Efficacy of Metered-Dose Inhaler Administration of Albuterol in Intubated Infants*

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Study objective: To compare the safety and efficacy of metered-dose inhaler (MDI) albuterol to nebulized (NEB) albuterol administration.

Design: A randomized, triple-blinded, crossover study.

Setting: A pediatric ICU in a tertiary care children's hospital.

Patients: Eleven intubated infants with bronchiolitis.

Interventions: Subjects received four puffs of MDI albuterol (360 μg) and 3 mL of NEB saline solution placebo or 0.3 mL of NEB albuterol (1.5 mg) and MDI saline solution placebo. Each set of albuterol and saline solution placebo was administered after direct attachment of delivery device to the endotracheal tube and bag-valve system. Subjects received the opposite sequence 4 h after the initial sequence. The second sequence was given first the next day, and the first sequence was administered 4 h later.

Measurements and results: Respiratory system compliance and resistance were measured at baseline and 30 min, 1 h, 2 h, and 4 h after each set of placebo and albuterol. There was an appreciable improvement in compliance and resistance for up to 2 h following both methods of administration. However, the degree of improvement was not significantly different (p>0.05) between the two methods. Neither method caused a significant change in resistance when measured at 4 h after albuterol/placebo administration. No evidence of toxicity was detected.

Conclusions: MDI-administered albuterol is as safe and efficacious as nebulized-administered albuterol in intubated infants with bronchiolitis. Generalizability of these results is limited by differences in drug delivery with different brands of nebulizers and spacers and sites of attachment.

(CHEST 1997; 112:484-90)

Abbreviations: CI=confidence interval; Crs=respiratory system compliance; ETT=endotracheal tube; FIO2=fraction of inspired oxygen; MDI=metered-dose inhaler; NEB=nebulized, nebulizer; PEEP=positive end-expiratory pressure; PICU=pediatric ICU; Rsx=respiratory system resistance; RSV=respiratory syncytial virus; SpO2=pulse oximeter arterial saturation; VT=tidal volume

There is a national movement to administer aerosolized medications to intubated patients with metered-dose inhalers (MDI). The Consensus Conference on Aerosol Delivery sponsored by the American Association of Respiratory Care and the American Respiratory Care Foundation concluded that MDI is the preferred route of administration of aerosolized medications to intubated patients with a tidal volume (VT)>100 mL. Although MDI delivers lower doses of β-agonists than a nebulizer, the safety and efficacy of these two methods in intubated adults are comparable. Furthermore, when compared with nebulized (NEB) administration of albuterol in hospitalized patients, MDI administration is associated with substantial cost savings. However, with no documentation of the safety and efficacy of MDI administration of albuterol in intubated children, there is less acceptance of MDI administration in this population. The purpose of this triple-blinded, randomized, crossover study was to compare the safety and efficacy of MDI to that of NEB administration of albuterol in intubated infants with bronchiolitis.

For editorial comment see page 303

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Clinical Investigations in Critical Care
Materials and Methods

Approval of the study protocol and informed consent were received from the Human Research Advisory Committee of the University of Arkansas for Medical Sciences. Informed consent was obtained from the parent(s) of all enrolled subjects prior to participation.

Subjects

Intubated, mechanically ventilated infants admitted to the pediatric ICU (PICU) during respiratory syncytial virus (RSV) season with bronchiolitis (ie, upper respiratory tract infection prodomate plus cough, tachypnea, wheezing, and low-grade fever) were enrolled consecutively into the study. Exclusion criteria included the following: (1) clinical instability (eg, tachycardia for age, evidence of shock, status asthmaticus, air leak); (2) clinical requirements of a fraction of inspired oxygen (FiO₂) ≥0.5 or positive end-expiratory pressure (PEEP) ≥8 cm H₂O; or (3) concurrent theophylline or aminophylline administration. Enrolled subjects received one dose of albuterol, 1.5 mg via jet NEB immediately preceded and followed in 30 min by measures of respiratory system resistance (Rrs) prior to randomization (see “Techniques” section). The subject was excluded if the post albuterol Rrs did not significantly decrease (ie, p<0.05 by a paired t test).

