

# Interfaces to Connect the HandiHaler and Aerolizer Powder Inhalers to a Tracheostomy Tube

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**BACKGROUND:** Patients with respiratory failure are often unable to inhale powdered aerosol medications such as long-acting  $\beta$  agonists and long-acting anticholinergics, which are important treatments for chronic obstructive pulmonary disease and asthma. **OBJECTIVE:** To explore delivery of aerosolized powder medications via tracheostomy tube. **METHODS:** We designed interfaces to connect the HandiHaler and Aerolizer devices to tracheostomy tubes, and to connect the HandiHaler to a manual resuscitator bag. With these interfaces, in 23 patients, we assessed the clinical ease/difficulty of delivery and delivery time of the first 3 administrations of powder-aerosol long-acting  $\beta$  agonists and long-acting anticholinergics from the HandiHaler and the Aerolizer. **RESULTS:** The powder aerosols were readily delivered to all the patients. Nineteen of the 23 patients (83%) were able to inhale the medication on their own. In the 4 patients who were unable to effectively inhale the medication on their own, bag-assist was successful. The aerosol delivery time was usually < 3 min. **CONCLUSIONS:** With a proper interface, powdered long-acting  $\beta$  agonists and long-acting anticholinergics can be easily delivered via tracheostomy tube, even if the patient cannot inhale on his or her own. Further studies are needed to assess particle size, dose delivery, and clinical efficacy with these interfaces and device modifications. *Key words: asthma, chronic obstructive pulmonary disease, COPD, tracheostomy, formoterol, inhaler, tiotropium.* [Respir Care 2007;52(2):166–170. © 2007 Daedalus Enterprises]

## Introduction

Chronic obstructive pulmonary disease (COPD) affects about 16 million people, and asthma affects about 11% of people in the United States. There are about 725,000 hospitalizations and 120,000 deaths annually from COPD,<sup>1</sup> making COPD the 4th leading cause of death in the United States.<sup>2</sup> Many of the hospitalized patients develop acute or chronic respiratory failure that requires intubation or tracheostomy. Some patients with asthma also develop respiratory failure

that requires intubation, and many patients with other causes of respiratory failure have asthma or COPD.

Current guidelines for asthma include inhaled steroids and long-acting  $\beta$ -agonists such as salmeterol and formoterol.<sup>3</sup> Long-acting  $\beta$  agonists provide better control than short-acting  $\beta_2$  agonists for both relief and maintenance medication.<sup>4</sup> Current COPD guidelines include long-acting  $\beta$  agonists and long-acting anticholinergics.<sup>5</sup> The long-acting anticholinergic tiotropium provides better control than the short-acting anticholinergic ipratropium in patients with COPD,<sup>6</sup> with better improvement in pulmonary function and fewer exacerbations and hospitalizations.

Long-acting medications are indicated for asthma and COPD, with long-acting  $\beta$  agonists and long-acting anticholinergics available in powder aerosol form, delivered from devices designed for oral delivery with a deep inspiration. The delivery devices for long-acting  $\beta$  agonists and long-acting anticholinergics are not designed for use with intubated and tracheostomized patients, so intubated and tracheostomized patients with asthma and COPD—those who need these treatments the most—are denied the ben-

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Douglas C Johnson MD has a patent pending for devices to connect inhalers to tracheostomy and endotracheal tubes.

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efits of long-acting  $\beta$  agonists and long-acting anticholinergics via inhalation.

Patients with respiratory failure are typically managed with frequent administration of short-acting  $\beta$  agonists (eg, albuterol) and/or short-acting anticholinergics (eg, ipratropium), because these medications can be given via metered-dose inhaler (MDI) or nebulizer.<sup>7</sup> Long-term frequent administration of short-acting  $\beta$  agonists has been associated with adverse effects, including greater risk of death,<sup>8</sup> whereas long-acting  $\beta$  agonists are much safer.<sup>9</sup> Long-acting  $\beta$  agonists and long-acting anticholinergics should be beneficial to appropriate patients with respiratory failure, since the long-acting medications are more effective and probably have less risk. However, the devices that deliver long-acting  $\beta$  agonists (Diskus delivers salmeterol 50  $\mu\text{g}$ , Aerolizer delivers formoterol 12  $\mu\text{g}$ ) and long-acting anticholinergics (HandiHaler delivers tiotropium 18  $\mu\text{g}$ ) are designed for oral delivery, not for endotracheal tube (ETT) or tracheostomy tube delivery.

