

Bronchodilator Delivery by Metered-dose Inhaler in Ventilator-supported Patients

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The optimal dose and technique for administration of bronchodilators with a metered-dose inhaler (MDI) in mechanically ventilated patients have not been established. We studied the efficacy and safety of 10 puffs (90 μ g/puff) of albuterol administered by an MDI in seven mechanically ventilated patients with chronic obstructive pulmonary disease (COPD). Rapid airway occlusions at constant flow inflation were performed before and at 5-min intervals after administration of albuterol for 60 min. Significant decreases in maximum (R_{rsmax} ; $p < 0.01$) and minimum inspiratory resistance (R_{rsmin} ; $p < 0.01$) were present at 5 min and persisted for 60 min after administration of albuterol ($p < 0.01$ for both parameters). R_{rsmax} indicates maximal inspiratory resistance while R_{rsmin} represents the ohmic flow resistance. Intrinsic positive end-expiratory pressure decreased significantly ($p < 0.05$) 15 min after albuterol administration. Heart rate, blood pressure, and arterial oxygenation did not show significant change after albuterol. In summary, 10 puffs of albuterol given by an MDI and spacer produced significant bronchodilation in ventilator-supported patients with COPD, without producing side effects. In conclusion, higher doses of albuterol given by an MDI and spacer could be used routinely in mechanically ventilated patients with COPD. Dhand R, Jubran A, Tobin MJ. Bronchodilator delivery by metered-dose inhaler in ventilator-supported patients. *Am J Respir Crit Care Med* 1995;151:1827-33.

In mechanically ventilated patients, the efficiency of aerosol delivery to the lower respiratory tract depends on several factors that are not a concern in ambulatory patients (1, 2). In particular, deposition of aerosol in the endotracheal tube and ventilator circuit causes a significant reduction in the fraction of aerosol reaching the lower respiratory tract (3, 4). Fuller and coworkers (4) observed that the deposition of aerosol delivered by metered-dose inhalers (MDI) in mechanically ventilated patients was lower than the values of 9 to 14% generally reported in nonintubated patients (5, 6). To compensate for the inefficient delivery of aerosols, it has been recommended that the dose of bronchodilator by an MDI should be increased in ventilator-dependent patients (7). However, the optimal dose is not known, as the efficacy of MDIs in delivering bronchodilator agents in ventilator-dependent patients has been examined by only a few investigators. These investigators employed different doses of bronchodilators and different techniques of administration (4, 8-12). A significant bronchodilator effect was shown in some studies (9, 10) but not in others (4, 8, 11).

The type of adapter used to connect an MDI to the ventilator circuit and the position of the aerosol generator in the ventilator circuit also influence aerosol delivery (1). Several commercial adapters (chamber devices, in-line devices, and elbow devices) can be used to connect an MDI to the ventilator circuit. The efficiency of these adapters in delivering aerosol can vary up to 100%

(13), and thus may have a considerable influence on the clinical response. Manthous and coworkers convincingly demonstrated that a swivel adapter connected to the endotracheal tube was very inefficient in delivering aerosol to the lower respiratory tract (2, 11).

With these issues in mind, we attempted to resolve some of the factors concerning the technique of administration, the dose requirement, the onset and duration of the response, as well as the safety of albuterol given by an MDI in mechanically ventilated patients. We investigated these factors in a homogenous group of mechanically ventilated patients with chronic obstructive pulmonary disease (COPD). Ten puffs of albuterol were actuated into a cylindrical spacer device placed at a distance of 15 cm from the endotracheal tube, and changes in mechanics of the respiratory system were assessed by rapid airway occlusion at constant flow inflation.

METHODS

Seven patients with COPD receiving mechanical ventilation for acute respiratory failure were enrolled in the study. The patients were clinically stable, without hypotension, cardiac arrhythmias, myocardial infarction, or unstable angina. Patients with pneumonia, pulmonary edema, pneumothorax, refractory hypoxemia, or excessive airway secretions were excluded. The patients, all men, were aged 59 to 82 yr (mean 70.1 ± 3.5 SE yr). The diagnosis of COPD was based on a history of productive cough, shortness of breath, and long-term smoking (83.6 ± 5.0 SE pack yr, range 60 to 100 pack yr). Their chest roentgenograms showed evidence of lung hyperinflation, decreased lung markings, and absence of other specific etiologies to explain these changes. Pulmonary function tests, done before the hospital admission when the patients were clinically stable, were available in 6 patients, and these confirmed the presence of airway obstruction that was not reversible with bronchodilators (ratio of forced expiratory volume in 1 s to forced vital capacity [FEV₁/FVC], 52.2 ± 2.4 SE %; FEF_{25-75%}, 31.7 ± 3.2 % of predicted normal; maximum increase in

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FEV₁ after bronchodilator, 9%). The study was approved by the Human Studies Subcommittee of Edward Hines Jr. Veterans Administration Hospital, and patients gave informed consent.

