Bronchodilator Effects of Nebulized Fenoterol*  
A Comparison With Isoproterenol

Suetaro Watanabe, M.D.; William G. Turner, M.D.;†  
Attilio D. Renzetti, Jr., M.D., F.C.C.P.; Keith W. Harless, M.D.;†  
Adelbert H. Bigler, Ph.D.; and Antonio Cutillo, M.D.

In an attempt to find the optimal single therapeutic dose of fenoterol inhalant solution administered by compressor-powered nebulization, bronchodilator and side effects of five different doses of fenoterol (0.5, 1.0, 1.5, 2.0, and 2.5 mg) and of placebo were compared with those of the recommended therapeutic dose delivered from a metered dose canister in 16 patients with reversible airway obstruction. The fenoterol (except for the metered dose) and the placebo were given in a double-blind, cross-over manner. In comparison with placebo, all doses of fenoterol produced a significant increase in average values of FEV₁, FEV₁/FVC, SG₅₀, and decrease in FRC for five to eight hours. There was a trend for the bronchodilator action to become greater and more prolonged with increasing doses of fenoterol. Compared with 0.4 mg given from a metered dose canister, 0.5 mg of fenoterol delivered by compressor-powered nebulization was equally effective in bronchodilator potency. Dose-by-dose comparison with isoproterenol indicates that fenoterol is a more potent and longer lasting bronchodilator and has no significant effect on heart rate and blood pressures. The most common side effects were shakiness or tremor of hands, which appeared to be dose-related in terms of incidence and intensity. The results of the present study suggest that 0.5 to 1.0 mg of fenoterol is a suitable single therapeutic dose when administered by compressor-powered nebulization.

Fenoterol hydrobromide (hydroxyphenyl orciprenaline, Th 1165a, Berotec), a recently introduced sympathomimetic bronchospasmolytic agent, is a chemical derivative of metaproterenol. It has characteristics of greater selectivity to β₂-adrenergic receptors with less cardiovascular stimulation and of prolonged action. It is effective orally as well as by inhalation. Fenoterol has been utilized clinically in the treatment of obstructive airway diseases in Europe for the past ten years. According to the previous reports, this agent appeared to be superior in every aspect to metaproterenol in therapeutic doses. Although fenoterol has not been available in the United States, results of clinical trials performed in this country have confirmed its high efficacy.

In the present study, the bronchodilating efficacy and side effects of various doses of nebulized fenoterol solution were evaluated in an attempt to establish dose-response relationships and to determine the optimal therapeutic dose in this form of administration in patients with chronic reversible airway obstruction. Furthermore, comparisons were made with a recommended therapeutic dose of fenoterol administered by a freon-propelled pocket canister and with a therapeutic dose of nebulized isoproterenol solution.

**Materials and Methods**

**Patient selection**

Nine male and seven female ambulatory patients were selected for the study. Their ages ranged from 17 to 62 years (average 40 years), with relatively stable, mild to severe chronic airway obstruction that was reversible or partly reversible as demonstrated by 15 percent or greater increase in forced expiratory volume in one second (FEV₁) over the baseline value within 30 minutes following inhalation of 0.15 mg of isoproterenol sulfate from a metered dose inhaler. Their ratios of FEV₁ to forced vital capacity (FVC) were between 42 and 70 percent, with a mean of 54.8 percent. Thirteen patients (eight male and five female) had diagnoses of bronchial asthma, and three (one male and two female) had chronic bronchitis according to the criteria of the American Thoracic Society classification. The latter three patients could be classified as having asthmatic bronchitis. None had histories of cardiac, hepatic, renal, or metabolic disease or hypertension. Patients receiving steroid medication were allowed to enter the study only when their conditions had been stabilized by minimal maintenance doses equivalent to less than 10 mg of prednisone daily for at least four weeks before...
the study. Four of the patients had been taking beclomethasone inhalant (Vanceril), two whiffs four times a day, and five were taking both prednisone and Vanceril. In these patients prednisone therapy was switched from single morning to single evening doses ten days before their first visit. Steroid inhalant therapy was modified to three times a day on test days without changing the total number of whiffs and starting the first dose at the conclusion of the test.

