Pulmonary Function and Exercise Challenge Test in Thai Children: 10 Years Post Respiratory Syncytial Virus Infection

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Abstract

Objective : To report the occurrence of asthma, pulmonary function and exercise challenge test abnormalities found in Thai children, who 10 years earlier had lower respiratory tract infection caused by respiratory syncytial virus (RSV-LRI).

Patients and Methods : 37 children, with RSV-LRI admitted at Ramathibodi Hospital during January 1986 through December 1987, were contacted, of whom 13 patients responded and completed history-review-questionnaires. Pulmonary function measurements at pre- and post-exercise and testing for bronchodilator response were performed.

Results : The occurrence of physician-diagnosed asthma in the patients with and without family history of allergic diseases was 75 per cent and 40 per cent, respectively. Of 11 patients who performed spirometry, 45 per cent had concave flow-volume curves, 36 per cent showed decreased ratio of forced expiratory flow in the first second (FEV_1) to forced vital capacity (FVC) and 27 per cent showed either decreased forced expiratory flow between 25-75 per cent of FVC ($FEF_{25-75\%}$) or peak expiratory flow rate (PEFR). Of 8 patients who completed exercise challenge tests, 87.5 per cent showed markedly decreased PEFR at post exercise challenge tests and 37.5 per cent had markedly decreased FEV_1. 62.5 per cent and 25 per cent showed markedly increased PEFR and FEV, respectively, after inhalation of bronchodilators.

Conclusion : This study suggests that the occurrence of asthma in children, who had previous RSV-LRI, is relatively high compared with that reported in general Thai children. Baseline pulmonary function tests showed evidence of airway obstruction as demonstrated by concave-shaped flow-volume curves, decreased FEV_1/FVC ratio, $FEF_{25-75\%}$ and PEFR. The presence of bronchial hyperreactivity to exercise challenge test and positive response to bronchodilators confirms the evidence of exercise-induced bronchospasm in children with history of RSV-LRI.

Key word : Pulmonary Function, Exercise Test, RSV

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Pneumonia is a leading cause of death in children under 5 years of age. In Thailand, 45 per cent of pneumonia in children under five were caused by viral infections and 45.2 per cent of these were respiratory syncytial virus (RSV) infection[1]. Lower respiratory tract infection caused by RSV (RSV-LRI) may lead to frequent hospitalization[2], apnea, pneumothorax, bronchial hyperreactivity, bronchiolitis obliterans, unilateral hyperlucent lung and chronic obstructive pulmonary disease in adulthood[3]. Most previous studies have shown evidence of abnormal pulmonary function tests (PFTs) indicating obstructive airway diseases and bronchial hyperreactivity after RSV infection[4-17].

In 1981, Stroke et al reported the increases in thoracic gas volume and inspired respiratory resistance in children who previously had acute bronchiolitis[6]. In 1982, Pullen et al reported the evidence of obstructive airway diseases from PFTs, 10 years after RSV infection[7]. In 1984, Hall et al showed evidence of decreased oxygen saturation and forced expiratory flow between 25-75 per cent of forced vital capacity ($FEF_{25-75\%}$)[8]. In 1993, Welliver et al found an abnormal methacholine challenge test and evidence of obstructive airway disease[9]. The objective of this study is to report the occurrence of asthma and the percentage of PFTs and exercise challenge test abnormalities found in Thai children, 10 years after RSV-LRI.

PATIENTS AND METHOD

This study is a cross-sectional, descriptive study. The patients with RSV-LRI, admitted at Ramathibodi Hospital during 1986 and 1987, were recruited from 49 patients with RSV-LRI participating in BOSTID project study on etiology and development of acute respiratory infections in Thai children[1]. Thirty-seven patients had complete address and of these 13 patients responded. Data were gathered from questionnaires and hospital records to determine the occurrence of physician-diagnosed asthma, wheezing and family history of allergic diseases. Baseline pulmonary function measurements were performed before exercise challenge tests. To achieve the maximal exercise level, patients were informed to exercise on a treadmill until their heart rates increased up to 189 beats per minute. Pulmonary function measurements were subsequently performed at 5, 10 and 15 minutes after exercise. Each patient received inhaled rapid acting bronchodilator, followed by a spirometric measurement to assess a bronchodilator response. We used the criteria of abnormal exercise challenge and positive bronchodilator response written in the exercise stress test protocol, 1994, Johns Hopkins Children's Center. The predicted values of all PFTs except peak expiratory flow rate (PEFR) were obtained from a study done in normal Thai children by Suwanjutha et al[18]. The predicted values of PEFR were obtained from a study by Hsu et al[19].