All patients were intubated with cuffed endotracheal tubes, with the exception of one patient who had a tracheostomy tube. Patients received mechanical ventilation in the control mode with a constant inspiratory flow (Servo 900C, Siemens Elema AB, Solna, Sweden). Proximal airway pressure (Paw) and airflow were monitored continuously by a pneumotachograph (Bicore, Irvine, CA) placed between the endotracheal tube and the Y-piece of the ventilator circuit. Validation of the pneumotachograph against a volumetric syringe revealed mean arithmetic differences of $-0.09 \pm 0.6\%$ (SE). This level of accuracy is similar to that reported by Nathan and colleagues (14). Validation of the pressure transducer against a water manometer over a range of ± 80 cm H₂O revealed a mean arithmetic difference of $-0.75 \pm 1.1\%$. The pressure and flow signals from the transducers were continuously digitized at 50 and 100 Hz, respectively, using a 12-bit analog-to-digital converter connected to a computer (Dell 316RX) and stored for analysis.

Protocol

The study was conducted with the patient lying in a semirecumbent position, with the head of the bed raised 20° from the horizontal position. All the patients were receiving aerosolized bronchodilators and these were withheld for at least 4 h before the study. Three patients were receiving theophylline and an equal number were receiving corticosteroids. Heart rate, respiratory frequency, and arterial pressure were recorded. Oxygen saturation was monitored with a pulse oximeter (SpO₂). Condensation of water vapor in the ventilator tubing was drained, and secretions were suctioned from the endotracheal tube. Patients were sedated with lorazepam, 2 to 4 mg intravenously. The back-up rate on the ventilator was gradually increased until all breathing efforts were suppressed. The absence of negative deflections of airway pressures and uniformity of the pressure contour and breath cycle duration confirmed that passive ventilation had been achieved. Tidal volume, breathing frequency, inspiratory airflow, and fractional concentration of inspired oxygen (FIO₂) were constant throughout the study.

An MDI canister containing albuterol (90 µg/puff, Schering Corp., Kenilworth, NJ) was connected to a cylindrical, collapsible spacer chamber (Aerovent, Monaghan Medical, Plattsburgh, NY; volume, 147 ml) placed in the inspiratory limb of the ventilator circuit 15 cm from the endotracheal tube. The MDI canister was inserted into a port situated at one end of the spacer so that the aerosol was directed towards the patient. After vigorous shaking, the MDI canister was actuated into the spacer immediately before initiation of airflow by the ventilator. Ten successive actuations were performed at approximately 20-s intervals. The canister was not shaken between actuations.

Computation of Physiological Indices

Breath-by-breath measurements of Paw and airflow were obtained. At the end of a mechanical inflation with a constant inspiratory flow, the airway opening was occluded for a duration sufficient to achieve a plateau airway pressure (15, 16). Five breaths with satisfactory end-inspiratory occlusions were recorded before and at 5-min intervals after albuterol administration. End-expiratory occlusions were also performed, which were for a duration sufficient to achieve a plateau pressure, thus allowing measurement of auto or intrinsic positive end-expiratory pressure (PEEP_i) (17). Again, five breaths with end-expiratory occlusions were recorded before and at 5-min intervals after administration of albuterol. Tidal volume was calculated by integration of the flow signal. From the recordings of Paw and airflow, graphs of individual breaths were obtained during passive inflation, end-inspiratory occlusion (Figure 1A), and end-expiratory occlusion (Figure 1B). Immediately after end-inspiratory occlusion, airway pressure exhibits a rapid decrease to a lower initial pressure (P_{init}). This is followed by a gradual decrease in airway pressure to reach a plateau pressure (P_{plat}), as shown in Figure 1A. Back extrapolation of the slope of the latter part of the airway pressure tracing to the time of airway occlusion was used to determine P_{init} (16, 18). Maximal inspiratory resistance (R_{rs}max, also previously described as R_{rs} or R_{iol}) was calculated as the difference between P_{peak} and P_{plat} divided by the inspiratory air-

