Changes in Pulmonary Functions in Children in Response to Pulmonary Hypertension Associated with Cardiac Diseases in Suez Canal Area in Egypt

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Abstract

Introduction: Alteration in pulmonary blood flow and respiratory mechanics are always present in infant and children with heart disease. We aimed to study the respiratory functions in subjects suffering from pulmonary arterial hypertension (PAH) associated with either congenital heart disease (CHD) or rheumatic heart disease (RHD).

Methods: 90 children were enrolled in this study. 30 children with CHD associated with PAH, 30 children with RHD associated with PAH and 30 normal control age matched children. Echocardiography was performed for calculating the systolic pulmonary artery pressure (SPAP). Spirometry was performed to evaluate pulmonary function: Forced vital capacity (FVC), forced expiratory volume in the first second (FEV1), FEV1/FVC and forced expiratory flow (FEF). Complete history, clinical examination and ECG were also performed for each subject before doing the echocardiography and pulmonary function test.

Results: The mean pulmonary arterial blood pressure (PABP) in the children with PAH was higher significantly in comparison to control group (p<0.0001). All pulmonary functions tests in the children suffering from cardiac diseases associated with PAH were lowered significantly in comparison to control group (p<0.0001). However, there were no statistically significant differences between children with CHD in comparison to RHD. The mean PABP of the children with restrictive and mixed patterns of pulmonary functions was higher significantly in comparison to obstructive ones. There were significant negative correlations between PABP and FVC (r=-0.386, p=0.003).

Conclusion: Deterioration of Pulmonary function tests is characteristic in children suffering from pulmonary hypertension, either due to CHD or RHD. Restrictive pattern is the most common respiratory abnormality accompanying PAH, followed by the mixed then the obstructive patterns.

Key Words: Pulmonary functions — Pulmonary hypertension — Cardiac diseases — Children — Suez Canal area — Egypt.

Introduction

CHD are the most common category of birth defect, occurring in 6.6 to 8.1 per 1000 live births, approximately 25% of these lesions are associated with cyanosis. Congenital heart defects associated with increased blood flow through the lung include; patent ductus arteriosis (PDA), atrial septal defects (ASD) and ventricular septal defects (VSD), and those associated with decreased blood flow through the lung include; tricuspid atresia, pulmonary atresia and Tetralogy of Fallot (TOF) III.

RHD is acquired heart disease and the most serious complication of rheumatic fever. As many as 39% of patients with acute rheumatic fever may develop varying degrees of pancarditis with associated valve insufficiency, heart failure and even death. With chronic RHD, patients develop valve stenosis with varying degrees of regurgitation, atrial dilatation and ventricular dysfunction. The mitral valve is most commonly and severely affected (65-70% of patients), the aortic valve is second in frequency (25%), the tricuspid valve is deformed in only 10% of patients and is almost always associated with mitral and aortic lesions [2].

Acute rheumatic fever (ARF) remains a major problem in tropical regions [3]. Estimations worldwide are that at least 15.6 million children and young adults have rheumatic heart disease, and 233,000 patients die from this disease each year [4].

Pulmonary hypertension is categorized as pulmonary venous hypertension and pulmonary hypertension due to left to right shunt. Pulmonary venous hypertension is the most common form and usually due to left-sided heart disease. It develops as a result of the obstruction of blood flow down-
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stream from the pulmonary veins. Causes of pulmonary venous hypertension include; coarctation of the aorta, aortic stenosis, aortic regurgitation (AR), mitral stenosis (MS) and mitral regurgitation (MR). Individuals with pulmonary hypertension due to left to right shunt have high blood flow to the pulmonary vessels which leads to increased pulmonary vascular resistance over time and includes; PDA, VSD and ASD [5].

Cardiorespiratory interaction occurs because the pulmonary and systemic circulation are in series and the lung and chest wall physically surround the heart and the great vessels exposing them to intra-thoracic pressure. As a result of this intimate relationship, the cardiovascular and respiratory systems should be considered to function as one unit (the cardiorespiratory system). Alteration in pulmonary blood flow and respiratory mechanics from cardio respiratory interactions are exaggerated in infant and children with heart disease [6].

Assessment of lung function in children is considered an important diagnostic and prognostic tool regarding lung diseases Pulmonary function tests are a group of tests that measure how well the lungs take in and release air and how well they move oxygen into the blood by Spirometer. In Spirometry test the patient breathes into a mouth piece that is connected to the Spirometer and records the amount and the rate of air that the patient breathes in and out over a period of time. Pulmonary function tests are helpful in defining the type of process (e.g. Obstruction or restriction), defining the degree of functional impairment, estimating the prognosis of different pulmonary diseases, pre-operative evaluation, confirmation of functional impairment in patients having subjective complains but normal physical examination [7].

