Abstract

Objective: to evaluate the alterations of heart rate, blood pressure, psychological aspects and oxygen saturation after continuous fenoterol inhalation (0.5 mg/Kg) by children with severe acute asthma.

Methods: we studied 30 patients with severe acute asthma who were treated at the pediatric ward of Hospital Universitário – UFMS. The patients inhaled 0.5 mg/Kg of fenoterol (two drops/Kg) during one hour. Psychological aspects, oxygen arterial saturation, heart rate and blood pressure were evaluated at three different moments: before, after and one hour after the fenoterol inhalation.

Results: there were 17 males (56.6%) and 13 females (43.4%). Sleepiness was observed in 16 (53.3%), psychomotor agitation in one (33%) and nausea and vomiting in 12 patients (40%). The average of oxygen arterial saturation increased from 90.9 ± 2.8% to 92.7 ± 2.5% (p<0.05) after inhalation. There was statistically significant increase in the average heart rate before and after inhalation (139.5 ± 13.5 beats/min, 166.5 ± 11.1 beats/min, respectively), p<0.05. A significant decrease in blood pressure rate was observed from 117.56 ± 10.3 / 74.6 ± 7 mmHg, to 107.6 ± 11 / 63.6 ± 9.3 mmHg (p<0.05).

Conclusions: continuous fenoterol (0.5 mg/Kg) inhalation by children with severe acute asthma caused sleepiness, nausea, vomits, palpitation and decrease in blood pressure rate. The authors suggest that patients submitted to this treatment need clinical monitorship at hospital settings. Children with concomitant diseases such as diarrhea, vomits, and dehydration require special attention.


Introduction

Severe acute asthma is characterized by an increase in airway obstruction, increase in breathing effort and a ventilation-perfusion imbalance, which possibly lead to hypoxia, respiratory muscle fatigue, CO₂ retention and respiratory acidosis.¹,²

The administration of aerosol bronchodilators has been recognized as the major method for treating acute exacerbations of asthma due to their excellent bioavailability, with direct deposition of the substance in the airway, thus causing fewer systemic side effects.³,⁴ Studies show that the inhalation of increasing doses of albuterol produces a significantly greater bronchodilator response⁵ and, when
continuously administered, prevents the recurrence of bronchospasms, allowing a greater distribution of the substance in the peripheral airways, with a more satisfactory clinical response. According to the II Brazilian Consensus on Asthma (1997), bronchodilators can be administered to a child with acute asthma in the form of continuous inhalation, in the dose of 0.5 mg/kg/hour.

In our setting, fenoterol is widely used, but studies about its side effects are still necessary.

The present study has the objective of evaluating the alteration of heart rate, blood pressure, psychological status and arterial oxygen saturation after continuous inhalation of fenoterol in the dose of 0.5 mg/kg/hour in children with moderate to severe acute asthma.

Materials and Methods

Thirty children with moderate to severe acute asthma treated at the Pediatric Emergency Room of the Teaching Hospital of Universidade Federal de Mato Grosso do Sul (UFMS) were studied. Each child was studied for two hours. The study was approved by the Medical Ethics Committee of UFMS. Permission and a signed consent form were obtained from the parents for the participation of their children in the study. Information about the treatment and its possible side effects was provided. Children with previous use of any medication or with heart, muscular, kidney or neoplastic diseases were not included in the study.

The clinical diagnosis of asthma and the intensity of the crisis (Table 1) were assessed according to the criteria established by the Guidelines for the Diagnosis and Management of Asthma (1991), and by the II Brazilian Consensus on Asthma (1998), following the survey below:

1. What is the age of onset, frequency and duration of crises?
2. Has the patient had wheezing, or cough?
3. Does it worsen during the day or night?
4. Does the patient have rhinitis, hives, drug or substance allergies?
5. Does the patient improve with bronchodilator nebulizers or inhalers?
6. Has the patient been exposed to dust, animals or chemical products?
7. Does the patient have a crisis while running, showing emotions, or laughing?
8. Is there a history of allergy in the family or smokers in the home?

Data collection and clinical evaluation of the patient were performed by one examiner only, according to Table 1.

During the study the psychological status of each patient was evaluated every 15 minutes as to the presence of drowsiness or irritability. Those patients who fell asleep soon after the start of the inhalation, and woke up only when aroused, were regarded as drowsy; and those patients who showed irritability, did not accept inhalation, and cried without an apparent cause (e.g.: pain, fear or separation from mother) were considered agitated.

Heart rate was checked on the arrival of the patient, at the end of inhalation and one hour after that, by direct reading on a heart monitor (Ecafix).