flow immediately before the occlusion ($R_{rs}max = [P_{peak} - P_{plat}]/\text{airflow}$). Initial or minimal inspiratory resistance (R_{rs}min, also termed R_{int} or R_{init}) was calculated as the difference between P_{peak} and P_{init} divided by the flow observed just before the airway occlusion ($R_{rs}min = [P_{peak} - P_{init}]/\text{airflow}$). The difference between R_{rs}max and R_{rs}min (ΔR_{rs}) was calculated as the difference between P_{init} and P_{plat} divided by the preocclusion value of airflow ($\Delta R_{rs} = [P_{init} - P_{plat}]/\text{airflow}$). R_{rs}min is considered to reflect ohmic airway resistance, while ΔR_{rs} is considered to represent the visco-elastic properties and regional inhomogeneities of the lung (16). Expiratory resistance was not computed because of the likelihood of expiratory flow limitation in this patient population. The static inflation compliance of the respiratory system (C_{rs}) was computed as the ratio between tidal volume and the difference between the end-inspiratory and end-expiratory plateau pressures ($C_{rs} = \text{tidal volume}/[P_{plat} - PEEP_i]$).

Data Analysis

Airway pressures, resistances, compliance, and vital signs recorded before aerosol administration were compared with values obtained at 5, 15, 30, 45, and 60 min after drug administration. Data were analyzed by using one-way analysis of variance (ANOVA) and the Newman-Keuls' method (multiple comparisons between individual means). The results are expressed as mean $\pm$ SE, and $p < 0.05$ was considered statistically significant.

RESULTS

The physiological measurements at baseline are shown in Table 1. Passive ventilation was achieved with tidal volumes ranging from 600 to 1,000 ml and respiratory frequencies of 8 to 16 breaths/min. Peak airway pressure varied from 30 to 48 cm H₂O, and the R_{rs}max was increased in all patients (range 18 to 24 cm H₂O/L/s). PEEP_i was at least 5 cm H₂O in 5 patients.

The changes in P_{peak}, P_{init}, P_{plat}, and PEEP_i after administration of albuterol are shown in Figure 2. After 5 min, significant decreases occurred in P_{peak} ($p < 0.01$, panel A), P_{init} ($p < 0.01$, panel B), and P_{plat} ($p < 0.05$, panel C). A decrease in PEEP_i was not significant until 15 min after albuterol administration ($p < 0.05$, panel D). These decreases in pressure persisted for 60 min following albuterol administration ($p < 0.01$ in all instances).

Decreases in R_{rs}max and R_{rs}min (Figure 3) occurred 5 min after albuterol administration ($p < 0.01$ for both parameters), which were sustained for at least 60 min ($p < 0.01$ for both parameters). Albuterol had a rapid onset of action, as manifested by a $15.4 \pm 3.7\%$ decrease in R_{rs}max at 5 min after drug administration; however, this response was variable among patients, range 2.4 to 28.5%. The greatest decrease in R_{rs}max was observed 15 min after albuterol administration (mean, $16.3 \pm 3.4\%$), although this value was not significantly different from the value at 5 min. R_{rs}max decreased by more than 15% in five patients, and all displayed a sustained effect with a decrease in R_{rs}max at 60 min, ranging from 16.1 to 29.5% (mean $20.8 \pm 2.0\%$); one patient showed a maximum decrease of 14.4% in R_{rs}max, and the remaining patient showed no change.

The decrease in P_{peak} was mainly due to the significant fall in R_{rs}max. The elastic component of Paw, i.e., C_{rs}, did not change significantly after albuterol administration ($p > 0.05$, Figure 4). Similarly, the values of ΔR_{rs} did not show a significant change after albuterol administration ($p = 0.9$, Figure 5).

Changes in heart rate, blood pressure and SpO₂ observed after administration of albuterol were not statistically significant ($p > 0.05$, Table 2).

