Original Article

Spirometric Assessment in Juvenile Idiopathic Arthritis

Md. Mahboob Alam1*, Biman Ray2, Sumantra Sarkar3, Oona Mandal2 and Rakesh Mondal4

1Department of Physiology, Institute of Post Graduate Medical Education & Research, Kolkata
2Department of Physiology, Malda Medical College, Malda
3Department of Pediatrics, Institute of Post Graduate Medical Education & Research, Kolkata
4Department of Pediatrics, Calcutta Medical College, Kolkata

Abstract

Objective: To estimate the prevalence of abnormal spirometry in Juvenile idiopathic arthritis (JIA) patients and to evaluate its relation with subtype, gender, disease activity and methotrexate therapy.

Methods: A cross-sectional study was carried out involving 5-12 years old JIA patients. Forced vital capacity (FVC), Forced expiratory volume in 1 second (FEV1), FEV1/FVC ratio, Forced expiratory flow between 25-75% of vital capacity (FEF25-75%) and peak expiratory flow rate (PEFR) were measured.

Result: Out of 33 patients, 18 were male. Six patients had oligoarthritis, 16 had polyarthritis and 11 had systemic JIA. Seventeen patients had clinically inactive disease and 16 received methotrexate. None had respiratory symptoms. Thirteen patients had decreased FVC with normal FEV1/FVC. One had decreased FEV1 and FEV1/FVC with normal FVC. Decreased FEF25-75% was found in 4 and decreased PEFR in 8 patients. JIA subtypes differed significantly with regard to prevalence of decreased FVC and FEV1.

Conclusion: Abnormal spirometry was present in 13 patients and affected all subsets in terms of subtypes, gender, disease activity and methotrexate therapy.

Keyword: Arthritis, Juvenile Idiopathic; Pulmonary Function Tests; Spirometry.

Introduction

Juvenile Idiopathic Arthritis (JIA) is the most common childhood rheumatic disorder. It comprises all forms of chronic arthritis of unknown etiology persisting for at least 6 weeks with onset prior to 16 years of age (1, 2). The disease is characterized by a fluctuating and ongoing course that varies over time, both between and within individuals. Extra-articular manifestations in the form of uveitis and growth failure are common but pulmonary involvement has also been described in JIA (3, 4). Some pathological and clinical similarities exist between JIA and adult rheumatoid arthritis (RA). While pulmonary
complication like interstitial lung disease affects 19-56% of adult RA patients in different studies, data on pulmonary function in JIA are sparse (5). However, there are few reports of pulmonary function abnormality and radiological evidence of parenchymal involvement in JIA (6, 7, 8).

Pulmonary involvement may be related to the illness itself, pre-existing any other lung disease, drugs used in treatment or secondary to infections amongst others (7, 9). Relation of pulmonary involvement with gender has not been elucidated so far, to the best of our knowledge. It is also not conclusively known whether spirometric abnormalities represent an early sign of progressive lung disease or whether they are just manifestation of disease activity. Decline in some pulmonary function parameters has also been observed with long-term methotrexate therapy (10).

This study was carried out to estimate the prevalence of spirometric impairment in JIA and whether this is more common in any subset in terms of subtype, gender, disease activity and methotrexate therapy.

**Methods**

This cross-sectional study was carried out from July 2013 through June 2014 in the Institute of Post-Graduate Medical Education & Research. Cases included all consecutive old and new JIA patients diagnosed on the basis of International League of Associations for Rheumatology (ILAR) criteria and attending the Rheumatology Clinic in the outpatient department of Pediatrics (1). New cases were followed up for at least 6 months to classify them into different subtypes as per ILAR criteria. Patients less than 5 years of age were not included because they usually fail to understand the instruction for spirometry (11). Those more than 12 years could not be evaluated because only up to the age of 12 years are treated in the pediatric outpatient department following the institutional policy. Patients with pre-existing chronic respiratory diseases, those having congenital defects like cleft lip and palate or having neuromuscular disorder or with history of surgery on head, neck or face or history of concurrent congenital heart disease were excluded from the study. Spirometry on patients having pneumonia, pleurisy or pleural effusion was done only after clinical and radiological resolution.