Table 1 - Estimation of the intensity of acute asthma in children

<table>
<thead>
<tr>
<th>Signs/Symptoms</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory frequency</td>
<td>Normal or 30% higher than the average</td>
<td>30% to 50% higher than the average</td>
<td>More than 50% higher than the average</td>
</tr>
<tr>
<td>Psychological status</td>
<td>Normal</td>
<td>Normal</td>
<td>Depressed</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>Absent or mild</td>
<td>Moderate, incomplete sentences</td>
<td>Intense, monosyllabic utterance, difficulty to eat</td>
</tr>
<tr>
<td>Accessory muscles</td>
<td>Mild intercostal retraction</td>
<td>Moderate intercostal, tracheosternal retraction, thoracic hyperinsuflation</td>
<td>Intense intercostal, tracheosternal retraction, fan-like motion of the alae-nasi</td>
</tr>
<tr>
<td>Color</td>
<td>Normal</td>
<td>Pale</td>
<td>Cyanotic</td>
</tr>
<tr>
<td>Auscultation</td>
<td>Expiratory wheezing</td>
<td>Inspiratory and expiratory wheezing</td>
<td>Inaudible respiratory noise</td>
</tr>
<tr>
<td>O₂ saturation</td>
<td>Higher than 95%</td>
<td>Between 90% and 95%</td>
<td>Lower than 90%</td>
</tr>
<tr>
<td>PaCO₂</td>
<td>Lower than 35 mmHg</td>
<td>Lower than 40 mmHg</td>
<td>Higher than 40 mmHg</td>
</tr>
</tbody>
</table>

Pulsus paradoxus and expiratory peak flow are part of this table, but were not considered, since pulsus paradoxus is difficult to assess in the presence of tachycardia, and expiratory peak flow can be assessed only in children older than 7 years, since its assessment depends on the patient’s cooperation. Once these variables could not be assessed in all patients of this study, they were not considered.
Systolic and diastolic blood pressures were measured before the beginning of treatment, at the end of inhalation and one hour after that, by Dixtal oscilloscope, with the cuff occupying 2/3 of the arm length and with the child in a half-sitting position. Normal values for each age group were considered according to the Second Task Force on Blood Pressure Control in Children, 1987.  

Pulse oximetry was carried out continuously with a digital oximeter (Ohmeda) from the arrival of the patient until the end of the second hour. 

Fenoterol was administered via a nebulizer with a face mask and a reservoir with a capacity of 20 ml and a flow of 6 liters per minute of compressed air. The nebulization solution consisted of physiological solution 0.9% and 0.5 mg/kg of fenoterol, a maximum of 15 mg (2 drops/kg), released into the reservoir via a syringe infusion pump with a flow of 30 ml per hour, adjusted to maintain a volume of 2 ml of the solution in the nebulizer (adapted from Craig et al., 1996), for an hour. 

In case of deterioration of the clinical status, that is, aggravation of hypoxemia, with cyanosis, psychomotor agitation and decrease in arterial oxygen saturation in relation to admission, oxygen inhalation was immediately initiated. 

Mean, standard deviation and percentage were used for statistical analysis. Wilcoxon signed-rank test was used to compare the differences between the groups, before and after treatment. A p value less than 0.05 was adopted. The statistical tests were done by the Stataquest 4.0 program for Windows 95, serial number: W-902103040, Stata Corporation, TX-USA. 

### Results 

Thirty children were included in the study between 1998 and 2000. The demographic characteristics are shown in Table 2. 

Drowsiness was observed in 16 children (53.3%), usually 45 minutes after the beginning of treatment. Only one child (3.3%) presented psychomotor agitation 30 minutes after the beginning of treatment. Nausea and vomiting occurred in 40% of the patients (Table 3). 

<table>
<thead>
<tr>
<th>Period (minutes)</th>
<th>During (n. of patients)</th>
<th>After (n. of patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>30</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>45</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>60</td>
<td>2</td>
<td>0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Period</th>
<th>HR (bpm)</th>
<th>Mean ± SD (bpm)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beginning</td>
<td>102 to 160</td>
<td>139.5 ± 13.5</td>
<td>p&lt; 0.05</td>
</tr>
<tr>
<td>End</td>
<td>145 to 190</td>
<td>166.5 ± 11.1</td>
<td>p&lt; 0.05</td>
</tr>
<tr>
<td>One hour after the end</td>
<td>105 to 163</td>
<td>147.3 ± 11.6</td>
<td>p&lt; 0.05</td>
</tr>
</tbody>
</table>

SD: standard deviation. 

Both systolic and diastolic blood pressures decreased at the end of fenoterol inhalation, with progressive elevation after its end, without reaching the baseline values obtained before the treatment (Table 5).
**Discussion**

ß2-adrenergic agents, medications of choice for the treatment of status asthmaticus, have a high therapeutic rate if inhaled, comparatively to oral, intravenous or subcutaneous administration, especially due to their local pulmonary effect and the consequent minimization of their systemic effects.4,18 High doses of ß2-adrenergics were used in children with severe acute asthma, 8,9 since only about 10% of the inhaled doses reached the lungs,5 due to the small diameter of the airways. Continuous nebulization can prevent the recurrence of bronchospasm, which occurs with the intermittent use of the medication, since it continually stimulates pulmonary ß2 receptors. This allows a better distribution of the drug in the peripheral airways.6

As frequent and greater doses were more effective, continuous nebulization started to play a key role in the treatment of severe acute asthma in children.9,10,18,19

Among the systemic effects provoked by beta adrenergics, tachycardia results from the action of these substances on ß2-adrenergic receptors, which are present in a small amount in the myocardium,20 and from the decrease of peripheral vascular resistance.4,21 In the group of children studied by Schuh et al. (1990)8 the heart rate varied from 108 to 180 bpm, with an average variation of 33.7% compared to the heart rate at admission. The highest heart rate observed by Katz et al. (1993),9 with a dose of 0.5 mg/kg every 20 or 30 minutes, was 174 bpm.