Two of the patients with asthmatic bronchitis were cigarette smokers. They were not allowed to smoke for at least two hours before reporting to the pulmonary laboratory and for the duration of the testing period.

Study Plan*

Each patient was studied at the same time of day (AM) at two- to three-day intervals for a total of seven visits. On test days, all short-acting bronchodilators and sympathomimetic drugs had been excluded for at least eight hours, and all long-acting bronchodilators and antihistamines for at least 12 hours before the start of and for the duration of the testing. Steroid medications were also withheld for at least eight hours before the testing and during the testing period. In those patients taking steroid medication, daily dosage was not changed throughout the study period.

Test Drugs and Doses

After the baseline evaluations, one of the following doses of the solution test drug was given on each study day: fenoterol (Th 1185a) solution: 0.5 mg, 1.0 mg, 1.5 mg, 2.0 mg, 2.5 mg; fenoterol metered dose inhalant: 2 whiffs (= 0.4 mg), or placebo solution: distilled water. The placebo and fenoterol solutions were administered in a double-blind, crossover fashion. Fenoterol solution of the test doses were prepared in 2-ml plastic syringes from a 0.5 percent fenoterol stock solution. The placebo solution was prepared in the same manner.

All of these doses except the fenoterol metered dose inhalant were administered by nebulization with a motor-driven, handheld nebulizer (Maxi Myst nebulizer, Mead Johnson Laboratories, Evansville, Ind.).

The patients were instructed to inhale the test drugs from functional residual capacity (FRC) to near total lung capacity (TLC) and to hold their breath for a few seconds at the end of the inhalation. The nebulization is made only when a small hole on the nebulizer is closed by a finger so that there is no loss of the test drug into the atmosphere.

It took 13 to 16 minutes at a rate of approximately ten inhalations per minute until 2 ml of the test drug solution had been nebulized. The metered dose inhalant (two whiffs) was administered by a technician immediately after the patient initiated inspiratory effort at FRC.

Ten of the 16 patients made an extra visit after they completed the seven visits. On this visit 1.0 mg of isoproterenol hydrochloride solution was administered by nebulization in the same manner as the fenoterol and placebo solutions.

Patients were allowed to have a light breakfast before reporting to the pulmonary laboratory and to eat a light lunch immediately after the third hour of testing.

Pulmonary Function Studies

In the morning of each test day, body plethysmography followed by spirometry were performed before the inhalation of the test drugs (baseline study). The measurements were repeated at % (spirometry only), % (spirometry only), 1, 2, 3, 4, 5, 6, and 8 hours after the drug administration.

The spirometry was performed with the patient sitting, with a dry spirometer incorporated by a X-Y recorder (Models 230 and 750A, CardioPulmonary Instruments Corp, Houston). At least two FVC maneuvers were repeated at each time interval. A tracing of the largest absolute sum of the FEV1 plus the FVC was selected, and the FVC, FEV1, and the mean forced expiratory flow during the middle half of the FVC (FEF25-75%) were measured.

The FRC, airway resistance (Raw), and thoracic gas volume (Vtg) at which Raw was determined were measured in a constant volume body plethysmograph described by Schmidt and Cohn using the method of DuBois and associates. Five measurements of each were made in sequence and the average of the last three were used in the calculations. The Raw was converted to its reciprocal, airway conductance (Gaw), and expressed as Gaw/Vtg (specific airway conductance [SGaw]).

Other Effects

Pulse rate and blood pressure were measured with the patient in the sitting position after two minutes of rest before each pulmonary function testing period. Each patient was asked to report such subjective side effects as headache, nausea, tremors, nervousness, and other adverse experiences throughout each test day. Each of the complaints was grouped according to the test drugs and dosages.