The aim of our research was to study the changes in respiratory functions in children suffering from either CHD or RHD associated with PAH in Suez Canal Area in Egypt.

Patients and Methods

90 children aged between 5 to 18 years were enrolled in this study. They were grouped as follows: Group I, children with CHD associated with PAH; Group II, children with RHD associated with PAH and Group III, normal control age matched children from Suez Canal area in Egypt.

Selection criteria: For the first two groups included children selected from the cardiology unit of pediatric clinic, Suez Canal University Hospital, Ismailia, Egypt during 2012, diagnosed as having chronic heart disease (congenital or rheumatic) associated with PAH by history, examination, ECG and echocardiography. Meanwhile children having current rheumatic activity, heart failure, acute or chronic pulmonary disease, airway anomalies or genetic abnormalities were excluded. All the subjects were able to successfully perform the required respiratory function tests in an acceptable and reliable technique.

Echocardiographic findings: Systolic pulmonary artery pressure (SPAP) was considered the same as the right ventricular systolic pressure (RVSP) in the absence of obstruction to right side flow (pulmonic valve stenosis or outflow tract obstruction). RVSP was generated using Doppler echocardiography by calculating the right ventricular to right atrial pressure gradient during systole using modified Bernoulli equation 4v², in which v is the velocity of the tricuspid jet in meters per second. RVSP was calculated by adding the estimation of right atrial pressure (RAP) to the gradient (RVSP=4v²+RAP). The RAP used was either a standardized number for some centers or based on echocardiographic characteristics of the inferior vena cava [8].

Spirometry testing: The following pulmonary function parameters were measured: Forced vital capacity (FVC), forced expiratory volume in the first second (FEV1) & FEV1/FVC. These were performed using pulmonary function analyzer: "Spirosift sp-5000 device with pneumotach". Signals detected were measured by the instrument microcomputer and plotted in the form of "real time data" and graphic analysis. Testing was performed in a calm, quiet and free from distraction atmosphere. Acceptable test required good start (omitting tests with slow rise in flow), no early termination, no variable flows and no coughing. The best trial was obtained from an average of three trials. Parameters evaluated were expressed as a percentage of the predicted value for age, sex, height and weight. Pulmonary functions obtained were classified to either normal, obstructed airways, restricted process or mixed (obstructed and restricted) patterns, according to table of expected patterns of pulmonary functions (Table 1).

Consents were taken from all parents before taking any data or doing any tests. All data were considered confidential and is not going to be used outside this study without patient’s approval.
Table (1): Expected patterns of pulmonary function test [9].

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Normal</th>
<th>Obstruction</th>
<th>Restriction</th>
<th>Mixed</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC</td>
<td>80% of predicted</td>
<td>Normal or slightly decreased</td>
<td>Severely decreased</td>
<td>Decreased</td>
</tr>
<tr>
<td></td>
<td>(70 to 80% of predicted)</td>
<td>(&lt;70% of predicted)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FEV1/FVC</td>
<td>75-85% of predicted</td>
<td>Severely decreased</td>
<td>Normal or increased</td>
<td>Decreased</td>
</tr>
<tr>
<td></td>
<td>(&lt;60% of predicted)</td>
<td>(&gt;85% of predicted)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Statistical analysis:

Data collected throughout: History, clinical examination and pulmonary functions were coded, entered and analyzed using Microsoft Excel software. Data was then imported into SPSS (statistical package for social sciences) software program version 10.0 for analysis. According to the type of data, Chi square and t-test were used with lesser significance difference (p<0.05) to test differences for significance.

Results

The mean age of the patients was 12.41±3.58 years, while the mean age of the control was 11.9±4.08 years. Both sexes were equal in the control group (50% each). There were no statistically significant differences between children with PAH and healthy control regarding age and sex (p>0.05). The mean age of the children with RHD was significantly higher than children with CHD (14.93 vs. 9.79 years, respectively) (p<0.0001). Sixty percent of CHD patients were males and 40% of them were females, whereas 36.7% of RHD patients were males and 63.3% of them were females. The frequency of males was significantly higher in children with CHD in comparison to children with RHD, while the frequency of females was significantly higher in children with RHD than children with CHD (p=0.001).