DISCUSSION

This study demonstrates that the administration of 10 puffs of albuterol (0.9 mg) from an MDI produced a significant decrease in

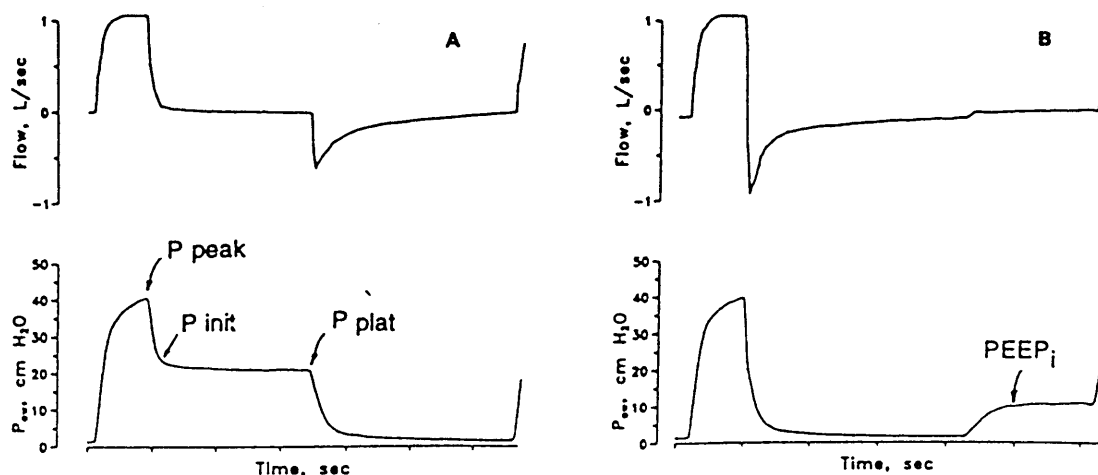


Figure 1. Recording of airflow and airway pressure (Paw) showing occlusion of the airway at end-inhalation (A) and at end-exhalation (B). An end-inspiratory occlusion produces a rapid decline from peak pressure (P_{peak}) to a lower initial pressure (P_{init}), followed by a gradual decrease to a plateau pressure (P_{plat}). Occlusion of the airway at end exhalation produces an increase in airway pressure, and its plateau value signifies the level of intrinsic PEEP (PEEP_i).

airway resistance in ventilator-supported patients with COPD. The bronchodilator effect was observed within 5 min and was sustained for at least 60 min. These effects were observed without any untoward cardiovascular effects.

Administration of bronchodilator agents to mechanically ventilated patients with COPD has several potential benefits, including reversal of bronchoconstriction, mobilization of secretions, and a reduction in work of breathing. A significant reduction in airway resistance occurred 5 min after administration of albuterol by an MDI in our patients. The decreases in R_{rs} min and PEEP_i are particularly important, as these parameters have been shown to be major determinants of the work of breathing in patients with COPD receiving mechanical ventilation (19). The baseline values of R_{rs} max in our patients are comparable with the values of 18.1 ± 6.4 cm H₂O/L/s obtained by Bernasconi and coworkers (20) in their ventilator-supported patients with COPD. Higher values of R_{rs} max (26.4 ± 4.74 cm H₂O/L/s) were obtained by Broseghini and coworkers (21) in patients with COPD studied on the first day of mechanical ventilation. All of these values are much higher than those reported using similar methodology in healthy subjects (22). While the increase in resistance is largely due to the presence of airway disease, an additional factor is the inspiratory flow resistance due to the ventilator circuit and endotracheal tube (23). Of interest, R_{rs} min values in our patients are comparable with those reported on the first day of ventilator support by Broseghini

and coworkers (21), indicating that airway resistance remained elevated in our patients even when they were in a relatively stable phase.

The magnitude of the bronchodilator effect in our patients was striking considering that the measurements were obtained during tidal breathing (in contrast to the use of a forced maneuver such as the FEV₁ in ambulatory patients). The decrease in R_{rs} max with 10 puffs of albuterol was comparable with the change in resistance of the lung and airways with 10 puffs of the same agent in intubated, spontaneously breathing patients (10), and greater than the decrease in R_{rs} max observed by Fernandez and coworkers (9) using two puffs, suggesting the presence of a dose response effect. Interestingly, the observed bronchodilation with 0.9 mg of albuterol from an MDI was comparable with that observed with cumulative doses of 7.5 mg of albuterol (11) or 2.4 mg of fenoterol (20) administered by a small volume nebulizer.