Data Analysis

The bronchodilating effect of the test doses were evaluated statistically for each pulmonary function variable in terms of magnitude and duration of change. The former was expressed as percentage of change from their respective baseline values. A response to a test dose at a specified time interval was defined to be significant when paired t test performed between an average change from baseline after placebo and after the test dose showed a significant difference (P < 0.05). Comparison of response among different test doses was made by comparing a pair of average values at each time interval after administration of the test drugs using the paired t test.

Average pulse rate and blood pressure at each time interval were compared with their average baseline values using the paired t test.

RESULTS

All 16 patients made their seven visits. Although the majority of the patients tolerated the eight-hour study on most of their visits, a few of them could not complete the study protocol because of increasing dyspnea. This was especially true when they received placebo. On placebo, although all 16 patients tolerated up to and including three-hour periods, only 11 of them remained in the study at the end of the eight-hour study protocol as shown in Table 2.

Pulmonary Function Data for Fenoterol vs Placebo

Table 1 shows the average baseline values of pul-

*Each patient signed a consent form approved by the institutional committee on human research after explanation of his role in the study.

CHEST, 80: 3, SEPTEMBER, 1981

BRONCHODILATOR EFFECTS OF NEBULIZED FENOTEROL 293
Table 1—Mean Baseline Values of Spirometric Variables, Functional Residual Capacity, Specific Airway Conductance, Heart Rate, and Blood Pressure for Seven Visits in 16 Patients With Reversible Airways Obstruction

<table>
<thead>
<tr>
<th></th>
<th>FVC, L</th>
<th>FEV₁, L</th>
<th>FEF₂₋₅₀, L/s</th>
<th>FRC, L</th>
<th>SGaw, L/s/cm H₂O/L</th>
<th>Heart Rate, beat/min</th>
<th>Blood Pressure, mm Hg</th>
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</thead>
<tbody>
<tr>
<td>Mean</td>
<td>3.47</td>
<td>1.96</td>
<td>1.06</td>
<td>3.68</td>
<td>.073</td>
<td>81.30</td>
<td>112.84</td>
</tr>
<tr>
<td>(SE)</td>
<td>(.34)</td>
<td>(.24)</td>
<td>(.19)</td>
<td>(.18)</td>
<td>(.007)</td>
<td>(3.26)</td>
<td>(2.15)</td>
</tr>
<tr>
<td>Coeff. Var.</td>
<td>8.97%</td>
<td>14.42%</td>
<td>24.32%</td>
<td>10.68%</td>
<td>28.47%</td>
<td>7.75</td>
<td>5.55</td>
</tr>
<tr>
<td>(SE)</td>
<td>(1.99)</td>
<td>(1.89)</td>
<td>(3.59)</td>
<td>(1.60)</td>
<td>(4.74)</td>
<td>(1.00)</td>
<td>(.49)</td>
</tr>
<tr>
<td>% Pred*</td>
<td>89.32%</td>
<td>59.33%</td>
<td>24.03%</td>
<td>143.77%</td>
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</tr>
<tr>
<td>(SE)</td>
<td>(4.77)</td>
<td>(4.14)</td>
<td>(3.17)</td>
<td>(8.03)</td>
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<td></td>
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</tbody>
</table>

*Predicted normal values were obtained from reference 17. FVC = forced vital capacity. FEV₁ = forced expiratory volume in one second. FEF₂₋₅₀ = mean forced expiratory flow during the middle half of the FVC. FRC = functional residual capacity. SGaw = specific airway conductance.

Pulmonary function variables over seven visits for 16 patients. Although considerable day-to-day variation in the baseline values was noted in some of the patients, there was no statistically significant difference between the highest and the lowest average values in all functional variables. Therefore, a mean of seven baseline values was used to compute the response for each of the patients in order to minimize the effect of baseline variation.

The mean response of the pulmonary function variables as percentage change from baseline during eight hours are shown in Figures 1, 2, and 3.

On placebo, no significant change from the baseline values (P < 0.05) occurred in any of the pulmonary function measurements throughout the eight-hour period.