Materials

Jet NEBs (Mistinebs; Baxter Healthcare Corp; Valencia, Calif) used were tested prior to the study to determine mass output and aerosol characteristics. The mass output or rate of nebulization (mL/min) for 12 NEBs was determined with a top-loading scale (ie, g weight loss/min=mL of solution NEB/min). The aerosol particle size distribution produced by the NEBs was characterized by nebulizing florescein dye solution through an eight-stage-cascade impactor (Andersen MK II; Graseby Andersen; Atlanta). The NEB florescein solution was collected on greased stainless steel plates that were rinsed with deionized water. The concentration of florescein in the solutions obtained from each filter was determined using a florescence spectrophotometer (Perkin-Elmer 203; Perkin Elmer Inc; Norwalk, Conn). Three NEBs were tested.

A spacing chamber (Airlife MediSpacer; Baxter Healthcare Corporation), with a volume of 130 to 145 mL, was used to administer MDI puffs to the subjects. All subjects received albuterol (Schering Corp; Kenilworth, NJ) and saline solution placebo (Glaxo Inc; Research Triangle Park, NC). Subjects received four puffs of MDI albuterol (360 μg) and 3 mL of NEB saline solution placebo or 0.3 mL of NEB albuterol (1.5 mg) in 3 mL of saline solution and MDI saline solution placebo. The NEB solutions were premixed and coded by a registered pharmacist with sole access to the code. The NEB with 6 inches of large-bore flex tubing and MDI with spacing chamber were attached directly to the subject’s endotracheal tube (ETT) for administration. All forms of albuterol and placebo were administered via hand ventilation with a 0.5-L anesthesia bag (Dupaco; Oceanside, Calif)—valve system (Anesthesia Associates; San Marcos, Calif) with a gas flow of 8 L/min and an FiO₂ equivalent to the subject’s baseline FIO₂. The MDI canister was shaken vigorously prior to each set of puffs. After the MDI canister was actuated at end-expiration, a sigh breath with 5-s breath-hold was administered. Thirty seconds of tidal breathing followed each puff to allow clearing of the chamber. The subject was hand ventilated with periodic sighs breaths followed by 5-s breath-holds during NEB administration until the solution or mist in the chamber was no longer visible.

Design

Each subject received either placebo MDI followed immediately by albuterol NEB or albuterol MDI followed immediately by placebo NEB in a blinded, randomized, crossover fashion. Respiratory system compliance (Crs) and Rrs were assessed at 0 min, 30 min, 1 h, 2 h, and 4 h after the first sequence. After 4 h, the alternate drug sequence was then administered. Crs and Rrs were again assessed at the same intervals. The following day, two blinded, crossover drug administration sequences were performed in the sequence opposite to that of the previous day with baseline and posttherapy Crs and Rrs. No chest physiotherapy or changes in ventilator settings were permitted during the time period of actual study. Tracheal suctioning with adequate time for clinical recovery was performed 5 min prior to each assessment of Crs and Rrs and administration of albuterol/placebo.

Techniques

While at rest or asleep, the subjects had baseline Crs and Rrs assessed with a specific system (SensorMedics 2600 Infant Pulmonary Function Laboratory; SensorMedics Corp; Yorba Linda, Calif). This system features a computer-controlled slide valve that occludes the airway at end-inspiration. This occlusion was held 0.1 to 0.5 s when a pressure plateau was achieved. Theoretically, it is at this point that stimulation of the inspiratory stretch receptors occurs which induces apnea or relaxation of the respiratory muscles, ie, the Hering-Breuer reflex. To facilitate this reflex, an inspiratory pause of 10% was added to the ventilatory pattern. The occlusion was then rapidly released, allowing the elastic recoil of the lungs to cause passive exhalation. Exhaled Vr was measured with a pneumotachograph (Hans Rudolph; Kansas City, Mo). Airway pressure was measured by a pressure transducer (MP45; Validyne; Northridge, Calif) connected to a side port of the valve at the attachment to the ET adapter. The respiratory system time constant was represented by the slope of the linear portion of the flow-volume curve. Rrs was calculated from the time constant and the measured Crs. Crs was determined by dividing passive exhaled volume by plateau pressure measured at the mouth during occlusion. For each set of measurements, the mean of five determinations of Crs and Rrs was obtained on records free of artifacts (ie, stable pressure plateau and sufficient linear portion on passive expiratory flow-volume curve). This passive flow-volume occlusion technique has been well described by LeSouef and colleagues.