The study commenced after obtaining the clearance from the Institutional Ethics Committee. Written consent was taken from parents of the patients. Height was measured in the standing posture using a stadiometer. Weight was measured using a spring-type weighing machine properly serviced and calibrated. Readings were taken in kilogram. Clinically inactive disease was defined using American College of Rheumatology criteria (12). Laboratory parameters included complete blood count, serum for rheumatoid factor (RF) & antinuclear factor (ANF), erythrocyte sedimentation rate, C-reactive protein and chest X-ray. Spirometry was done using windows based digital spirometer, Spirowin version 2.0 and forced vital capacity (FVC), forced expiratory volume in 1 second (FEV1), FEV1/FVC ratio, forced expiratory flow between 25-75% of vital capacity (FEF 25-75%) and peak expiratory flow rate (PEFR) were measured. The procedure of spirometry was explained and demonstrated to the children. The nose was manually closed by the examiner while they were asked to take the maximal inspiration and then to blow into the mouthpiece as quickly, forcefully and maximally as possible. American Thoracic Society (ATS) criteria for acceptability and repeatability of spirometry as standardized by M. R. Miller et. al. were strictly followed (13). Individual spiromograms were considered acceptable if they had satisfactory start and satisfactory exhalation with adequate effort. On obtaining a minimum of three acceptable spiromograms, it was observed whether the two largest values of FVC were within 0.150 L of each other or not. The procedure was repeated until the two largest values of FVC were within 0.150 L of each other. Those with unacceptable spirometry and/or inadequate effort were excluded. Manoeuvre that showed largest sum of FVC and FEV1 was used (13). Predicted values for spirometric parameters of each patient were calculated from regression equations derived from a study in north India (14). Lower limit of normal for a parameter was calculated as its predicted value minus 1.645 times standard error of estimate (SEE) provided (15). FVC, FEV1, FEF 25-75% and PEFR were considered to be decreased.
if their values were below lower limit of normal. FEV1/ FVC was considered to be decreased if it was less than 70%.

GraphPad Prism version 5 [San Diego, CA: GraphPad Software Inc., 2007] were used for statistical analysis. The data were analyzed by Fisher’s exact test and Chi square test. P value less than 0.05 was considered significant.

Results

Initially 48 JIA patients were enrolled for the study. A total of 15 patients had to be excluded of which two had pre-existing asthma. Seven of them failed to perform acceptable spirometry while 6 failed to produce repeatable curve. Of the remaining 33 subjects included in the study, 18 were male and 15 were female. Mean age, height and weight of JIA patients were 9.48 years, 126.69 cm and 25.42 kg respectively. Categorization of subtypes of JIA patients showed that 6 had oligoarthritis, 4 had rheumatoid factor positive (RF-positive) polyarthritis, 12 had rheumatoid factor negative (RF-negative) polyarthritis and 11 had systemic JIA. Clinical and laboratory evaluation revealed inactive disease in 17 patients. 16 patients required methotrexate and of them 9 had active disease. Mean duration of the disease was 3.12 yrs. Mean duration of treatment with methotrexate was 358 days.

FVC was decreased in 13 patients with all having normal FEV1/FVC ratio. Of them 11 had decreased FEV1. Two oligoarthritis patients had decreased FVC but normal FEV1. One female systemic JIA patient had decreased FEV1 and FEV1/FVC ratio with normal FVC. Out of 12 RF-negative polyarthritis patients, 11 had normal FVC and FEV1 and 9 had normal PEFR. Only 4 patients had reduced FEF25-75% of which three had systemic JIA. One RF-negative polyarthritis patient had reduced FEF25-75% with normal FVC, FEV1 and FEV1/FVC ratio. There were 8 patients with decreased PEFR and 3 of them had normal FVC and FEV1. Three patients had reduced FVC, FEV1, FEF25-75% and PEFR with normal FEV1/FVC ratio. Figure 1 depicts minimum, 25th percentile, median, 75th percentile and maximum values of FVC, FEV1, FEF25-75% and PEFR in the form of box and whisker plot.