All doses of the test drug including the lowest dose (0.4 mg) from the metered dose inhaler (MDI) produced significantly greater response in all the spirometric and the plethysmographic measurements over placebo up to at least six hours after

![Figure 1](http://publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21247/)

**Figure 1.** Mean percentage changes from baseline in FEV₁, after inhalation of 6 doses of fenoterol and placebo in 16 patients. *Indicates statistically significant difference between the two mean values marked (0.05 > P > 0.01); †, ††, significantly greater mean response over placebo (*0.05 > P > 0.01, †† P < 0.01).
sustained the drug action over their baseline for three hours and 1.0 mg, 1.5 mg, and 2.0 mg did for four hours, and the highest test dose (2.5 mg) for five hours.

Figures 1 to 3 show that peak responses were achieved within the first two-hour periods, and a substantial portion of maximal responses was reached at 15 minutes after the test drug administration. The time interval for attaining peak responses did not appear to be dose related and varied among pulmonary function variables; for instance, it took 15 minutes to one hour in FEV₁ to reach peak responses, but one to two hours in FEF₂₅₋₇₅. At the 15 minutes period, an average of 93.8 percent (87.3 to 100.0 percent) of mean peak FEV₁ responses from various doses was achieved, whereas only 88.8 percent (77.8 to 97.3 percent) was reached in FEF₂₅₋₇₅ at the same period. This difference, however, was not statistically significant.

It should be noted in Figure 1 that there were significant differences in magnitude of response in FEV₁ between the highest dose (2.5 mg) and the lowest dose (0.4 mg) from two-hour to six-hour periods and between 2.0 mg and 0.4 mg at one-hour periods when the response to 2.0 mg exceeded 2.5 mg. Differences in response among other test doses did not reach significant levels at any time periods. In SGaw (Fig 3A), responses to 2.5 mg were significantly greater than those to 0.4 mg MDI from three-hour to six-hour time periods, but at one- and two-hour periods, responses to 1.0 mg exceeded 2.5 mg and were significantly greater than responses to 0.4 mg MDI. It should also be noted in Figures 1 to 3 that the magnitude of response to 1.0 mg was consistently greater than responses to the lower doses (0.4 mg MDI, and 0.5 mg) from 15 minutes to six-hour time periods in all the functional parameters except for FVC, and that 1.0 mg exceeds in response to 2.0 mg in SGaw, and to 1.5 mg in FEV₁ and FEF₂₅₋₇₅ up to six-hour periods, although the differences in magnitude of response between 1.0 mg and these two test doses were not statistically significant. In FEF₂₅₋₇₅ and FVC, differences in response between higher doses and lower doses were less obvious than in FEV₁ and SGaw, and only at a few time periods (at 15 min, 30 min, and one hour in FEF₂₅₋₇₅, at four hours and five hours in FVC) did the differences reach significant levels.

In FRC (Fig 3B), a dose-response relation was not apparent, although all doses of the test drug reduced the size of FRC to a significant degree compared to placebo for at least six hours and five of the six doses for eight hours.
Table 2—Time-related Responses of Mean Values (± SE) for FEV₁ After Placebo and Fenoterol Inhalation in 16 Patients With Reversible Airways Obstruction