The duration of response to bronchodilators delivered by an MDI in mechanically ventilated patients is not known. Fuller and colleagues reported that the effect of fenoterol (0.8 mg) on peak airway pressure had dissipated by 30 min (4). In our study, the decreases in R_{rs} max and R_{rs} min remained undiminished for 60 min after albuterol administration. The duration of the response may be related to the delivered dose, with larger doses producing a longer action (24, 25). Unfortunately, the dose response relationship to beta-adrenergic bronchodilator agents given by an MDI

TABLE 1
VENTILATORY DATA AND PULMONARY MECHANICS AT BASELINE*

Pt	V _T (ml)	f (br/min)	V _E (L/min)	$\dot{V}$ (L/min)	F _{IO₂}	T _I (s)	T _E (s)	T _I /T _{TOT}	P _{peak} (cm H ₂ O)	P _{plat} (cm H ₂ O)	PEEP _i (cm H ₂ O)	R _{rs} max (cm H ₂ O/L/s)
1	800	8	6.4	48	0.5	1.0	6.5	0.13	30	13	0	21.3
2	850	10	8.5	60	0.5	0.85	5.2	0.14	43	20	3	23.0
3	600	10	6.0	48	0.5	0.75	5.3	0.13	35	17	5	22.5
4	1,000	12	12.0	60	0.3	1.0	4	0.20	35	17	5	18.0
5	800	10	8.0	50	0.3	0.96	5.0	0.16	43	23	8	24.0
6	800	12	9.6	50	0.4	0.96	4.0	0.19	43	24	6	22.8
7	800	16	12.8	70	0.4	0.69	3.1	0.18	48	22	10	22.3

Definition of abbreviations: V_T = tidal volume; f = breathing frequency; V_E = minute volume; $\dot{V}$ = inspiratory flow rate; F_{IO₂} = fractional concentration of inspired oxygen; T_I = inspiratory time; T_E = expiratory time; T_I/T_{TOT} = duty cycle; P_{peak} = peak airway pressure; P_{plat} = plateau pressure; PEEP_i = intrinsic PEEP; R_{rs}max = maximal inspiratory resistance.

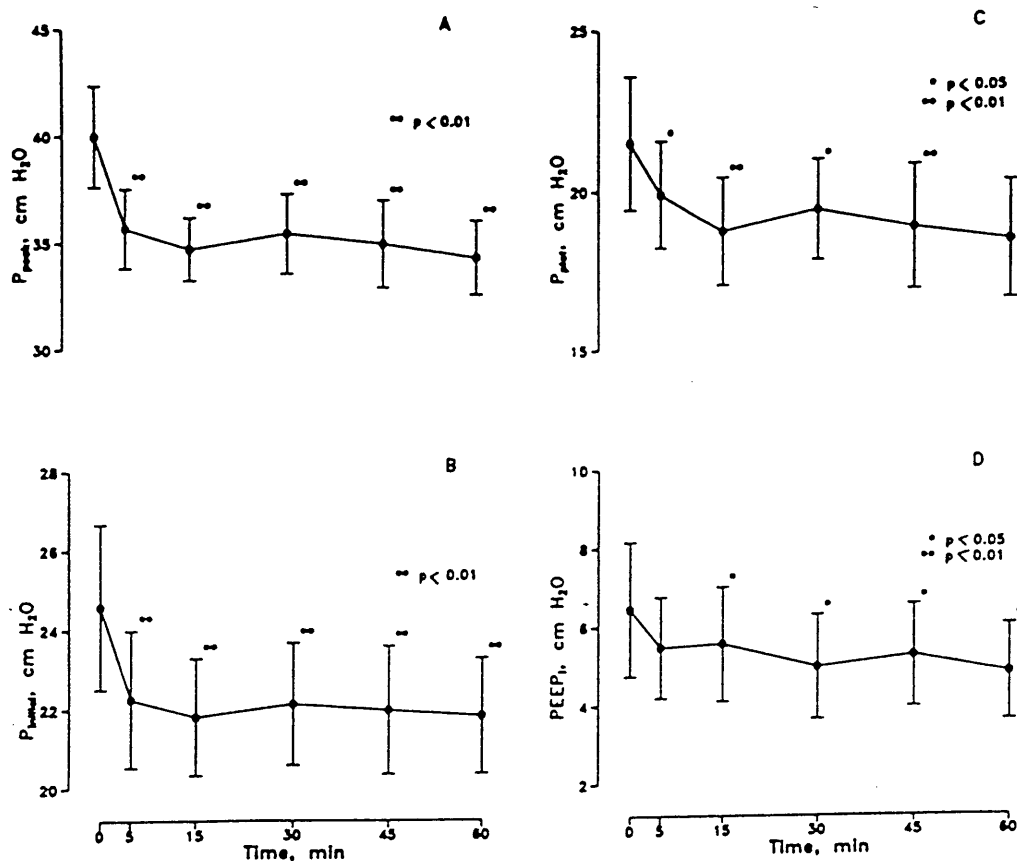


Figure 2. Effect of albuterol on peak airway pressure (P_{peak} , panel A), initial pressure (P_{init} , panel B), plateau pressure (P_{plat} , panel C), and intrinsic PEEP ($PEEP_i$, panel D). Significant decreases in P_{peak} , P_{init} and P_{plat} were observed at 5, 15, 30, 45 and 60 min after albuterol administration ($p < 0.01$ for each parameter). The decreases in $PEEP_i$ were significant at 15, 30, 45 ($p < 0.05$) and 60 min ($p < 0.01$) after drug delivery. Bars represent SE. * = $p < 0.05$; ** = $p < 0.01$.

