Yao et al.[10] also reported COPD and concluded that this may be related to the degree of hepatic involvement. In patients with more severe hepatic disease, there is greater interstitial lung edema and therefore more extensive involvement of alveoli and bronchioles, causing premature closure of the airways during expiration, as well as obstructive disorders.

According to Chao et al.,[21] the effects of ascites on the respiratory system are probably mediated by the hydrostatic pressure exerted on the diaphragm. Under these circumstances, the extent to which gas exchange is altered is closely related to lung volume reduction.

Since only 3 of the 8 patients with obstructive defects were smokers, we were unable to establish a correlation between smoking and COPD. We believe, in agreement with Yao et al.,[10] that pulmonary changes due to severe chronic hepatic disease alone can better explain our findings.

In evaluating the pulmonary function of cirrhotic patients with and without ascites, Ordialez Fernandez et al.[22] observed restrictive patterns and reduced ERV. When respiratory muscle force was measured in patients with and without ascites, the authors found decreases in the evaluated parameters, indicating that the accessory muscles in the chest wall were less effective, which could have contributed to the functional changes observed.

In concordance with our findings, most studies in the literature show that FVC, FEV_1, ERV, and functional residual capacity decrease before and increase after paracentesis.[10,12,14,15,21,24]

In some patients, we observed that spirometric results returned to normal after paracentesis or after clinical treatment with diuretics, demonstrating that reduction of ascites improves respiratory parameters.

There were no significant differences between pretreatment and posttreatment FEV_1/FVC ratios. This indicates that the increase in FEV_1 was proportional to the FVC increase, approximating the predicted value of 80%. Such decreases in FEV_1 and FVC, together with FEV_1/FVC ratios remaining at the predicted value, are seen in RLD and could therefore be related to the obstructive disorders observed in our patients.

The small decrease in $FEF_{25-75\%}$ found before treatment may be related to the bronchiolar involvement and lung compression, involving premature narrowing of the small airways, which can occur in patients with hepatic diseases and ascites.

In our study, ERV values were markedly below normal prior to ascites treatment. In accordance with previous studies, we observed significant improvement after treatment. We also believe that the lower intra-abdominal pressure resulting from reduction of the ascites volume was responsible for the ERV improvement.[11,14,22]

According to Chao et al.,[21] ascites may impair pulmonary perfusion by reducing blood flow in the lung bases, which are mechanically compressed, thereby aggravating hypoxemia in cirrhotic patients. Some studies have reported hypoxemia in patients with ascites prior to the treatment and considerable improvement in PaO_2 after therapy with diuretics.[15,23] According to the authors, the use of diuretics may reduce interstitial lung edema and yield a more favorable V/Q ratio.

In the present study, we observed mild hypoxemia, which improved after treatment. There was also improvement in SaO_2 after the reduction of ascites, but $PaCO_2$ was unaffected. Increased lung volume, combined with improved pulmonary ventilation, may have contributed to better oxygenation. All patients were prescribed diuretics during the study and this may have contributed to PaO_2 improvement, in accordance with the previously cited studies.

In summation, the reduction of ascites volume significantly improved pulmonary ventilation in the patients evaluated in this study. Therapeutic paracentesis seems to be an alternative treatment for rapid relief of symptoms such as dyspnea and abdominal discomfort, or for patients who do not satisfactorily respond to diuretic therapy.

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CHART 1
Child – Pugh classification

Variable	Score		
	1 points	2 points	3 points
Encephalopathy	Absent	Mild to moderate	Severe to coma
Ascites	Absent	Slight	Moderate
Bilirubin (mg/dl)*	<2	2–3	>3
Albumin (g/L)	>3.5	2.8–3.5	<2.8
Prothrombin time (sec above normal)	1–4	4–6	>6

If the total score if 5 or 6, The cirrhosis is designated class A; if the score is 7 to 9, the cirrhosis is class B; if the score is 10 or higher, the cirrhosis is class C. The prognosis is directly related to the score. Adapted from Pugh et al.
** To convert values for bilirubin to micromoles per liter, multiply by 17.1.*

Courtesy of the New England Journal of Medicine. From: Gastrooesophageal Variceal Hemorrhage; Shahara AI and Rocky DC; NEJM 345 (9), 30 august 2001, p669-681

TABLE 1
Frequency distribution according to etiological diagnosis in patients evaluated between March, 1996 and October, 2000 at the ISCMSP

Diagnosis	*Number of patients*	*(%)*
Alcoholic cirrhosis	5	33.33
Schistosomiasis (SS)	2	13.33
Alcoholic cirrhosis and SS	1	6.66
Alcoholic cirrhosis and hepatitis C virus	2	13.33
Alcoholic cirrhosis and hepatitis B virus	1	6.33
Cirrhosis caused by hepatitis B virus	1	6.33
Cryptogenic cirrhosis	2	13.33
Portal vein thrombosis	1	6.33
Total	15	100

TABLE 2
Spirometric results prior to and after paracentesis or clinical treatment of ascites in patients evaluated between March, 1996 and October, 2000 at the ISCMSP

Patient	*Pre-treatment*	*Post-treatment*
1	COPDSA	COPDSA
2	COPDSA	NL
3	COPDSA	COPDSA
4	NL	NL
10	MLD	NL
11	MdCOPD	MCOPD
12	MCOPD	NL
13	MCOPD	NL
14	MCOPD	MCOPD
15	MLD	MLD
16	RLD	NL
17	MLD	MCOPD
18	RLD	NL
19	MCOPD	NL
20	NL	NL

Source: Pulmonary Function Tests, Laboratory of Santa Casa de São Paulo; NL: Normal; COPD: Chronic obstructive pulmonary disease; MCOPD: mild COPD; MdCOPD: moderate COPD; COPDSA: COPD in the small airways; RLD: restrictive lung disease; MdRLD: moderate RLD; MLD: mixed lung disease

TABLE 3
Comparison of spirometric variables and blood gas tests before and after paracentesis or clinical treatment of ascites

VARIABLE	*Mean and Standard Deviation BEFORE*	*Mean and Standard Deviation AFTER*	*p value*
FVC (L)	2.67±0.67	3.13±0.83	*0.002
FVC (%)	82.40±17.00	97.53±12.51	*0.001
FEV_1 (L)	2.10±0.53	2.45±0.61	*0.001
FEV_1 (%)	78.33±19.59	93.80±16.74	*< 0.001
FEV_1/FVC (%)	78.07±10.02	78.40±7.58	0.727
$FEF_{25-75\%}$ (L/sec)	2.12±1.00	2.35±0.85	0.127
$FEF_{25-75\%}$ (%)	75.40±38.94	83.87±33.43	0.170
ERV (L)	0.73±0.34	1.0 ±0.50	*0.019
ERV (%)	73.27±40.60	100.00±37.42	*0.033
PaO_2 (mmHg)	68.25±16.63	75.84±17.01	*0.027
$PaCO_2$ (mmHg)	31.95±7.89	28.70±4.59	0.217
SaO_2 (%)	91.71±5.99	94.32±4.18	*0.032

Test: paired Student's *t*-test; source: Pulmonary Function Tests, Laboratory of Santa Casa de São Paulo
FVC: forced vital capacity; $FEV_{1:}$ forced expiratory volume in one second; $FEF_{25-75\%}$: forced expiratory flow between 25 and 75% of forced vital capacity; ERV: expiratory reserve volume; PaO_2: Arterial oxygen tension; $PaCO_2$: Arterial carbon dioxide tension; SaO_2: arterial oxygen saturation
*significant