<table>
<thead>
<tr>
<th>Time</th>
<th>Placebo</th>
<th>0.4 mg MDI†</th>
<th>0.5 mg</th>
<th>1.0 mg</th>
<th>1.5 mg</th>
<th>2.0 mg</th>
<th>2.5 mg</th>
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<td></td>
<td>2.031</td>
<td>1.847</td>
<td>2.068</td>
<td>1.951</td>
<td>1.940</td>
<td>1.922</td>
<td>1.938</td>
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<tr>
<td></td>
<td>(.283)</td>
<td>(.236)</td>
<td>(.258)</td>
<td>(.226)</td>
<td>(.233)</td>
<td>(.236)</td>
<td>(.232)</td>
</tr>
<tr>
<td>15 min</td>
<td>2.069</td>
<td>2.598*</td>
<td>2.746*</td>
<td>2.781*</td>
<td>2.771*</td>
<td>2.865*</td>
<td>2.835*</td>
</tr>
<tr>
<td></td>
<td>(.317)</td>
<td>(.297)</td>
<td>(.300)</td>
<td>(.276)</td>
<td>(.271)</td>
<td>(.290)</td>
<td>(.283)</td>
</tr>
<tr>
<td>30 min</td>
<td>2.006</td>
<td>2.643*</td>
<td>2.752*</td>
<td>2.819*</td>
<td>2.810*</td>
<td>2.891*</td>
<td>2.907*</td>
</tr>
<tr>
<td></td>
<td>(.292)</td>
<td>(.289)</td>
<td>(.310)</td>
<td>(.279)</td>
<td>(.289)</td>
<td>(.297)</td>
<td>(.294)</td>
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<tr>
<td>1 hr</td>
<td>2.084</td>
<td>2.676*</td>
<td>2.822*</td>
<td>2.854*</td>
<td>2.851*</td>
<td>2.968*</td>
<td>2.901*</td>
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<tr>
<td></td>
<td>(.305)</td>
<td>(.302)</td>
<td>(.307)</td>
<td>(.283)</td>
<td>(.285)</td>
<td>(.295)</td>
<td>(.298)</td>
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<tr>
<td>2 hr</td>
<td>2.151</td>
<td>2.692*</td>
<td>2.789*</td>
<td>2.900*</td>
<td>2.851*</td>
<td>2.942*</td>
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<td></td>
<td>(.330)</td>
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<td>(.322)</td>
<td>(.296)</td>
<td>(.297)</td>
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<tr>
<td>3 hr</td>
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<td>(.305)</td>
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<tr>
<td>4 hr</td>
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<td>2.496</td>
<td>2.661*</td>
<td>2.584*</td>
<td>2.714*</td>
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<td>(.319)</td>
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<td>(.298)</td>
<td>(.282)</td>
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<tr>
<td>5 hr</td>
<td>2.244††</td>
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</tr>
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<td>(.274)</td>
<td>(.288)</td>
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<td>(.305)</td>
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<tr>
<td>6 hr</td>
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<td>2.333*</td>
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<td>2.262</td>
<td>2.484*</td>
<td>2.460</td>
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<td>(.301)</td>
<td>(.262)</td>
<td>(.289)</td>
<td>(.279)</td>
<td>(.286)</td>
</tr>
<tr>
<td>8 hr</td>
<td>2.265††</td>
<td>2.279*</td>
<td>2.283*</td>
<td>2.263*</td>
<td>2.360*</td>
<td>2.264*</td>
<td>2.236</td>
</tr>
<tr>
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<td>(.285)</td>
<td>(.286)</td>
<td>(.270)</td>
<td>(.251)</td>
<td>(.242)</td>
<td>(.291)</td>
<td>(.275)</td>
</tr>
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</table>

*Statistically significant increase over baseline (P < 0.05) by paired t test.
†MDI: metered dose inhaler.
††Numbers indicate the number of patients remaining.

Pulmonary Function Data for Fenoterol vs Isoproterenol

Results of a comparison of 1.0 mg fenoterol to 1.0 mg isoproterenol in ten patients are presented in Figure 4. Fenoterol sustained a highly significant increase in FEV₁ over placebo from 30 minutes to three hours after administration of the drug, whereas isoproterenol produced a significant effect for only one hour. The magnitude of response with fenoterol was significantly greater than isoproterenol at one-, two-, and three-hour time periods.

Heart Rate and Blood Pressure

There were no significant differences in average heart rate or systolic or diastolic blood pressure from the respective mean baseline values during the eight-hour test periods on any of the test doses and the placebo. However, the higher doses of fenoterol (1.5, 2.0, and 2.5 mg) tended to increase the heart rate slightly within the first hour and decrease both systolic and diastolic blood pressures slightly within the first three hours.

