Bronchodilating Effect of Terbutaline Powder in Acute Severe Bronchial Obstruction

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The bronchodilating effect of terbutaline dry powder inhaled via Turbuhaler was compared with terbutaline inhaled via a conventional, chlorofluorocarbon (CFC) inhaler and Nebuhaler (750 ml spacer) in 68 consecutive patients attending the emergency department with acute severe bronchial obstruction. The study was done as an open, randomized, parallel group design with one study day. Patients were treated with 2.5 mg of terbutaline 15 min apart, either as dry powder via Turbuhaler or with a CFC inhaler in conjunction with Nebuhaler. Data from 62 patients were analyzed. The mean baseline FEV₁, values were 0.81 L (SD, 0.64; range, 0.14 to 2.74 L) in the Turbuhaler group (n = 33), and 0.90 L (SD, 0.90; range, 0.27 to 2.60 L) in the Nebuhaler group (n = 29). The mean increases in FEV₁ from baseline were 0.40 L (SD, 0.40; range, 0.06 to 2.36 L) and 0.21 L (SD, 0.25; range, −0.05 to 0.95 L) 10 min after the last inhalation via Turbuhaler and Nebuhaler, respectively. The difference between mean values of the increase in FEV₁ after terbutaline treatment with Turbuhaler and the CFC inhaler and Nebuhaler was statistically significant (p = 0.0004, ANOVA). This study showed that inhalation of terbutaline via Turbuhaler produced a significantly greater increase in FEV₁ compared with the same dose of terbutaline administered via the CFC inhaler and Nebuhaler in patients attending the emergency department with acute severe bronchial obstruction. (Chest 1994; 105: 697-700)

METHODS

Patients

All patients attending the emergency department with acute severe obstructive lung disease and an age of more than 18 years were included during a 5-month period. The study was done as an open, randomized, parallel group design.

Patients in need of acute respiratory intensive care were to be excluded as were patients with significant cardiac disease or known hypersensitivity to sympathomimetics.

The study was approved by the local Ethics Committee in Copenhagen and the National Board of Health and was performed in accordance with the Declaration of Helsinki.

All measurements were performed by the principal investigator. On admission, basal FEV₁, peak expiratory flow (PEF), respiratory rate, heart rate, and blood pressure were measured and arterial blood gas analyses were performed. Patients were asked about all drug intake during the last 24 h before arrival at the hospital. Immediately thereafter, patients were randomized to treatment with either terbutaline, 0.5 mg five deep inhalations via Turbuhaler, or terbutaline, 0.25 mg ten deep inhalations via the conventional CFC inhaler and Nebuhaler. Inhalations were taken in accordance with the user’s instruction for each device and treatments were carefully monitored by the principal investigator. Ten minutes later, FEV₁, PEF were measured as well as pulse rate, blood pressure, and respiratory rate. Fifteen minutes from study start, asthma, inhalation via Bricanyl Turbuhaler has been shown to give a good bronchodilating effect. Thus, Turbuhaler would be an alternative to Nebuhaler (750-ml spacer) for administering terbutaline to patients with acute severe bronchoconstriction. However, this hypothesis has to be proved. In the present study, the bronchodilating effect of terbutaline sulfate powder inhaled via Turbuhaler or via the CFC inhaler and Nebuhaler was compared in patients with acute severe bronchial obstruction.

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another and equal dose of terbutaline was administered by the same route as the first and 10 min later the same measurements were performed. No administration of other asthma treatment was allowed during the study which lasted for approximately 1 h per patient. Patients were excluded from data analysis if FEV₁ increased less than 10 percent on the day of hospital admission and less than 15 percent at a subsequent visit within 2 months.

Comparison between treatments, with respect to changes, was based on intrapatient changes from pretreatment to posttreatment. Ranked values for these differences were subjected to an analysis of variance (ANOVA) model. Ranked values were used in order to avoid dependence on distributional assumptions. A difference in p values of less than 0.05 was considered significant.

RESULTS

A total of 93 patients with acute obstructive lung disease attended the emergency department from May to October 1990. Twenty-five patients were not included at times when the principal investigator was not on call. None of the patients with acute obstructive lung disease attending the department during the 5-month study period required acute intensive respiratory care. Sixty-eight patients, 34 in each treatment group, were randomized. One patient did not wish to continue after the initial lung function test. Five patients showed an increase in FEV₁ of less than 10 percent of the study day and a reversibility of less than 15 percent when reexamined within 2 months at the clinic. The patient demographic data were similar in both treatment groups (Table 1).