in mechanically ventilated patients has not been reported. The only study examining the use of increasing doses of albuterol given by an MDI in ventilator-supported patients did not demonstrate a significant bronchodilator effect (11). Nebulized fenoterol in doses of 0.4, 0.8, and 1.2 mg produced a significant bronchodilator effect for only 1 h, with very little response noted after 3 h in mechanically ventilated patients with COPD (20). Furthermore, administration of higher doses of fenoterol (0.8 and 1.2 mg) was not

associated with a significantly greater response than that observed with 0.4 mg of fenoterol.

The values of C_{rs} in our patients were slightly lower than normal for healthy, anesthetized, paralyzed subjects (26) but were similar to those observed by Broseghini and coworkers (21) in their patients with COPD on the first day of mechanical ventilation. The lack of change in C_{rs} with albuterol indicates that the latter did not significantly influence the elastic properties of the lung. The

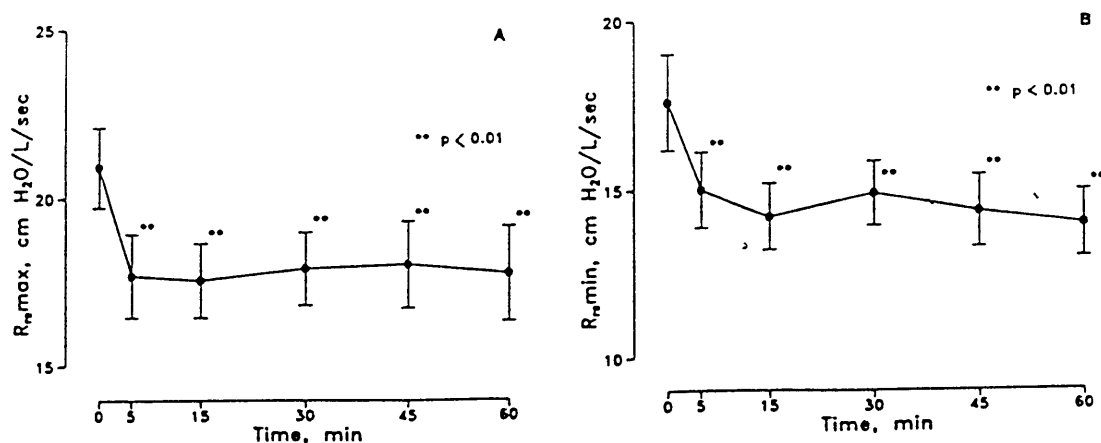


Figure 3. Effect of albuterol on maximal inspiratory resistance (R_{rsmax} , panel A) and minimal inspiratory resistance (R_{rsmn} , panel B). Significant decreases in R_{rsmax} and R_{rsmn} were observed 5 min after albuterol administration, which were sustained for 60 min ($p < 0.01$). Bars represent SE. ** = $p < 0.01$.

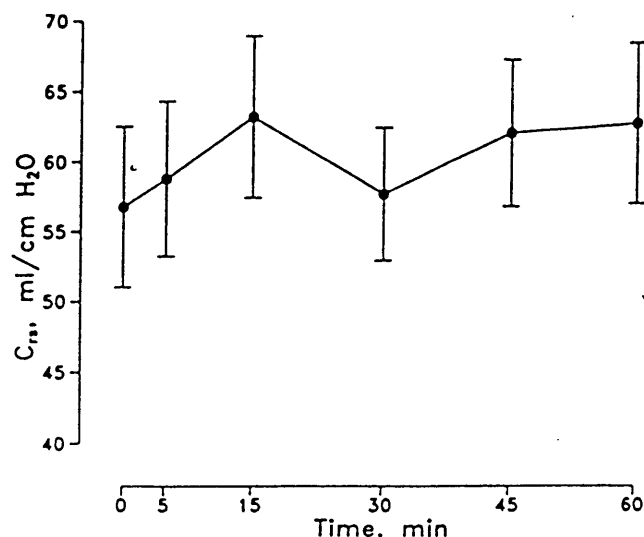


Figure 4. Effect of albuterol on respiratory system compliance (C_{rs}). No significant change in C_{rs} was observed after albuterol administration. Bars represent SE.