Figure 5 shows changes in mean heart rate following inhalation of the test doses. With placebo, mean heart rate decreased slowly with time by about 10 percent in three hours, returned to the
baseline level in two hours after lunch, and decreased slowly again afterward. The lower doses (0.4 mg MDI, and 0.5 mg, and 1.0 mg) followed a similar pattern of change to the placebo with smaller magnitudes of change. With the higher doses (1.5 mg, 2.0 mg and 2.5 mg) of fenoterol, the mean heart rate increased by 2.4 beats/min (3.0 percent) to 7.4 beats/min (9.1 percent) in 30 minutes to one hour and returned to their baseline levels at two-hour periods; thereafter, patterns of change were similar to the placebo.

The greatest change in the mean systolic and diastolic blood pressures were a decrease of 4.4 mm Hg and 5.0 mm Hg, which occurred at two-hour and 30-minute periods, respectively, following inhalation of 2.5 mg of fenoterol. There was no consistent trend in the change in blood pressures following inhalation of the lower doses of fenoterol and the placebo.

Subjective Adverse Effects

The number of patients reporting adverse effects during the eight-hour test periods is summarized in Table 3. Most of these side effects were of mild degree, transient, and tended to occur within 30 minutes after drug administration and disappear after 30 minutes to one hour. The most common adverse effect was tremor or shakiness of hands, which appeared to be dose-related. None of the patients had to terminate the study because of these side effects.

Discussion

Previous reports have shown that aerosolized fenoterol is a potent and long-acting bronchodilator, and one- to two-puffs from a MDI (0.2, 0.4 mg) has been recommended as a single therapeutic dose. The results of the present study have confirmed these findings, and have shown that inhaled fenoterol was a far more potent and long-acting bronchodilator than inhaled isoproterenol in dose-by-dose comparison.

Significant bronchodilation as evaluated by spirometric and body plethysmographic measurements was observed at less than 15 minutes following administration of fenoterol, and the effect lasted for about eight hours compared to placebo in all the test doses including the lowest dose (0.4 mg) delivered from MDI. Although significant airway responses were seen in all the functional parameters, the time to reach peak responses was greater and the duration of the drug action was shorter in
FEF25-75 and FVC than in FEV1 and SGaw. It may be that the inhaled fenoterol was effective in dilating both large and small airways, but the deposition of the drug was less in the small airways. Comparing the magnitude and duration of response to the six different test doses of fenoterol, there was a consistent trend indicative of a dose-dependent phenomena, so that with an increasing dose of fenoterol, the magnitude and duration of response increased in the doses tested.

The results were similar to an earlier report by Steen et al1 in which the bronchodilator effect of three dose levels (0.5, 1.25, and 2.5 mg) of fenoterol solution, one dose level each of isoproterenol solution (2.5 mg), isetharine solution (5 mg), and placebo administered by a motorized mist nebulizer (Maxi-Myst aerosol unit) were compared in 20 patients with reversible chronic airways obstruction. They found that mean FEV1 values of all drugs showed responses higher than placebo and that the highest dose of fenoterol produced significantly greater and longer drug action than the lower doses of fenoterol and the other bronchodilators. Beardshaw et al7 compared bronchodilating effects of 0.4 mg and 0.8 mg of aerosol fenoterol administered from MDI and found no advantage with doubling the dose. On the other hand, Pellon et al15 reported that there was no significant increase in FEV1 caused by increasing the dose of aerosol fenoterol from 0.1 to 0.4 mg in 20 patients with asthma, but the responses of FEF25-75 and SGaw with 0.4 mg were significantly greater in the initial two hours than with 0.1 mg. Alvarado et al14 found a dose-dependent increase in duration of response when 0.1, 0.2, and 0.4 mg doses of fenoterol by MDI were administered to 22 patients with asthma. The results of the present study cannot be compared directly to these previous studies with MDI because of differences in method of delivery and the range of doses tested.