In our study population we could not find any statistically significant differences between children with PAH and healthy control regarding weight and height (p>0.05). Meanwhile, the mean weight and height of the children with RHD was significantly higher compared to children with CHD (54.93kg, 152.67cm vs. 36.2 lkg, 132.86cm, respectively) (p<0.0001) (Table 2).

The most frequent congenital defect detected in this study was VSD (43.3%), followed by PDA and ASD (23.3% and 20%, respectively). The most frequent valvular affection detected in this study was MR (40%), followed by MS-MR (26.7%) and AR-MS (20%) (Figs. 1, 2).

The mean pulmonary arterial blood pressure (PABP) in the children with PAH was higher significantly than in healthy children (42.07 vs. 21.35 mmHg, respectively) (p<0.0001). There was no statistically significant difference between children with CHD and RHD regarding mean PABP (41.028 vs. 42.07mmHg, respectively) (p>0.05).

The results of pulmonary function tests of the studied patients and healthy controls are shown in Table (3). The mean FVC, FEV1, FEV1/FCV ratio and the mid-flow rate or forced expiratory flow occurring in the middle 50% of the patient’s exhaled volume (FEF25-75%) were measured in both groups. All pulmonary function tests in the children with PAH was lower significantly than healthy children (p<0.0001).

There were no statistically significant differences between children with CHD and RHD regarding the results of pulmonary function tests (p>0.05) (Table 4).

The total number of patients with restrictive pattern of pulmonary functions was higher than obstructive ones in all different degrees of pulmonary arterial blood pressure in both CHD and RIM patients. There were no statistically significant differences between children with obstructed, mixed and normal patterns of pulmonary functions regarding mean PABP (p>0.05). The only statistically significant difference was between children with restrictive and children with normal patterns of pulmonary functions regarding categories of PABP (p=0.012) (Tables 5, 6).

Restrictive pattern of functions was present in 65% of all PAH children, obstructive pattern was present in 20%, mixed pattern was present in 5% and 10% of the children show normal pulmonary functions (Fig. 3).

There were significant negative correlation between PABP and FVC (r=-0.386, p=0.003). This means that children with higher PABP had lower FVC (Fig. 4). The other pulmonary variables such as FEV1 and FEV1/FCV showed insignificant correlations (p>0.05).
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Table (2): Anthropometric measurements of CHD and RHD groups.

<table>
<thead>
<tr>
<th>Variable</th>
<th>CHD (n=30)</th>
<th>RHD (n=30)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight</td>
<td>36.21 ± 12.04</td>
<td>54.93 ± 8.61</td>
<td>&lt;0.0001*</td>
</tr>
<tr>
<td>Height</td>
<td>132.86 ± 13.28</td>
<td>152.67 ± 12.17</td>
<td>&lt;0.0001*</td>
</tr>
</tbody>
</table>

*Significant p-value at <0.05.

Table (3): Results of pulmonary function tests of the studied patients and healthy control.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Total PAH (n=60)</th>
<th>Control (n=30)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC</td>
<td>64.47 ± 11.63</td>
<td>65.45 ± 6.07</td>
<td>&lt;0.0001**</td>
</tr>
<tr>
<td>FEV1</td>
<td>63.76 ± 15.07</td>
<td>90.75 ± 7.30</td>
<td>&lt;0.0001**</td>
</tr>
<tr>
<td>FEV1/FVC</td>
<td>98.95 ± 19.04</td>
<td>105.35 ± 9.71</td>
<td>0.035*</td>
</tr>
<tr>
<td>FEF25-75</td>
<td>71.22 ± 19.56</td>
<td>102.00 ± 7.88</td>
<td>&lt;0.0001**</td>
</tr>
</tbody>
</table>

*Significant p-value at <0.05.

Table (4): Results of pulmonary function tests of the studied patients.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>CHD (n=30)</th>
<th>RHD (n=30)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC</td>
<td>64.45 ± 11.62</td>
<td>64.50 ± 11.84</td>
<td>0.99</td>
</tr>
<tr>
<td>FEV1</td>
<td>63.24 ± 15.23</td>
<td>64.27 ± 15.17</td>
<td>0.78</td>
</tr>
<tr>
<td>FEV1/FVC</td>
<td>98.62 ± 20.04</td>
<td>99.27 ± 18.37</td>
<td>0.89</td>
</tr>
<tr>
<td>FEF25-75</td>
<td>73.90 ± 19.50</td>
<td>68.63 ± 19.59</td>
<td>0.30</td>
</tr>
</tbody>
</table>