In this study, the average heart rate varied significantly, with a progressive increase during inhalation and a gradual decrease up to the end of the second hour of observation (Table 3). However, this rate was not considered a complication of treatment but an indication of the pharmacological effect of the substance on myocardial beta receptors.20,21 One hour after the end of inhalation, the heart rate maintained an average above the pretreatment values (p<0.05), indicating that the effects of fenoterol were still present.

The increase in average arterial oxygen saturation at the end of inhalation was statistically significant; however, five patients presented a decrease in arterial saturation after the beginning of treatment, and oxygen inhalation was started. This decrease was possibly due to the alteration of the ventilation/perfusion ratio, in which the fenoterol-induced stimulus over ß2-adrenergic receptors leads to vasodilatation, with an increase in pulmonary blood flow and an increase in cardiac output. As reported by Tal et al.,22 a sudden increase in blood perfusion in poorly ventilated lung areas resulted in initial reduction of arterial oxygen saturation, as observed in our patients. There was no correlation between arterial oxygen saturation and heart rate at the end of inhalation.

One of the adverse effects of fenoterol is nervousness or agitation.23 In this study, agitation was observed in two patients (6.6%) and drowsiness, a more frequent signal, was observed in 16 cases (53.3%) and predominantly occurred in the first 45 minutes after the beginning of inhalation.

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Of the 30 children studied, six presented systolic blood pressure above the normal limits (from 126 to 140 mmHg) before fenoterol inhalation. This possibly occurred due to tachycardia and to the physical effort imposed by the asthma crisis.

Arterial blood pressure results are contradictory in the literature, as shown by Chapman et al.13 and Bauer et al.,14 who observed an increase in systolic blood pressure and a decrease in diastolic blood pressure. In contrast, Papo et al.10 reported that there was no alteration in blood pressure in the group of children they studied.

In the present study, the average blood pressure suffered an evident and significant decrease at the end of the first hour, with a progressive increase by the end of the second hour, but did not reach the initial values. In spite of the significant decrease, 29 patients maintained blood pressure within the normal values for age, except for one patient, who presented hypotension (77/40 mmHg). Drowsiness

<table>
<thead>
<tr>
<th>Period</th>
<th>Time (minutes)</th>
<th>ABP (mmHg)</th>
<th>Mean and SD of ABP</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before</td>
<td>0</td>
<td>90 / 67 to 140 / 85</td>
<td>117.56 ± 10.3 / 74.6 ± 7.0</td>
<td></td>
</tr>
<tr>
<td>After</td>
<td>60</td>
<td>77 / 43 to 128 / 74</td>
<td>107.6 ± 11.0 / 63.6 ± 9.3</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>One hour later</td>
<td>120</td>
<td>100 / 70 to 130 / 87</td>
<td>110.8 ± 7.3 / 70.7 ± 8.1</td>
<td>p&lt;0.05</td>
</tr>
</tbody>
</table>

ABP: arterial blood pressure, mmHg: millimeters of mercury, SD: standard deviation.
was the only clinical sign observed in this patient. Four patients presented a decrease in diastolic blood pressure, which varied from 40 to 50 mmHg, levels considered to be below the normal values for age; drowsiness was observed in three of these patients. At the end of the second hour of observation, blood pressure rose again but did not reach the pretreatment values.

According to the literature, a decrease in blood pressure in patients using beta adrenergics occurs because of a decrease in peripheral vascular resistance, induced by the vasodilator action mediated by ß2 adrenergics. In addition to the decrease in peripheral vascular resistance, drowsiness may have contributed to the reduction in arterial blood pressure.

The occurrence of nausea and vomiting presented by the patients was interpreted as an adverse effect of fenoterol, although such effect has not been reported by other authors. Although comparing the adverse effects of continuous and intermittent inhalation in asthmatic children was not the object of this study, it allowed us to observe sinusal tachycardia, decrease in arterial blood pressure, drowsiness, initial decrease in arterial oxygen saturation, nausea and vomiting when fenoterol was continuously inhaled in the dose of 0.5 mg/kg during one hour. The clinical effects observed in this study were not compared with those presented by other treatment methods in children with severe acute asthma, and we are therefore unable to compare their intensity.

Authors suggest that continuous fenoterol inhalation in the dose used in this study should be performed preferably with clinical monitoring, in a hospital environment, and with special attention to those children with concomitant diseases, such as diarrhea, vomiting, dehydration, on which the systemic effect of therapy could be more intense because of those of the underlying diseases.

New studies are necessary to verify whether the adverse effects observed in this study occur in other treatment regimes for children with severe acute asthma.

References
2. Sociedade Brasileira de Pneumologia e Tisiologia, Sociedade Brasileira de Alergia e Imunologia; Sociedade Brasileira de Pediatria. II Consenso Brasileiro no Manejo da Asma. 1998.