Efficacy of the Ipratropium Bromide in Moderate and Severe Asthma Attack in Children

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Abstract

Introduction: Standard therapy for acute asthma attack includes beta 2 agonists, O₂, and systemic corticosteroids. Although there is a widespread usage of this therapy protocol in recent years, as some of the children still need hospitalization because of incomplete responses, adjunctive therapy measures should be considered. We planned this study protocol to assess the effects of ipratropium bromide (IB) for moderate and severe childhood asthma attacks.

Methods: All of the consecutive 50 children admitted to the Pediatric Emergency Service of Istanbul University Cerrahpaşa Medicine Faculty were included in our study. All patients received short duration β2-adrenergic agonists and methylprednisolone consistent with current practice guidelines; then, they were randomized into two groups. While the first group received IB (250 µg/dosage) three times with 20 minutes of intervals, the second group received serum physiologic. Before each therapy regimen and at the 72nd hour, clinical asthma scores (CAS) and peak expiratory flow rates (PEF) of the patients were screened and their hospitalization status was recorded.

Results: There was not any significant difference in the hospitalization status of the two groups, which included patients aged three to 18 years. Clinical asthma scores and PEF of the first and second group of patients had a statistically significant difference beginning from the 40th minute.

Discussion and Conclusion: In our study, we reported that IB added to the standard therapy regimen of moderate and severe childhood asthma attacks was efficient and did not have any adverse effect.

Keywords: Acute asthma attacks; childhood; ipratropium bromide.

Asthma is a chronic inflammatory disease presenting with acute asthma attacks. National diagnoses and management reports recommend oxygen, short-acting β2-adrenergic agonists and systemic corticosteroids for the management of acute asthma attack[¹,²]. As some patients do not respond completely to the optimal therapy regimen applied, adjunctive therapy measures should be considered. Ipratropium bromide (IB) is a quaternary anticholinergic and when it is used in conjunction with β2-adrenergic agonists, they have additive effects in improving the pulmonary function[³-⁶]. The bronchodilator effect of ipratropium bromide starts at 30-120 minutes, lasts 4-8 hours and has a half-life of 3.2 hours[⁶,⁷].

In our study, the efficacy and adverse effects of (if there is)
nebulised IB, added to the β2-agonist therapy regimen was evaluated by observing the symptom scores three times with 20 minutes of intervals and observing pulmonary function tests (PFT) of childhood moderate and severe asthma attacks.

**Materials and Methods**

Children admitted to the Pediatric Emergency Service of Istanbul University Cerrahpaşa Medicine Faculty with moderate and severe childhood asthma attacks were included in our study this study approved by our hospitals institutional boards. Patients aged three to 12 years and with clinical asthma scores (CAS)\(^8\) and with PEFR <70% participated with the consent of their families. Patients who received corticosteroids during the last three days and bronchodilator drugs during the last six hours, who had prior intensive care unit history and who had diseases like glaucoma and cardiac disorders, and who had known hypersensitivities to the drug were excluded from the study. The severity of the asthma attacks of our cases was classified according to the PEFR or CAS (Table 1). The patients were randomized into two groups; and PEFR, clinical asthma scores, heart rate, minute respiration rate, \(O_2\) saturation and blood pressure of each patient was recorded. Each patient participated in this study received nebulised salbutamol dosages (if the patient’s weight was <30 kg, 2.5 mg salbutamol; if the patient’s weight was >30 kg, 5 mg salbutamol) three times with 20 minutes of intervals in between and one dosage of 2 mg/kg (max. 60 mg) intravenous methylprednisolone. First group of patients received 250 µg/dosage of nebulised ipratropium bromide (Boehringer Ingelheim) three times with 20 minutes of intervals, and the second group of patients received 2 ml nebulised serum physiologic three times with 20 minutes of intervals (Fig. 1). \(O_2\) therapy was with pulse oxymeter and when \(O_2\) saturation (BCI International Waukesha, Wisconsin USA) was ≤94%, it was 6 liters/minute.