The two groups of patients were comparable with respect to use of previous antiasthma treatment during the previous 24 h. Seventeen and 16 patients, respectively, in the 2 groups had used inhaled β₂-agonists up to 1 h before attending the emergency department. Inhaled steroids were used by 12 patients in each group. Eight and three patients suffered from chronic obstructive lung disease in the CFC and Turbuhaler group, respectively.

The mean baseline value of FEV₁ was 0.81 L (SD, 0.25; range, 0.14 to 2.74 L) corresponding to 26 percent (range, 5 to 74 percent) of predicted normal values before inhalation via Turbuhaler. Before inhalation via Nebuhaler, the mean baseline value of FEV₁ was 0.90 L (SD, 0.53; range, 0.27 to 2.60 L) corresponding to 29 percent (range, 11 to 72 percent) of predicted normal values. There was no statistical difference between means of initial values in the two groups (p = 0.53) (Fig 1). After the first treatment, FEV₁ increased on average to 1.07 L after inhalation via Turbuhaler and to 1.06 L after inhalation via Nebuhaler. After the second treatment there was a further increase in FEV₁ to 1.20 L after inhalation via Turbuhaler and to 1.12 L after inhalation via Nebuhaler. The mean total increase in FEV₁ was 0.40 L after terbutaline Turbuhaler treatment (SD, 0.40; range, 0.06 to 2.36 L) and 0.21 L after terbutaline Nebuhaler treatment (SD, 0.25; range, 0.05 to 0.95 L). The difference between the mean increases in FEV₁ was statistically significant (p = 0.0004) (Table 2).

The mean percentage increases in FEV₁ from baseline were 59 percent and 57 percent after the first and second treatment, respectively, in patients inhaling terbutaline via Turbuhaler. After inhalation via Nebuhaler, the corresponding mean increases were 16

![FIGURE 1. Mean of FEV₁ before and after each inhalation.](image)

**Table 1** — Demographic Data and Arterial Blood Test*

<table>
<thead>
<tr>
<th></th>
<th>Bricanyl Turbuhaler</th>
<th>Bricanyl CFC Inhaler and Nebuhaler</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>33</td>
<td>29</td>
</tr>
<tr>
<td>Male/female</td>
<td>11/22</td>
<td>11/18</td>
</tr>
<tr>
<td>Age, yr</td>
<td>50 (20)</td>
<td>51 (19)</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>69 (16)</td>
<td>69 (11)</td>
</tr>
<tr>
<td>Height, cm</td>
<td>168 (8)</td>
<td>169 (9)</td>
</tr>
<tr>
<td>PIF, L/min</td>
<td>100 (46)</td>
<td>111 (53)</td>
</tr>
<tr>
<td>Arterial blood test</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P₀₂</td>
<td>8.7 (2.4)</td>
<td>8.5 (2.0)</td>
</tr>
<tr>
<td>Pco₂</td>
<td>5.6 (1.2)</td>
<td>5.2 (0.9)</td>
</tr>
<tr>
<td>pH</td>
<td>7.4 (0.1)</td>
<td>7.4 (0.1)</td>
</tr>
<tr>
<td>BE</td>
<td>1.2 (2.8)</td>
<td>2.4 (3.5)</td>
</tr>
<tr>
<td>SO₂</td>
<td>89 (10)</td>
<td>91 (6)</td>
</tr>
<tr>
<td>HCO₃⁻</td>
<td>25 (3)</td>
<td>27 (3)</td>
</tr>
</tbody>
</table>

*Values are mean (±SD).

**Table 2** — Before and 15 min After Second Inhalation

<table>
<thead>
<tr>
<th></th>
<th>Bricanyl Turbuhaler</th>
<th>Bricanyl CFC Inhaler and Nebuhaler</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood pressure, mm Hg</td>
<td>146/98</td>
<td>130/77</td>
</tr>
<tr>
<td>Pulse rate, beats per min</td>
<td>98</td>
<td>87</td>
</tr>
<tr>
<td>Respiratory rate, breaths per min</td>
<td>23</td>
<td>19</td>
</tr>
<tr>
<td>PEF, L/min</td>
<td>172</td>
<td>210</td>
</tr>
<tr>
<td>PEF, % of predicted</td>
<td>39</td>
<td>47</td>
</tr>
<tr>
<td>FEV₁, L</td>
<td>0.81</td>
<td>1.20</td>
</tr>
<tr>
<td>FEV₁, % of predicted</td>
<td>26</td>
<td>38</td>
</tr>
</tbody>
</table>
percent and 23 percent.