RESULTS

Thirteen patients with RSV-LRI were recruited. Eleven patients performed acceptable spirometry. Two patients were unable to perform spirometry due to mild to moderate mental retardation. Eight patients were able to complete exercise challenge tests. Three patients had oxygen desaturation during exercise and had to terminate the tests before they could achieve the maximal exercise level.

Among 13 patients, the mean age at onset of RSV-LRI was 1 1/12 years. The mean age at the last follow-up was 12 2/12 years. Male to female ratio was 5 to 8 (1:1.6). The clinical histories and previous respiratory illnesses obtained by the questionnaires and hospital records are shown in Table 1.

Table 1. Clinical histories and respiratory illnesses of 13 patients.

	N	%
Family history for allergic diseases	8	62
Physician-diagnosed asthma	8	62
Recurrent wheeze	8	62
History of exercise-induced bronchospasm	6	46
Breathing difficulties improved by bronchodilators	6	46
Presence of wheeze at onset of RSV infection	4	31
Parental smoking in house	5	39

Table 2. Baseline pulmonary function tests of 11 patients.

	N	%
Normal	6	55
FEV_1 < 80% of predicted value	1	9
FEV_1/FVC ratio < 80%	4	36
$FEF_{25-75\%}$ < 65% of predicted value	3	27
PEFR < 80% of predicted value	3	27
Concave flow-volume curve	5	45

Table 3. Exercise challenge test and bronchodilator response of 8 patients.

	N	%
Normal	1	12.5
Wheeze during and after exercise	0	0
Decreased $FEV_1 \geq 10\%$ at 5 or 10 or 15 min after exercise	3	37.5
Decreased PEFR $\geq 12.5\%$ at 5 or 10 or 15 min after exercise	7	87.5
Increased $FEV_1 \geq 10\%$ after bronchodilators	2	25.0
Increased PEFR $\geq 12.5\%$ after bronchodilators	5	62.5

The occurrences of physician-diagnosed asthma in children with and without a family history of allergic diseases were 6 of 8 (75%) and 2 of 5 (40%), respectively. This percentage is relatively high compared with the occurrence of asthma reported in general Thai children[20].

The results of PFTs were analyzed and interpreted by using the American Thoracic Society standard method. Of 11 patients, 6 (55%) had normal baseline PFTs, 5 (45%) had concave shape of flow-volume curves indicating variable intrathoracic airway obstruction, 4 (36%) showed decreased ratio of forced expiratory flow in the first second (FEV_1) to forced vital capacity (FVC) and 3 (27%) showed either decreased $FEF_{25-75\%}$ or PEFR, as shown in Table 2.

The results of exercise challenge testing are shown in Table 3. Of 8 patients, 7 (87.5%) showed significant decreases in either FEV_1 or PEFR after exercise. Only one patient had decreases in both FEV_1 and PEFR. Five (62.5%) showed marked increases in either FEV_1 or PEFR after inhalation of bronchodilators.

DISCUSSION

We found that children with RSV-LRI, whose family had atopic diseases, had a higher occurrence of physician-diagnosed asthma than children whose families were free of these diseases. In comparison with the occurrence of asthma in general Thai children surveyed by ISAAC (International Study of Asthma and Allergy in Children) questionnaires[20]. In this study, the occurrence of asthma was 75 per cent and 40 per cent in children with a without family history of atopy, respectively. The occurrence of recurrent wheezing is also high, approximately 62 per cent, and mostly appeared 2-5 years after RSV infection, which is similar to other previous studies[7,9,11,14].

Abnormal baseline PFTs were found in nearly half of the children with RSV-LRI. The most common abnormality is the concave shape of flow-volume curves followed by decreased FEV_1/FVC ratio, decreased $FEF_{25-75\%}$ and decreased PEFR, all of which indicate the evidence of airway obstruction without restrictive pulmonary disease. Most of the children, who completed exercise challenge testing, showed exercise-induced-bronchial hyperreactivity as demonstrated by the decreases in either PEFR or FEV_1. This evidence is comparable to earlier studies[4,7,9], that found positive exercise challenge test between 22-70 per cent, depending on methods and criteria of positive test. Furthermore 62.5 per cent of the children revealed good responses to rapid acting bronchodilators. These findings additionally suggest that RSV may lead to lower airway obstruction and bronchial hyperreactivity in children[4-17].