Initial parameters were assessed at the beginning of this study, and then measured again at the 20th, 40th and 60th minutes after each therapy regimen. Patients were followed for adverse effects (defined by the patient or observed by the primary physician). The need for adjunctive therapy measures after the initial one hour of therapy and the need for hospitalization should be assessed by the physician observing the patient clinically. The patients were hospitalized when there were clinical and PEFR changes, or when the \(O_2\) saturation of the room-air was <94%. Time for each nebulisation therapy, hospitalization status of the patients and discharge day from the hospital was recorded with details. Out-patients were admitted to controls 72 hours later to re-evaluate all of the tests initially measured. PEFR was measured with SensorMedics Vmax Series 20C spirometers (SensorMedics Corporation Yorba Linda California). The highest level measured at the end of 3 measure performed is defined as a PEFR.

<table>
<thead>
<tr>
<th>Severity</th>
<th>Wheeze score</th>
<th>Dyspnea score</th>
<th>Accessory muscle score</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No wheeze and well</td>
<td>Absent dyspnea</td>
<td>No retractions</td>
</tr>
<tr>
<td>1</td>
<td>End-expiratory wheeze</td>
<td>Normal activity and speech, minimal dyspnea</td>
<td>Interkostal retractions</td>
</tr>
<tr>
<td>2</td>
<td>Pan-expiratory ± inspiratory wheeze</td>
<td>Decreased activity; 5- to 8-word sentences; moderate dyspnea</td>
<td>Interkostal and suprasternal retractions</td>
</tr>
<tr>
<td>3</td>
<td>Wheeze audible without a stethoscope</td>
<td>Concentrates on breathing; ≤5-word sentences; severe dyspnea</td>
<td>Nasal flaring</td>
</tr>
</tbody>
</table>

**Table 1. Evaluation of the clinical asthma scores**

**Figure 1.** Study plan.
Patients in the therapy group and control group were compared for the beginning time of the disease, the number of attacks experienced during the last year, hospitalization rates because of attacks experienced during the last year, and for ECP levels, with the Mann-Whitney U test. Kruskal-Wallis test was used to compare the PEFR and CAS before and after the two therapy regimens. The difference was statistically significant when the "p"-value was <0.05, and data were evaluated with “SPSS” statistical program.

**Results**

A total of 50 children, 30 male (60%) and 20 female (40%), admitted to the Pediatric Emergency Service of Istanbul University Cerrahpaşa Medicine Faculty with acute asthma attack participated in our study and all of the patients completed this study.

While of 25 cases (15 male, 10 female) in the first group had a "median age of 6.61±2.21 years; 25 cases (15 male, 10 female) in the second group had a "median age of 6.68±2.92 years and there was not any statistically significant difference in the demographical characteristics of these groups (Table 2).

It was found that while nine patients had a severe asthma attack (5 patients in the first group; 4 patients in the second group), 41 patients had a moderate asthma attack (20 patients in the first group; and 21 patients in the second group) (Table 3).

One patient (4%) in the first group and three patients (12%) in the second group were hospitalized. Although the number of patients hospitalized in the combined therapy group was lower than the other group, there was not a statistically significant difference (p>0.05) (Table 3). None of the discharged patients were admitted to the Emergency Service within 72 hours.

There was not any adverse effect defined by the physician or by the patient in both groups.

PEFR was evaluated in 19 children (10 patients in group I; and 9 patients in group II) who are over seven years of age. PEFR was significantly improved at the 60th minute in both groups (p<0.001), but when the two groups were compared, there was a statistically significant difference as soon as the second therapy had been started (40th minute), and this difference continued at the 72nd hour (p<0.05) (Table 4).

At the end of the first hour, CAS of both groups had decreased significantly (p<0.001) (Table 4). However, when the two groups were compared, like improvement in PEFR, there was a statistically significant difference after the second therapy had been completed (40th minute), and this difference continued at the 72nd hour (p<0.05) (Table 4).