Data Collection and Analysis

Subjects were monitored for signs of albuterol toxicity (eg, tachycardia, tremors, vomiting). Pulse oximetry was monitored continuously. Pulse oximeter arterial saturation (SpO₂) and heart rate were recorded prior to drug/placebo administration and prior to each pulmonary function measurement. Based on clinical experience, an SpO₂<93% and a heart rate ≥200 beats/min were considered abnormal. All variables were entered into a statistical software program (SPSS for Windows; Chicago) for analysis. The statistician was blinded to the modes of administration during the analysis. The average coefficients of variations for Crs and Rrs were calculated on five measurements obtained at baseline (SD/mean×100) and expressed as a mean percentage ± 1 SD. The Wilcoxon signed ranks test was used to test the median Crs and Rrs pre-MDI and pre-NEB for a difference. The percent change in Rrs and Crs post-MDI albuterol administration and the post-NEB administration values were tested for a difference with the Wilcoxon signed ranks test (α=0.05, β=0.2, 80% power to detect a 25% difference in mean percent change in Crs and Rrs.
between post-MDI and post-NEB administration values). The 95% confidence intervals (CIs) were determined for the mean percent change in Rrs and Crs at each time interval for both administration methods to provide the range of values within which the true magnitude of effect lies. Biological (weight, compliance, resistance) and demographic (age) data are reported as either mean±1 SD or median (range).

## Results

A total of 16 infants were enrolled from January 1 to May 1, 1994. Five of the 16 infants had insignificant decreases in Rrs after a dose of NEB albuterol and were excluded from further participation. Table 1 contains the demographic and biological data of the 11 subjects. Seven of the 11 infants had RSV infections confirmed by culture. All subjects were mechanically ventilated with a conventional ventilator (Servo Ventilator 300 or Servo 900C; Siemens Medical Systems; Piscataway, NJ) in the synchronized intermittent mandatory ventilation mode plus pressure support of 5 cm H2O. The mean (±SD) peak inspiratory pressure, PEEP, and FIO2 during the days of study were 36±8 cm H2O, 5±2 cm H2O, and 0.28±0.14, respectively. The inspiratory time and inspiratory pause time for all subjects were 0.5 s and 0.15 s, respectively. All subjects completed 2 days of study without any tremors or vomiting noted. One subject had a temporary decrease in SpO2 to 91% 60 min after MDI albuterol administration on the first day and 30 min after NEB albuterol administration on the second day.

The median (range) rate of nebulization of 12 jet NEBs tested prior to use was 0.229 (0.188 to 0.25) mL/min with a unit-to-unit variability of 33%. Table 2 lists mass output, mass median aerodynamic diameter, and geometric SD for the three NEBs undergoing cascade impactor measurements. These measurements represent wet droplet particle size. The mean Rrs and Crs before MDI (0.166±0.102 cm H2O/mL/s, 0.65±0.53 mL/cm H2O/kg) and NEB (0.192±0.116 cm H2O/mL/sec, 0.62±0.50 mL/cm H2O/kg) administration of albuterol were not significantly different (p=0.183 and 0.385, respectively). Though the improvement in compliance after both delivery modes persisted 4 h, the decrease in resistance persisted only 2 h (Figs 1 and 2). There was no significant difference in percent change in Crs and Rrs following NEB vs MDI administration of albuterol at the various time intervals (Tables 3 and 4). The baseline coefficients of variation for Rrs and Crs were 7.2±3.3% and 8.7±6.0%, respectively.