The Table I shows significant difference in abnormal spirometry among different subtypes. Decreased FVC and FEV1 were more common in male while PEFR was more commonly decreased in female patients as shown in Table II. A higher percentage of clinically inactive patients and those not receiving methotrexate

![Figure 1: Box and whisker plot showing minimum, 25th percentile, median, 75th percentile and maximum value of spirometry parameters of JIA patients.](image)

<table>
<thead>
<tr>
<th>Oligoarthritis (n=6)</th>
<th>RF-positive polyarthritis (n=4)</th>
<th>RF-negative polyarthritis (n=12)</th>
<th>Systemic arthritis (n=11)</th>
<th>Total (n=33)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decreased FVC 4 (66.67)</td>
<td>2 (50)</td>
<td>1 (8.33)</td>
<td>6 (54.55)</td>
<td>13 (39.39)</td>
<td>0.0468*</td>
</tr>
<tr>
<td>Decreased FEV1 2 (33.33)</td>
<td>2 (50)</td>
<td>1 (8.33)</td>
<td>7 (63.63)</td>
<td>12 (36.36)</td>
<td>0.0469*</td>
</tr>
<tr>
<td>Decreased PEFR 1 (16.67)</td>
<td>1 (25)</td>
<td>3 (25)</td>
<td>3 (27.27)</td>
<td>8 (24.24)</td>
<td>0.2475</td>
</tr>
</tbody>
</table>

p value obtained by Chi-square test for individual parameters, * indicates significance.
had decreased FVC and FEV1 as displayed in table 3 and 4 respectively. Overall, there was no significant difference in terms of prevalence of spirometric impairment between male and female, clinically active and inactive, methotrexate receiving and methotrexate non-receiving groups.

Discussion

Spirometric impairment has been documented in JIA in different studies but they show varying results regarding correlation of pulmonary function parameters with subtype and disease activity (7, 10, 16-18). Published data by the authors generated from a case control study had also demonstrated a significant spirometric alteration in JIA patients as a whole (19). In this study, 13 out of 33 (39%) patients had decreased FVC with normal FEV1/FVC ratio, suggesting possible restrictive defect. There was significant difference in prevalence of decreased FVC and FEV1 among different subtypes with 11 out of 12 RF-negative polyarthritis patients having normal FVC and FEV1. No significant difference in spirometric parameters was found between male and female and between clinically active and inactive patients. PEFR was also reduced in 8 (24%) patients. JIA patients might have some degree of muscle weakness resulting in lower PEFR value as reported in an earlier study (20).

Though short-term methotrexate therapy has been found to be safe in different studies, certain pulmonary function parameters are affected during its long-term use (10, 18). Methotrexate usage has also been reported to cause acute exacerbation of ILD in adult RA (21). In this study, mean duration of treatment with methotrexate was small (358 days) and no significant difference in terms of abnormal FVC and FEV1 was observed between those receiving and those not receiving methotrexate.

A limitation of the study is the small sample size. This is because of the narrow age window of the
patients included for this study. Since this was a cross-sectional study, it was not possible to find out whether there is any change in pulmonary function with duration and disease activity. Diffusing capacity for carbon monoxide (DLCO) could not be done due to lack of facility.

The normative spirometric data in the Bengali children is not yet available. The normal data for the north Indian children, from which lower limit of normal has been calculated might not be truly representative. This is another limitation of this study. But a study has shown approximation in spirometric data between North and East Indian population (22).

In conclusion, abnormal spirometry affected JIA in terms of subtypes, gender, disease activity and methotrexate therapy. A longitudinal multicentric study is needed to evaluate the course of spirometric impairment with duration and disease activity and the long-term effect of methotrexate therapy.

Acknowledgements

The authors express heart-felt gratitude to the postgraduate trainees of department of Pediatrics, I.P.G.M.E.&R., Kolkata for their unconditioned help.

References