This study describes interfaces and methods to deliver aerosolized powder medications from the HandiHaler and Aerolizer inhalers, via inhalation and a manual assisted-breath (bag-assist) technique to tracheostomized patients in a ventilator weaning program. We assessed the ease/difficulty of use of the device interfaces and the time required to administer the aerosols.

### Methods

Patients who had tracheostomy tubes and were unable to inspire deeply via mouth were eligible for the study. The hospital physicians were informed that powdered tiotropium and formoterol could be delivered to tracheostomized patients. We included all tracheostomized patients who were in the ventilator weaning program who had these medications ordered, from June 2004 to April 2005, and who provided informed consent for participation. Our institutional review board approved the study and protocol.

The respiratory therapists (RTs) collected data for up to 3 doses of each powder (tiotropium and formoterol) per patient. The data included the type of tracheostomy tube, whether the cuff was inflated or deflated during aerosol delivery, the time taken to deliver the medicine, the inhaler device (HandiHaler or Aerolizer), and how many attempts it took to deliver the medicine. Forced vital capacity (FVC), peak inspiratory pressure ( $P_{I\text{max}}$ ), peak expiratory pressure ( $P_{E\text{max}}$ ), and rapid shallow breathing index were measured while the patient was off the ventilator, as part of respiratory mechanics measurements with each patient.

Interfaces were designed to connect the HandiHaler (Fig. 1) and Aerolizer (Fig. 2) to a tracheostomy tube (proximal end 15-mm outer diameter), via adapters (15-mm inner diameter, 22-mm outer-diameter plastic adapter, catalog no. 1422, Hudson RCI, Durham, North Carolina),

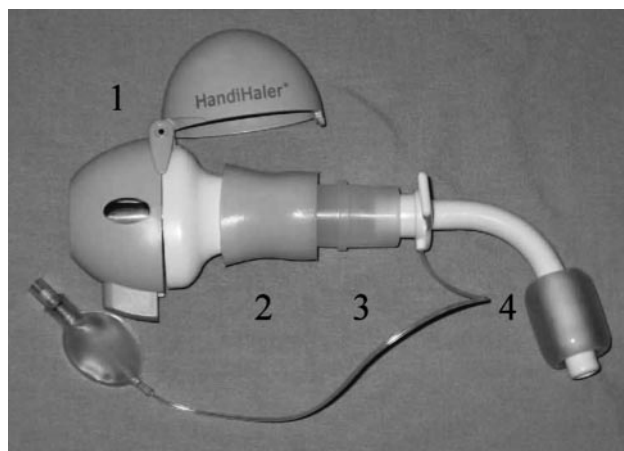


Fig. 1. Setup for delivering powder aerosol from the (1) HandiHaler, via a (2) 22-mm inner-diameter silicone connector and a (3) 22-mm outer-diameter plastic adapter, to a (4) tracheostomy tube.

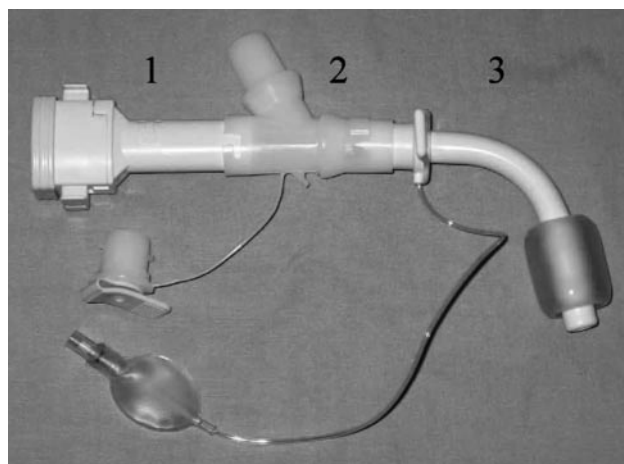


Fig. 2. Setup for delivering powder aerosol from the (1) Aerolizer, via a (2) silicone connector, to a (3) tracheostomy tube.

connectors (22-mm inner-diameter silicone connector, catalog no. 2200, RC Medical, Tolland, Connecticut, and connector model SHER-I-SWIV/FO, catalog no. 5-15401, Hudson RCI, Durham, North Carolina), T-pieces (catalog no. 838-407-250F, King Systems, Noblesville, Indiana), and tubing (oxygen supply line, catalog no. 1115, Hudson RCI, Durham, North Carolina), which allowed delivery of the powder aerosol from the medication capsule to the tracheostomy tube. The silicone connector fit securely between the inhaler mouthpiece and the tracheostomy tube.