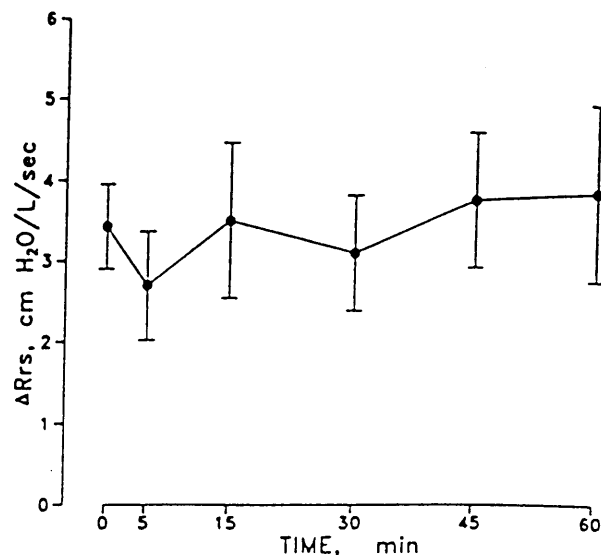


Figure 5. Effect of albuterol on additional respiratory resistance (ΔR_{rs}). No significant change in ΔR_{rs} was observed after albuterol administration. Bars represent SE.

decrease in P_{plat} was mainly due to a decrease in $PEEP_i$. There was no change in values of ΔR_{rs} after albuterol administration, even though time constant inequalities have been shown to make a significant contribution to ΔR_{rs} in patients with COPD (19). Values of ΔR_{rs} in our patients were lower than ΔR_{rs} values reported on the first day of mechanical ventilation in patients with COPD (21), suggesting that an improvement in time constant inequalities and stress relaxation behavior of the lung may occur with improvement in the patients' clinical status. Therefore, it appears that the changes in airflow resistance following albuterol administration were mainly due to a decrease in R_{rsmin} without much apparent effect on visco-elastic behavior or time constant inhomogeneities in the lung. When R_{inh} or R_{rsmin} was partitioned into lungs and chest wall components, the contribution from the chest wall was found to be negligible (27). Hence, the decrease in R_{rsmin} probably reflects the relaxant effect of albuterol on bronchial smooth muscle and supports the notion that R_{rsmin} reflects airway resistance.

Bronchodilators have been administered to critically ill patients by MDIs in different dosages, with different techniques of administration, and different degrees of efficacy (Table 3). The variability in efficacy underscores the importance of selecting the appropriate dose and technique of administration. All but one of our patients showed a consistent and sustained decrease in R_{rsmax} and R_{rsmin} following albuterol administration. We selected a dose of 10 puffs of albuterol based on the findings of decreased respiratory tract deposition of aerosol in mechanically ventilated pa-

tients described by Fuller and colleagues (4). One possible reason for increased deposition of aerosol in the circuit could be hygroscopic growth of aerosol due to increased humidity in the ventilator circuit (28). In addition, two other factors are important in determining the therapeutic response: the type of spacer and its location in the ventilator circuit, and the timing of the MDI actuation in relation to the ventilator breath.

The technique of aerosol administration should be simple and preferably avoid disconnection of the ventilator circuit. We used a collapsible cylindrical spacer that remained in the ventilator circuit between actuations of the MDI. In a mechanically ventilated lung model, Rau and colleagues (29) showed that the combination of an MDI and a chamber device resulted in a fourfold greater delivery of aerosol to a lung model when compared with actuation of the MDI into a connector placed directly at the endotracheal tube. Fuller and colleagues (13) also reported that a chamber type adapter in the inspiratory limb of the ventilator circuit significantly improved pulmonary deposition compared to a commercially available device that allows MDI actuation into the inspiratory limb but lacks a chamber (Instrumentation Industries Inc., Bethel Park, PA). Connecting the adapter directly to the endotracheal tube results in considerable deposition of aerosol within the tube itself, thereby reducing the fraction available for delivery to the respiratory tract. Consequently, the therapeutic effect obtained with such an adapter may be small or negligible, as shown by Manthous and coworkers (11) with up to 100 puffs (9 mg) of albuterol given by an MDI. Therefore, a spacer device with a chamber placed at a distance