## Discussion

To our knowledge, this clinical study is the first to demonstrate that MDI administration of albuterol is as efficacious and safe as NEB albuterol in intubated infants with bronchiolitis. A similar magnitude of improvement in pulmonary functions was noted after both administration methods despite the large difference in albuterol dosages (ie, 360 μg MDI vs 1.5 mg

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**Table 1—Subject Information**

<table>
<thead>
<tr>
<th>Subject/Age, mo/Weight, kg/Sex</th>
<th>ETT Size, mm, ID</th>
<th>Vt, mL</th>
<th>f</th>
<th>Initial Rrs, cm H2O/mL/s</th>
<th>Initial Crs, mL/cm H2O/kg</th>
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<tbody>
<tr>
<td>1/1.5/2.7/F</td>
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<td>22</td>
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<td>0.472</td>
<td>0.21</td>
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<td>2/2.0/4.3/M</td>
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<td>25</td>
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<tr>
<td>3/3.0/6.2/M</td>
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<td>10</td>
<td></td>
<td>0.112</td>
<td>0.34</td>
</tr>
<tr>
<td>4/19/6.0/F</td>
<td>4.0, 90</td>
<td>18</td>
<td></td>
<td>0.160</td>
<td>0.24</td>
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<td>5/22/8.7/F</td>
<td>4.5, 120</td>
<td>12</td>
<td></td>
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</tr>
<tr>
<td>6/3.5/5.2/M</td>
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<td>12</td>
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<td>0.225</td>
<td>0.17</td>
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<tr>
<td>7/1.0/2.6/F</td>
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<td>16</td>
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<td>0.124</td>
<td>1.74</td>
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<td>16</td>
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<td>0.426</td>
<td>0.41</td>
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<td></td>
<td>0.136</td>
<td>0.60</td>
</tr>
<tr>
<td>Mean±SD 5.3±7.6/4.6±1.8</td>
<td>71±26</td>
<td></td>
<td></td>
<td>0.220±0.137</td>
<td>0.57±0.49</td>
</tr>
</tbody>
</table>

*f=set respiratory frequency; ID=inner diameter.

1 Spontaneous Vt while mechanically ventilated prior to drug/placebo administration.

1 Rrs prior to any drug/placebo administration.

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**Table 2—Output Parameters for Three Jet NEBs**

<table>
<thead>
<tr>
<th>Nebulizer No.</th>
<th>Mass Output, mg/min</th>
<th>MMAD, mm</th>
<th>GSD</th>
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<tr>
<td>6</td>
<td>238</td>
<td>5.8</td>
<td>2.8</td>
</tr>
<tr>
<td>10</td>
<td>188</td>
<td>4.92</td>
<td>2.65</td>
</tr>
<tr>
<td>11</td>
<td>225</td>
<td>5.15</td>
<td>2.48</td>
</tr>
</tbody>
</table>

*MMAD=mass median aerodynamic diameter; GSD=geometric SD.
NEB). Although an appreciable improvement in Rrs was noted up to 2 h following administration of albuterol with both methods, there was minimal change in Rrs at 4 h following either method.

There is sufficient evidence demonstrating MDI plus spacer-administered medications are as efficacious as NEB administration in nonintubated asthmatic children\(^\text{13-15}\) and intubated adults.\(^\text{2}\) Penetration of the lungs with MDI-administered \(\beta\)-agonists has been documented to be almost five times greater than NEB administration in intubated adults (5.65±1.09\% vs 1.22±0.35\%).\(^\text{2}\) Efficacy of MDI-delivered albuterol in intubated infants has also been investigated but not well established.\(^\text{9,16,17}\) The study by Denjean et al\(^\text{17}\) used a specially designed spacing chamber and the study by Brundage et al\(^\text{9}\) administered a combination of albuterol and ipratropium to intubated infants. Our study was designed to assess the aerosol administration equipment and methods utilized in clinical practice at our institution.

Efficacy of an aerosolized medication is highly dependent on the materials and specific methods used for administration.\(^\text{18-20}\) The NEB utilized in this study had acceptable particle size distribution and rates of nebulization for a reasonable comparison.

Alvine and colleagues\(^\text{8}\) performed \textit{in vitro} tests of eight different manufacturers’ brands of jet NEBs. They suggest the median rate of nebulization should be 0.2 mL/min and the unit-to-unit variability should be <75\%. \textit{In vitro} tests of the NEBs used in our study showed that they performed within these standards. Different brands of spacer devices also perform differently \textit{in vitro}.\(^\text{20,21}\)

The treatment time, duty cycle, volume fill of the NEB, and presence of a humidification device also influence the efficacy of aerosol drug delivery during mechanical ventilation.\(^\text{18}\) O’Riordan et al\(^\text{18}\) documented a variable response to volume fill among the NEBs tested. O’Doherty et al\(^\text{22}\) demonstrated increased deposition with increased volume fills. The volume fills and NEBs tested, however, were not clinically applicable in the pediatric population. The optimal volume fill for pediatric jet NEBs is unknown.