Table (5): Mean PABP according to patterns of pulmonary functions.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Restrictive (n=39)</th>
<th>Obstructive (n=12)</th>
<th>Mixed (n=3)</th>
<th>Normal (n=6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean PABP</td>
<td>44±10.2</td>
<td>38.2±2.7</td>
<td>41.7±2.9</td>
<td>39.3±5.3</td>
</tr>
</tbody>
</table>

Table (6): Mean PABP according to the patterns of pulmonary function results in both types of cardiac lesions.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Restrictive (n=39)</th>
<th>Obstructive (n=12)</th>
<th>Mixed (n=3)</th>
<th>Normal (n=6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHD RHD</td>
<td>25&lt;45mmHg (14)</td>
<td>65&lt;75mmHg (6)</td>
<td>40-45mmHg</td>
<td>&gt;45mmHg</td>
</tr>
<tr>
<td>CHD RHD</td>
<td>45-60mmHg (7)</td>
<td>60-70mmHg (8)</td>
<td>30-40mmHg</td>
<td>&gt;70mmHg</td>
</tr>
</tbody>
</table>

(No) is the number of subjects.
Discussion

Peripheral airways affection follows the pulmonary vasculature, so, it is reasonable to postulate that pulmonary function might be affected by the development of PHT. However, previous studies of pulmonary function in pulmonary hypertension have been contradictory, with normal lung volumes, restrictive ventilator pattern, and airway obstruction [10].

The mean age of our patients with RHD was higher significantly than children with CHD (14.93 vs. 9.79 years respectively). This was expected because congenital diseases are present since birth so its complications as pulmonary hypertension will happen earlier than the complication of rheumatic heart diseases which occurs relatively later in the childhood period [11,12].

In our study and in another study done by Van Albada ME [13], it was found that the mean weight of the children with RHD was higher significantly compared to children with CHD. Also same observation was found in a study done by Varan et al. [12], who found that patients with CHD are prone to malnutrition and growth failure, and pulmonary hypertension appears to be the most important factor, and cyanotic patients with pulmonary hypertension are the ones most severely affected. This was expected because CHD are a group of chronic disease starting very early in life so its effect on growth is more than the effect on RHD on growth which usually starts later in life. Benn et al. [11], stated that RHD probably has no inhibition effect on the growth of children once the infection has subsided.

Our study revealed that there were no statistically significant differences between children with CHD and RHD regarding the results of pulmonary functions tests (p>0.05). The same observations were found by Jing et al. [14]. They reported that lung volumes such as FVC, FEV1 were reduced (67.34% of predicated, 62.27% respectively) in CHD and RHD- PAH patients compared with controls.

The mean FVC, FEV1, and FEF25-75 in the children with PAH were lower significantly than healthy children. These findings indicate that the early pattern of impairment in pulmonary function in these patients is usually the restrictive type caused by lung stiffness and reduced compliance secondary to increased pulmonary pressure. With the time, there is more increase in pulmonary congestion with edema of bronchial mucosa. More cardiac enlargement with its compressing effect and more left ventricular dysfunction cause impaired respiratory muscle perfusion. All of which add an obstructed element. Thus a combined pattern of impaired pulmonary function can ensue [15].

We found significant negative correlation between PAP and FVC (r=-0.386, p=0.003). This could be explained as progressive medial hypertrophy and intimal proliferation of pulmonary blood vessels might decrease lung distensibility and result in lower lung volume measurements. The same observation was found by Leonard et al. [16] They found that children with congenital heart disease with severe pulmonary hypertension demonstrated significant reduction in FVC Changes appeared to correlate with degree of pulmonary hypertension than with specific lesion or size of shunt. In contrast, Jing et al. [14] found that no hemodynamic measurements (PAP) or capacity parameters correlated well with pulmonary function indices.

Conclusion:

Lung compliance is affected in children suffering from pulmonary hypertension. This is proved by the restrictive pattern associated with most of the patients of the study. Mixed and restrictive patterns were less common. Deterioration of the Pulmonary function tests are correlated to the severity of the pulmonary hypertension. Being easy and reliable tests, pulmonary functions can be introduced among the follow-up tools in children with pulmonary hypertension either diagnosed as CHD or RHD.

References

1- Rectors and visitors of the University of Virginia. University of Virginia health system, last modified on Jan., 24: 434-924, 2008.