A limitation of this study was a small sample size mainly due to inability to contact or search for the target patients who 10 years earlier had RSV-LRI. Recruited children might have more serious illness and the parents were probably more concerned about the child's condition. On the contrary, parents of children without ongoing respiratory illness might be less concerned and refused to participate in the study. This selection bias may contribute to the high occurrence of asthma, abnormal PFTs and exercise challenge test found in our study. A cohort study is preferably needed to avoid this specific problem.

In conclusion, we have strengthened the postulation that RSV-LRI is one of the precipitating cause of asthma[4-17]. The occurrence of physician-diagnosed asthma in children with RSV-LRI is relatively high compared with that found in general Thai children. Baseline PFTs showed evidences of airway obstruction as demonstrated by concave-shaped flow-volume curves, decreased FEV_1/FVC ratio, $FEF_{25-75\%}$ and PEFR. The presence of bronchial hyperreactivity to exercise challenge test and positive response to bronchodilators demonstrates the evidence of exercise-induced bronchospasm among children with history of RSV-LRI.

(Received for publication on October 15, 1999)

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การทดสอบสมรรถภาพปอด และความไวต่อการกระตุ้นของหลอดลมด้วยวิธีออกกำลังกายในเด็ก 10 ปี ภายหลังการติดเชื้อไวรัส อาร์เอสวี ในระบบทางเดินหายใจส่วนล่าง

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ผู้ป่วยเด็กที่มีการติดเชื้อของระบบหายใจส่วนล่างจากเชื้อ respiratory syncytial virus (RSV) มักพบอุบัติการของโรคหอบหืดและการมีความไวเกินต่อการกระตุ้นของหลอดลมในระยะต่อมาสูงกว่าปกติ ผู้วิจัยได้ทำการศึกษาผู้ป่วยจำนวน 13 ราย ซึ่งคัดมาจากผู้ป่วยเด็กที่มีการติดเชื้อของระบบหายใจส่วนล่างจากเชื้อ RSV ที่เข้ารับการรักษาในโรงพยาบาลรามาธิบดี ระหว่างปี พ.ศ.2529-2530 จำนวน 37 ราย พบว่ามีอุบัติการของโรคหอบหืดมากกว่าในประชากรปกติ โดยพบผู้ป่วยที่ได้รับการวินิจฉัยจากแพทย์ว่าเป็นหอบหืดทั้งที่มีและไม่มีประวัติโรคภูมิแพ้ในครอบครัว คิดเป็นร้อยละ 75 และร้อยละ 40 ตามลำดับ ผลการทดสอบสมรรถภาพปอดในผู้ป่วยจำนวน 11 ราย พบความผิดปกติของรูปร่าง flow-volume curve เป็นแบบ concave ซึ่งบ่งชี้ถึง small airway obstruction ร้อยละ 45 พบว่ามีการลดต่ำลงของค่า FEV_1/FVC ร้อยละ 36 มีการลดต่ำลงของ $FEF_{25-75\%}$ หรือ PEFR อย่างใดอย่างหนึ่ง เท่ากับร้อยละ 18 ผลการทดสอบ exercise challenge test ในผู้ป่วย 8 ราย พบมีการลดต่ำลงของ PEFR ร้อยละ 87.5 มีการลดต่ำลงของค่า FEV_1 ร้อยละ 37.5 เมื่อทดสอบการตอบสนองต่อการสูดยาขยายหลอดลมพบว่ามีการเพิ่มขึ้นของค่า PEFR และ FEV_1 เท่ากับร้อยละ 62.5 และ 25 ตามลำดับ

สรุป การศึกษาครั้งนี้ชี้ให้เห็นว่า ผู้ป่วยเด็กที่มีการติดเชื้อของระบบหายใจส่วนล่างจากเชื้อ RSV มีอุบัติการของหอบหืดมากกว่าอุบัติการในเด็กไทยปกติ และมีความผิดปกติของค่าสมรรถภาพปอดค่อนข้างสูง โดยพบความผิดปกติแบบ concave flow-volume curve มากที่สุด ความผิดปกติส่วนใหญ่บ่งชี้ถึง peripheral airway obstruction นอกจากนี้ยังพบว่าผู้ป่วยบางรายมีความไวเกินต่อการประตุ้นของหลอดลมด้วยวิธีการออกกำลังกาย และตอบสนองดีต่อการสูดยาขยายหลอดลมด้วย

คำสำคัญ : Pulmonary Function, Exercise Test, RSV

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