The efficacy of aerosolized albuterol can be altered by the difference between delivery in-line with the ventilator circuit vs direct attachment to the ETT. Bishop and associates\(^\text{23}\) demonstrated that >90\% of the weight of the aerosol was in the elbow and ETT when three MDI in-line adapters were tested in the laboratory. Watterberg et al\(^\text{24}\) estimated that <1\% of cromolyn penetrated the lungs of intubated infants with bronchopulmonary dysplasia regardless of the proximity of the NEB to the ETT in-line with the ventilator circuit. An in-line spacer may increase the compressible volume of the ventilator circuit and potentially reduce the tidal volume delivered to the patient.\(^\text{25}\) Excellent reviews on aerosolized bronchodilator delivery during mechanical ventilation are recommended to interested readers.\(^\text{26-28}\)

MDI administration of albuterol to intubated children in our PICU with a bag-valve system is preferred over in-line administration due to concern of significant washout of drug from the continuous bias flow present on most new-generation ventilators. However, patients requiring elevated amounts of PEEP may not tolerate temporary ventilator disconnection to attach the MDI-spacer-bag-valve system. These patients would likely need in-line administration of aerosolized medications, which was not evaluated in this study. Though inflation pressures used during bag-valve delivery were monitored with a
manometer, other ventilatory parameters such as Vt, respiratory cycle, and inspiratory flow were not measured.

Significant reduction in drug penetration occurs in the presence of an ETT.\textsuperscript{29-31} In one clinical study, the ETT was partially responsible for the significant decrease in lung deposition of NEB-administered, radiolabeled aerosol in intubated adults (2.9±0.7% vs 11.9±2.2% in nonintubated adult volunteers).\textsuperscript{29} Two in vitro studies demonstrated significantly smaller amounts of MDI-delivered medication with smaller internal diameter ETTs.\textsuperscript{29,31} One set of authors recommended doubling the MDI dose of drug when a 6.0-mm internal diameter ETT is in place and quadrupling the dose if a 4.0-mm internal diameter ETT is in place.\textsuperscript{29} Although larger doses for use in intubated pediatric patients may be necessary, the optimal MDI dose of albuterol producing the greatest clinical response with the least amount of adverse effects needs to be determined in a prospective clinical study.

MDI administration of albuterol to intubated infants is further encouraged by reports of adverse effects to NEB albuterol.\textsuperscript{32,33} Yuksel and Greenough\textsuperscript{32} documented a 16% deterioration in airways resistance immediately after NEB albuterol, compared to a 3% improvement following MDI albuterol in 15 children with a history of prematurity. O’Callaghan et al\textsuperscript{33} also discovered a worsening in bronchoconstriction for up to 15 min after NEB albuterol. They demonstrated that a solution containing 0.5 mL of albuterol in 1.5 and 2.5 mL of saline solution is initially hypo-osmolar and with nebulization becomes increasingly hyperosmolar (>400 mmol/kg at 15 min). They reported that the pH of the 0.5 mL albuterol+1.5 mL saline solution was 4.75. We did not encounter deteriorations in results of clinical examination or Rrs after NEB albuterol in our study.

One concern regarding MDI administration is the possibility of inducing hypoxemia in infants with VT <100 mL.\textsuperscript{1} A potentially hypoxic mixture may result when a small VT is combined with the MDI aerosol volume. In our study, MDI-albuterol administered with a bag-valve system and no change in FIO\textsubscript{2} did not induce hypoxemia in the nine infants with VTs <100 mL. One subject had transient hypoxemia several minutes after both administration modes of albuterol, possibly secondary to an increased ventilation-perfusion mismatch.

The single occlusion technique utilized for determining Rrs and Crs assumes the occlusion during expiration will result in total relaxation of the respiratory muscles—the Hering-Breuer reflex.\textsuperscript{34} The reflex was not inducible in some of the early study subjects. We soon discovered addition of a 10% inspiratory pause facilitated induction of the reflex in subjects unresponsive to occlusion.