We also designed an interface to connect an adult manual-assist resuscitator (model 8500, Portex, Waukesha, Wisconsin) to the HandiHaler to deliver the aerosol to patients who are unable to generate a deep inhalation (Fig. 3). We did not design an interface to connect the Diskus inhaler to a tracheostomy tube.

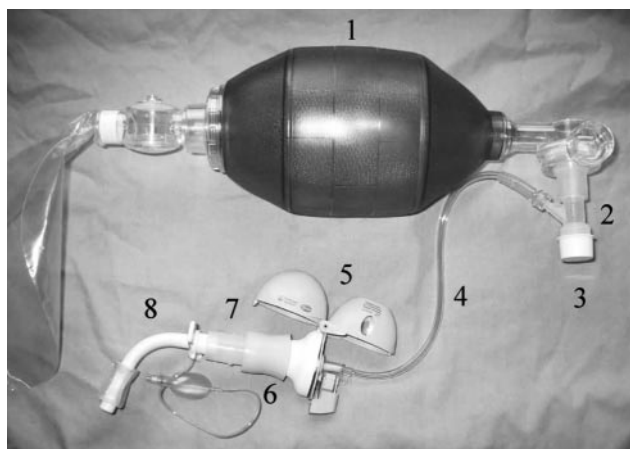


Fig. 3. Setup for bag-assist delivery of powder aerosol, including (1) manual resuscitator, (2) T-piece, (3) cap, (4) tubing, (5) HandiHaler, (6) silicone connector, (7) plastic adapter, and (8) tracheostomy tube.

The standard protocol for delivery via HandiHaler and Aerolizer was used to ready the medication. The medication capsule was inserted into the chamber and the device was squeezed to puncture the capsule. If the patient was on a ventilator, the ventilator was briefly disconnected to administer the medication. Instead of placing the inhaler into the patient's mouth, the inhaler was connected via the interface to the tracheostomy tube. With the HandiHaler, the patient was asked to breathe out, then the interface was connected to the tracheostomy tube, and the patient was asked to breathe in deeply. The technique was similar for the Aerolizer, but the RT occluded the side port with a gloved thumb during inspiration. If the medication was given via bag-assist, the HandiHaler was used for both formoterol and tiotropium, and the resuscitator was squeezed to deliver aerosol along with a breath of air. If the patient had any inspiration ability, the squeeze was timed to assist the patient's inspiration.

Delivery was first attempted by having the patient inhale deeply. Effective delivery was determined based on hearing the capsule spin and finding no powder remaining in the capsule. For the first dose, bag-assist was used if delivery was unsuccessful after 5 tries with the patient's own inhalation. For subsequent doses, if the patient had previously required bag-assist, inhalation delivery was tried again only if the RT deemed that the patient had improved enough to allow effective inhalation. The RT rated the inhaled and bag-assist administrations as either very easy, fairly easy, moderately difficult, or very difficult, and noted the time needed for delivery.

Values are reported as mean  $\pm$  standard deviation.

## Results

Seventy-seven medication doses were administered to 23 patients. Their mean age was  $58 \pm 17$  y. Four patients

(17%) required bag-assist, and one of those 4 later did not need bag-assist. Two patients were unable to perform the respiratory mechanics maneuvers. Among the remaining 21 patients, the mean FVC was  $760 \pm 362$  mL, the mean rapid shallow breathing index was  $90 \pm 64$ , the mean  $P_{I_{max}}$  was  $-40 \pm 13$  cm H<sub>2</sub>O, and the mean  $P_{E_{max}}$  was  $35 \pm 16$  cm H<sub>2</sub>O. Eleven patients had FVC < 700 mL, 10 had rapid shallow breathing index > 100, 6 had  $P_{I_{max}} > 40$  cm H<sub>2</sub>O, and 13 had  $P_{E_{max}} < 40$  cm H<sub>2</sub>O. The reasons for bag-assist were severe respiratory muscle weakness with very low FVC (3 patients) and inability to cooperate (1 patient).

The RT inflated the cuff for nearly all administrations via inhalation. Only one patient had an uncuffed tube, and that patient had very easy administration on the first effort. Two patients had the cuff deflated during administration. For one of those the administration was very easy, whereas for the other administration failed with the cuff deflated, but was very easy once the cuff was inflated. The cuff was always inflated for bag-assist.