Although the MDI is a convenient and popular way to deliver bronchodilators, there are certain circumstances that administration by devices other than MDI, such as the compressor-powered nebulization system (CPN) used in this study, are preferred as recommended by Posey and Tinkelman.25 Examples of such are patients who have an adverse reaction to Freon propellant or who have a tendency to abuse MDI. Little information concerning the optimal therapeutic dose of fenoterol solution for use with CPN has been available. In this study, the test doses were chosen on the basis of the previous knowledge that when bronchodilator is delivered by IPPB (Bird Mark 7 respirator and nebulizer), only 10 to 15 percent of nebulized dose reaches the lung, and the remainder is retained in the mouthpiece, nebulizer, tubings, and the expired air. When administered from a pressurized canister, nearly all of the dose is retained by the patient.26 In accordance with this, Weber et al24 found that when terbutaline was administered by both IPPB and CPN, six to eight times as much drug was required to achieve the same degree of bronchodilation as when administered from MDI. In the present study, therefore, five test doses of fenoterol solution, ranging from 1.25 to 6.25 times the recommended therapeutic dose from MDI (0.4 mg) were administered by CPN. Contrary to the previous studies, the results of this study do not seem to indicate that much larger doses are required to achieve the same degree of functional improvement when delivered by CPN compared to the dose by MDI, since there was no significant difference in response between 0.4 mg of fenoterol from MDI and 0.5 mg by the CPN. This is probably due to one or both of the following: (1) there may have been only a negligible waste of the drug in the expired air and in the nebulization system used in the present study in which no tubing was placed distal to the nebulizer. Patients participating in this study had been well instructed in how to inhale the aerosol without wasting it into the atmosphere; and (2) the administration of the drug was made by multiple inhalations over a period of time that may have helped greater penetration of the drug into peripheral airways.

There has been no conclusive evidence to support that multiple inhalation of bronchodilator produces better results than a single inhalation of the same dose. Weber et al24 compared the bronchodilator effect of four inhalations of 0.125 mg of terbutaline (total dose = 0.5 mg) at one-minute intervals from a MDI to a single inhalation of the same dose (0.5 mg) in patients with bronchial asthma. They found that the mean response in FEV1 to terbutaline as a single dose was consistently less than the response to terbutaline in divided doses, although the results did not reach a level of statistical significance. They suggested that the bronchodilator response is related to the total dose inhaled, not to the number of inhalations required to achieve that dose.

Most of the adverse reactions to fenoterol were very mild, transient, and well-tolerated phenomena and did not seem to be dose-related in the dose range tested except for a sensation of shakiness and tremor of the hands. The latter was the most frequent side effect and seemed to be dose-related in terms of incidence and degree.
From the results of the present study, we concluded that 0.5 mg of aerosolized fenoterol delivered by compressor-powered nebulization is almost equal in bronchodilating potency to 0.4 mg from MDI. Furthermore, 1.0 mg of fenoterol is recommended as a single therapeutic dose when administered by a compressor powered nebulization, since this dose produced a significantly greater functional improvement and sustained the drug action for longer periods without significant increase in side effects than 0.4 mg from MDI.

We do not have any information on the effect of long-term repetitive use of this drug. Steen et al.14 and Chervinsky15 studied the therapeutic effectiveness of fenoterol aerosol following administration of 0.4 mg from MDI several times per day for a 90-day period in asthmatic patients and found that fenoterol aerosol sustained a useful bronchodilating effect for that period without any serious side effects. However, the results of Steen et al suggest that some drug tolerance may develop following the repetitive use for several weeks.

ACKNOWLEDGMENT: The authors wish to thank Charles W. Serby, M.D., Paul Irwin, and James Clifford of Boehringer Ingelheim Ltd., Elmsford, N.Y., for their close support; Bill Rush of the Division of Pharmacy, University of Utah Medical Center, for the preparation of the study agents; Angela DeVito and Bruce Mortensen for their technical assistance; and Jeanette Jensen for the preparation of the manuscript.

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