The cost-effectiveness associated with MDI administration has led national organizations to recommend MDI as the preferred mode of aerosol administration.\textsuperscript{1} The cost savings of MDI administration of

<table>
<thead>
<tr>
<th>Time</th>
<th>Method</th>
<th>Mean</th>
<th>Mean − 95% CI</th>
<th>Mean + 95% CI</th>
<th>p Value</th>
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<tr>
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<td>MDI</td>
<td>−25</td>
<td>−32</td>
<td>−18</td>
<td>0.83</td>
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<tr>
<td></td>
<td>NEB</td>
<td>−28</td>
<td>−38</td>
<td>−20</td>
<td></td>
</tr>
<tr>
<td>1 h</td>
<td>MDI</td>
<td>−22</td>
<td>−30</td>
<td>−13</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td>NEB</td>
<td>−29</td>
<td>−39</td>
<td>−19</td>
<td></td>
</tr>
<tr>
<td>2 h</td>
<td>MDI</td>
<td>−17</td>
<td>−25</td>
<td>−8</td>
<td>0.29</td>
</tr>
<tr>
<td></td>
<td>NEB</td>
<td>−22</td>
<td>−35</td>
<td>−8</td>
<td></td>
</tr>
<tr>
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<td>MDI</td>
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<td></td>
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<td>−23</td>
<td>4</td>
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<table>
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<th>Mean + 95% CI</th>
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<tbody>
<tr>
<td>30 min</td>
<td>MDI</td>
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<td>5</td>
<td>46</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td>NEB</td>
<td>19</td>
<td>5</td>
<td>33</td>
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<tr>
<td>1 h</td>
<td>MDI</td>
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<td>−11</td>
<td>46</td>
<td>0.35</td>
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<tr>
<td></td>
<td>NEB</td>
<td>18</td>
<td>9</td>
<td>27</td>
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<td>8</td>
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<tr>
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<tr>
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<td>12</td>
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aerosolized medications over NEB administration has been well documented. Bowton et al calculated a cost savings to the hospital ranging from $32,000 to $83,000 per year and a reduction in patient charges of $300,000 per year. Moreover, Jasper and colleagues have estimated switching all non-ICU patients to MDI administration would save approximately $250,000 per year. We estimated reducing administration time by 7 min per treatment with MDI for the 11,000 aerosolized medication doses delivered in the PICU annually would decrease hospital personnel costs by approximately $25,000.

The largest limitations of our study were the dosages of MDI and NEB albuterol chosen. The dosages of 360 μg of MDI albuterol and 1.5 mg of NEB albuterol were based on clinical experience. The MDI dose of albuterol chosen was probably insufficient based on the evidence presented above. A larger MDI dose would likely reduce further any difference in response between the two administration methods under similar conditions. A higher incidence of adverse effects might occur with increasing dosages of either form.

MDI administration of albuterol in intubated patients is safe, cost-effective, and, therefore, encouraged. Our study demonstrated MDI albuterol is as effective and safe as NEB albuterol in intubated infants with bronchiolitis responsive to treatment with the medication. However, generalizability of these findings is limited to the administration equipment and methods used. MDI administration of albuterol via direct attachment to the ETT with supplemental oxygen is safe in infants with VTs <100 mL. The optimal dose of MDI albuterol delivered by direct ETT attachment or in-line requires investigation.

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REFERENCES

1 Aerosol Consensus Statement, Chest 1991; 100:1106-09
7 Hess D. Aerosol bronchodilator delivery during mechanical ventilation: nebulizer or inhaler? [editorial]. Chest 1991; 100:1100-09
19 Silverman M. Aerosol therapy in the newborn. Arch Dis Child 1990; 65:906-08
23 Bishop MJ, Larson RP, Buschman DL. Metered dose inhaler aerosol characteristics are affected by the endotracheal tube actuator/adaptor used. Anesthesiology 1990; 73:1263-65
31 Taylor RH, Lerman J. High-efficacy delivery of salbutamol with a metered-dose inhaler in narrow tracheal tubes and catheters. Anesthesiology 1991; 74:360-63
32 Yuksel B, Greenough A. Comparison of the effects on lung function of two methods of bronchodilator administration. Respir Med 1994; 88:229-33