Tiotropium was delivered to 22 patients, 6 of whom also received formoterol. One patient received only formoterol. Tiotropium was delivered only via HandiHaler, whereas formoterol was delivered via either Aerolizer (4 patients) or HandiHaler (3 patients). Inhalation delivery was not attempted in one patient, because he had no inspiratory volume. Inhalation delivery was attempted in 22 of the 23 patients, with successful delivery in 58 of 63 (92%) administrations on the first attempt. Forty-two (72%) of the successful first attempts were rated as very easy, and 16 (28%) as fairly easy. Of the 7 unsuccessful first attempts in 4 patients, one of the patients was confused and uncooperative, but the first attempt on other days was easily successful. The other 3 attempts were unsuccessful despite good cooperation, due to very severe lung disease and respiratory muscle weakness.

In the 4 patients who were unable to get effective delivery with inhalation, bag-assist was successful. Bag-assist was rated as very easy on the first attempt in all patients, except for one dose that required 2 bag squeezes to empty the capsule. The 3 patients who were cooperative and required bag-assist had vital capacities of 0 mL, 225 mL, and 332 mL, and peak inspiratory pressures of 0 cm H<sub>2</sub>O,  $-18$  cm H<sub>2</sub>O, and  $-16$  cm H<sub>2</sub>O.

The mean medication delivery time with inhalation was  $2.5 \pm 1.7$  min. Twenty of the inhalation administrations were  $\leq 1$  min, 37 were  $\leq 2.5$  min, and all were  $\leq 5$  min. The mean time for bag-assist delivery was  $5.6 \pm 8.1$  min. Most bag-assist delivery times were 2–3 min, but one administration time was 20 min, which included locating and initial setup of the bag-assist assembly. The RTs reported that most of the time involved getting the device and loading the capsule into the device, with very little time required for the inhalation (usually one breath or one bag-assist). With bag-



assist there was a little more time required to connect the tubing from the bag to the HandiHaler.

The RTs generally preferred using the HandiHaler over the Aerolizer. They reported that occasionally patients would not time the breath properly and would exhale into the Aerolizer and blow the powder out the back of the Aerolizer. This is unlikely to happen with the HandiHaler, because the capsule occludes the inspiratory port on exhalation.

### Discussion

The present study demonstrates ease of use with these inhaler/tracheostomy-tube interfaces to deliver powdered tiotropium and formoterol. Traditionally, inhaled bronchodilator therapy in mechanically ventilated patients has involved nebulizers or MDIs adapted for use in ventilator circuits.<sup>10</sup>

Long-acting  $\beta$ -adrenergic and anticholinergic medications have become the mainstay for treatment of patients with obstructive lung disease because they have greater efficacy than short-acting agents. Long-acting anticholinergics and long-acting  $\beta$  agonists are not available in MDI or nebulizer forms, and until now there has been no way to administer these important medications to patients via tracheostomy tube or ETT.

Several studies have raised concern about frequent use of short-acting  $\beta$  agonists, which leads to  $\beta$ -receptor down-regulation and increased airways reactivity in many patients, and has been associated with increased risk of death among asthmatics.<sup>8,11</sup> Increased use of short-acting  $\beta$  agonists is associated with unstable angina and myocardial infarction in COPD patients,<sup>12</sup> and with heart failure, hospitalization, and death in patients with left-ventricular systolic dysfunction.<sup>13</sup> Thus, there is a concern that frequent short-acting  $\beta$  agonists may cause more harm than benefit in some hospitalized patients. Long-acting  $\beta$  agonists appear to be much safer than short-acting  $\beta$  agonists, without causing increased airways reactivity in adults or increased mortality.<sup>9</sup>

Inhaled corticosteroids are recommended as first-line therapy for asthma,<sup>14</sup> and they reduce the frequency of COPD exacerbations, with further reductions in exacerbations with the combination of inhaled corticosteroids and long-acting  $\beta$  agonists.<sup>15</sup> Inhaled corticosteroids reduce the risk of short-acting  $\beta$  agonists in asthmatics.<sup>16</sup> Though monotherapy with long-acting  $\beta$  agonists is not recommended for asthma, the combination of long-acting  $\beta$  agonists and inhaled corticosteroids is believed to be effective and safe.<sup>17</sup> Standard practice is to treat patients receiving long-acting  $\beta$  agonists also with inhaled corticosteroid via MDI.