All patients, except one, treated with terbutaline Turbuhaler showed an increase > 10 percent in \( \text{FEV}_1 \) from baseline to 10 min after the second inhalation. After treatment via terbutaline Nebuhaler, 13 patients showed no change or a decrease (ie, ≤ 10 percent) in \( \text{FEV}_1 \) during that time (Table 3).

The mean PEF baseline value was lower before inhalation via Turbuhaler and was 172 L/min compared with 206 L/min before inhalation via Nebuhaler. After the second treatment, the mean PEF values were 210 L/min and 215 L/min after inhalation via Turbuhaler and Nebuhaler, respectively. The mean increases in PEF were 38 L/min after inhalation via Turbuhaler and 9 L/min after inhalation via Nebuhaler (\( p = 0.08 \)).

The mean percent predicted normal value of baseline PEF was 39 percent (range, 5 to 107 percent) before inhalation via Turbuhaler and 46 percent (range, 14 to 81 percent) before inhalation via Nebuhaler. After the second treatment, the values had increased on average to 47 percent and to 48 percent after Turbuhaler and Nebuhaler treatment, respectively. The difference in the mean increases between the treatments was not statistically significant (\( p = 0.17 \)).

Respiratory rate fell in both patient groups with mean decreases of four to six breaths per minute. After the second treatment, there was a decrease in diastolic blood pressure of 11 mm Hg after inhalation via Turbuhaler and 6 mm Hg after inhalation via Nebuhaler. The decreases in systolic blood pressure were equal, 16 mm Hg, after inhalation of terbutaline both via Turbuhaler and via the CFC inhaler and Nebuhaler.

Six patients in each treatment group experienced either tremor or palpitations. One patient had noticed a rise in pulse rate after the second treatment using terbutaline Turbuhaler. No serious adverse events were reported.

**DISCUSSION**

The standard treatment of acute bronchial obstruction in patients attending the emergency department at our hospital is inhalation of \( \beta_2 \)-agonists using handheld electric compressor nebulizers whereby it is possible several times to administer the dose that can be administered by the conventional CFC inhalers.

However, it has been shown that terbutaline inhaled via the CFC inhaler and Nebuhaler is as effective as nebulized terbutaline in the treatment of severe asthma.\(^9\) Inhalation of terbutaline via CFC inhaler and Nebuhaler is an effective treatment during exacerbations of asthma in both adults and children.\(^11-13\)

Administration of terbutaline via Turbuhaler is as effective as nebulized terbutaline in the treatment of severe chronic obstructive lung disease.\(^14\) In addition, the same doses of terbutaline given via Turbuhaler or via a CFC inhaler and Nebuhaler were shown to be equally effective.\(^15,16\)

We chose a randomized open design as the most appropriate method of evaluating the two treatments, because in this type of investigation, a double-blind placebo-controlled design could not be used for obvious ethical and methodologic reasons. We acknowledge the risk of bias by having one investigator performing all the tests. However, by doing so we made sure that as many as possible of patients consecutively attending the hospital were included. Furthermore, we have strengthened the study by uniform instructions and measurements.

The present study showed increases in \( \text{FEV}_1 \), of 0.40 L and 0.21 L after inhalation via Turbuhaler and Nebuhaler, respectively. These increases might seem small but blood pressure decreased after both Turbuhaler and Nebuhaler terbutaline inhalation. Consistent with the better bronchodilation after inhalation via Turbuhaler, there was a larger decrease in diastolic blood pressure after inhalation via Turbuhaler. Furthermore, approximately two thirds of the patients showed an increase in \( \text{FEV}_1 > 30 \) percent after terbutaline Turbuhaler inhalation (Table 3).

The initial \( \text{FEV}_1 \) values showed a big variation. This corresponds very well with normal clinical observations in these patients. Furthermore, the patients included in the present study had acute severe lung diseases and were the type of patients who attend the emergency department. We are not aware of any other study that documents intensive lung function measurements in patients just on the door step to the hospital. We are convinced that our data are unique in showing a variety of severely impaired lung functions in a group of unselected patients with acute severe lung diseases.

The fact that the initial \( \text{FEV}_1 \) values in the Turbuhaler group were lower compared with the values in the CFC group may contribute to the statistically significant greater increase in \( \text{FEV}_1 \) in the Turbuhaler group.

Chlorofluorocarbon propellants will be abandoned in the near future in order to avoid further destruction...
of the ozone layer and their safety of use has also been questioned.1,2,17

To our knowledge, this is the first study that documents that inhaled terbutaline powder from the multidose inhaler Turbuhaler probably has better bronchodilating effects than the conventional CFC inhaler and Nebuhaler in patients with acute severe bronchial obstruction.

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