TABLE 2
VITAL SIGNS BEFORE AND AFTER ADMINISTRATION OF ALBUTEROL*

	Heart Rate (b/min)	Systolic BP (mm Hg)	Diastolic BP (mm Hg)	S_pO_2 (%)
0 min	91.4 ± 6.2	121.0 ± 8.9	64.9 ± 6.3	96.7 ± 1.3
5 min	87.7 ± 7.2	120.7 ± 8.5	64.6 ± 6.9	96.9 ± 1.1
15 min	93.3 ± 6.3	125.6 ± 8.8	64.3 ± 5.9	97.3 ± 1.3
30 min	92.3 ± 5.9	122.7 ± 8.8	64.3 ± 6.3	96.4 ± 1.3
45 min	93.4 ± 5.8	125.6 ± 9.9	62.9 ± 5.9	96.6 ± 1.1
60 min	90.9 ± 5.9	120.9 ± 8.8	64.1 ± 5.6	96.1 ± 1.1

Definition of abbreviations: BP = blood pressure; S_pO_2 = oxygen saturation by pulse oximetry.

*Values represent mean ± SE.

TABLE 3
TECHNIQUE OF ADMINISTRATION AND RESPONSE TO BRONCHODILATORS
IN MECHANICALLY VENTILATED PATIENTS

Authors	Drug/Dose	Canister and Adapter	Inflation	Results
Gay and colleagues (8)	Albuterol 0.27 mg	Connected to ETT	Manual with breath hold	Increase in expiratory flow not significant
Fernandez and colleagues (9)	Albuterol 0.20 mg or Ipratropium 0.04 mg	Connected to ETT with short catheter into ETT	Manual with breath hold	Significant decrease in P_{peak} , PEEP _i
Fuller and colleagues (4)	Fenoterol 0.8 mg	Cylindrical spacer, 15 cm from ETT	Ventilator breaths	Decrease in P_{peak} not significant
Mancebo and colleagues (10)	Albuterol 0.9 mg	Conical spacer connected to ETT	Spontaneous breathing	Significant decrease in R_{aw}
Manthous and colleagues (11)	Albuterol 9.0 mg	Connected to ETT	Ventilator breaths	No change in R_{aw}
Fernandez and colleagues (12)	Ipratropium 0.04 mg or Ipratropium 0.04 mg + Fenoterol 0.1 mg	Connected to ETT with short catheter into ETT	Manual with breath hold	No change in R_{aw} with Ipratropium; significant decrease in R_{aw} with combination
Present study	Albuterol 0.9 mg	Cylindrical spacer, 15 cm from ETT	Ventilator breaths	Significant decrease in R_{aw}

Definition of abbreviations: ETT = endotracheal tube; P_{peak} = peak airway pressure; PEEP_i = intrinsic PEEP; R_{aw} = airway resistance.

from the endotracheal tube appears to be the preferred method for delivery of an aerosol by MDIs in mechanically ventilated patients.

Higher doses (1 to 4 mg) of albuterol given by MDIs in nonintubated COPD patients produce a mild increase in heart rate, non-sustained supraventricular tachycardia, tremors, and fall in arterial oxygen saturation (24, 25, 30). In contrast, no significant peripheral cardiovascular effects were observed with up to 100 puffs of albuterol by an MDI in mechanically ventilated patients with COPD (10, 11). Similarly, albuterol produced no significant changes in heart rate, blood pressure, or S_pO_2 in our patients. The relative safety of albuterol given by MDIs to mechanically ventilated patients is probably due to the decreased lower respiratory tract deposition of aerosol (4). Moreover, actuation of the aerosol into the ventilator circuit would be expected to decrease absorption of the drug from the oropharynx and gastrointestinal tract, and thereby limit systemic side effects.

In summary, this study demonstrates the efficacy of 10 puffs of albuterol (0.9 mg) given by an MDI in mechanically ventilated patients using a cylindrical spacer placed in the inspiratory limb of the ventilator circuit. The technique of administration was simple and applicable to routine clinical use. The effect of albuterol was rapid in onset, sustained for at least 1 h, and resulted in no significant side effects. In conclusion, the bronchodilator effect observed with an MDI actuated into a spacer was comparable with that reported for small volume nebulizers. Routine use of MDIs with a spacer in mechanically ventilated patients could result in substantial reduction in the cost of bronchodilator therapy without compromise in efficacy.

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