Powder inhalers require a deep inhalation at an inspiratory flow of  $\geq 1$  L/s for optimal dispersion of the powder into respirable particles.<sup>18,19</sup> It is likely that a lower flow rate and smaller inspired volume is required for effective delivery of the medication via tracheostomy than via mouth, because the oropharynx is bypassed. Most patients in the

present study had vital capacities in the range 600–900 mL, and they easily inhaled the medication via tracheostomy tube. They were believed to be unable to take the medication effectively via mouth, often because the tracheostomy tube interfered with oral inhalation. Though these patients effectively emptied the medication capsule, it is possible that some of them would have had more effective lung deposition with bag-assist. The few patients who required bag-assist to empty the capsule had much lower FVC ( $< 350$  mL) or were uncooperative. Therefore, bag-assist is recommended for patients with vital capacities  $< 500$  mL and patients unable to cooperate with deep inhalation. Further studies to correlate lung deposition to inspired volume and flow could help determine which patients would benefit from bag-assist.

There are many techniques and devices for inhalation of drugs. A relatively low proportion of the total dose is deposited in the lung.<sup>20</sup> With oral administration there is usually substantial drug deposition in the oropharynx.<sup>20</sup> A tracheostomy tube would probably have less deposition than the oropharynx, so even patients capable of a relatively deep breath through the mouth might benefit from delivery via a short tracheostomy tube.

In our interface setup, the short piece of tubing between the Aerolizer or HandiHaler and the tracheostomy tube is not expected to change particle size. There would probably be more deposition in an ETT than in a tracheostomy tube because of the ETT's greater length. More patients in intensive care settings would probably need bag-assist than do weaning-program patients, who are usually alert and cooperative.

HandiHaler has the advantage over the Aerolizer of allowing attachment of tubing to deliver positive pressure via bag-assist. The HandiHaler also has the advantage of blocking accidental loss of medication caused by exhalation, because the capsule occludes the inhalation port. The HandiHaler was sometimes used to deliver Foradil, which has a similar size capsule as Spiriva. The present study found that the Foradil capsule emptied when given via HandiHaler, but future studies are needed to evaluate whether particle size or drug delivery differ when Foradil is administered via HandiHaler versus Aerolizer. If other powder medications (eg, salmeterol, steroids) were available in capsules, then they could be studied as well.

Though this study reports data from only the first 3 medication administrations for each patient, it is important to note that many patients received tiotropium and/or formoterol for weeks or months via tracheostomy-tube inhalation or bag-assist. There were no occurrences of being unable to deliver the medication via tracheostomy tube in well over 1,000 administrations. Occasionally, bag-assist was needed for patients who usually did well with inhalation. No complications were noted from tracheostomy-tube administration of the medications. The RTs did not

note any problems with cough, increased dyspnea, or increased airway resistance during or after administration.

Though this study did not evaluate the efficacy of these medications in treating airway obstruction, these patients' airways obstruction seemed well controlled with long-acting  $\beta$  agonists, long-acting anticholinergics, and inhaled corticosteroids. There was very infrequent wheezing or need for albuterol in patients with underlying airways obstruction, and all the patients were tapered off of prednisone. Most patients were ventilator-dependent at the time of the study, but were sooner or later weaned from the ventilator and were able to switch to taking the medications orally when their tracheostomy tubes were down-sized or capped.

The present study used combinations of available connectors and adapters to connect the inhalers to a tracheostomy tube or resuscitator. It should be possible to produce more convenient devices to deliver tiotropium, formoterol, and other powder aerosol medications to intubated and tracheostomized patients. Further research is needed to determine the effects of flow rate and inspired volume on particle size and deposition. Ideally, studies would evaluate lower-respiratory-tract deposition of inhaled powders delivered via tracheostomy and via ETT, and would compare the clinical response (including measures of airway resistance, respiratory mechanics, and clinical outcome) of patients with respiratory failure managed with long-acting versus short-acting bronchodilators.

### Conclusions

These new interfaces and methods allow delivery of aerosolized tiotropium and formoterol powder via tracheostomy tube or ETT. The methods are very easy, even in patients unable to breathe on their own. Given the advantages of long-acting  $\beta$  agonists and long-acting anticholinergics over short-acting agents, providing the long-acting agents should improve the care of patients with respiratory failure and COPD or asthma. This study provides feasibility data. Further studies are needed to assess particle size, dose delivery, and clinical efficacy before these device interfaces are adopted.

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