**Discussion**

Acute severe asthma attacks in children are life-threatening emergencies. According to pediatric guidelines, three dosages of β2-agonist (with 20 minutes of intervals in between), systemic corticosteroids and O₂ therapy is rec-

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**Table 2. Baseline characteristics of the study groups: Clinical demographics**

<table>
<thead>
<tr>
<th></th>
<th>Group I (n=25)</th>
<th>Group II (n=25)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>6.61±2.21</td>
<td>6.86±2.92</td>
<td>0.93</td>
</tr>
<tr>
<td>M/F</td>
<td>15/10</td>
<td>15/10</td>
<td></td>
</tr>
<tr>
<td>The beginning age for the disease</td>
<td>2±2.14</td>
<td>2.14±1.33</td>
<td>0.63</td>
</tr>
<tr>
<td>The number of admittances to the Emergency Service with an acute asthma attack during the last year</td>
<td>2.96±1.38</td>
<td>3.12±2.99</td>
<td>0.36</td>
</tr>
<tr>
<td>The number of hospitalizations during the last year</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>The number of allergens positive with prick test</td>
<td>2.82±1.42</td>
<td>3.30±1.46</td>
<td>0.15</td>
</tr>
<tr>
<td>Atopy (patient or family history)</td>
<td>48%</td>
<td>56%</td>
<td>0.57</td>
</tr>
<tr>
<td>Receiving prophylactic drug therapy</td>
<td>72%</td>
<td>84%</td>
<td>0.31</td>
</tr>
<tr>
<td>Respiratory rate (breaths/min)</td>
<td>48.08±8.82</td>
<td>48.44±6.78</td>
<td>0.87</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>125.96±16.55</td>
<td>124.80±14.45</td>
<td>0.79</td>
</tr>
<tr>
<td>Initial O₂ saturation % (room air)</td>
<td>94.2±1.29</td>
<td>94.78±1.42</td>
<td>0.18</td>
</tr>
<tr>
<td>Accessory muscle contractions</td>
<td>1.92±0.4</td>
<td>2±0.41</td>
<td>0.24</td>
</tr>
<tr>
<td>Wheeze score</td>
<td>2.2±0.41</td>
<td>2.16±0.37</td>
<td>0.48</td>
</tr>
<tr>
<td>Dyspnea score</td>
<td>1.68±0.47</td>
<td>1.6±0.5</td>
<td>0.71</td>
</tr>
<tr>
<td>Clinical asthma score</td>
<td>5.80±1</td>
<td>5.76±1.01</td>
<td>0.88</td>
</tr>
<tr>
<td>ECP (IU/ml)</td>
<td>25.27±20.62</td>
<td>30.3±18.84</td>
<td>0.17</td>
</tr>
<tr>
<td>PEFR (% predicted)</td>
<td>55.30±6.93</td>
<td>53.78±9.95</td>
<td>0.70</td>
</tr>
</tbody>
</table>
agonists have been reported in many studies [11-16]. Studies the IB for adult patients and its synergistic effects with β2-
measures is frequently discussed. The efficacy and safety of
recover completely. Thus, usage of adjunctive therapy
standard therapy, it is reported that some patients do not
+ IB (with 20 minutes of intervals) [23]. In our study, com-
coming six dosages of β2-agonist (with 20 minutes of intervals)
again, FEV1 has improved significantly in children receiv-
ing three dosages of β2-agonist (with 20 minutes of intervals), it is proved to
In our study, group I receiving three dosages of β2-agonist (with 20 minutes of intervals) + IB and group II receiving
three dosages with 20 minutes of intervals, it is proved to
In our study, group I receiving three dosages of β2-agonist
and dosage intervals was efficient in moderate and severe
symptom scores and pulmonary function tests of child-
hood asthma beginning from the fourteenth minute and
do not have any adverse effects.

**Peer-review:** Externally peer-reviewed.

**Authorship Contributions:** Concept: M.O.; Design: M.O., HC.; Data Collection or Processing: M.O.; Analysis or Interpretation: M.O., H.C.; Literature Search: M.O.; Writing: M.O., H.C.

**Conflict of Interest:** None declared.

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