Spinal Muscular Atrophy Type 1*
A Noninvasive Respiratory Management Approach

John R. Bach, MD, FCCP; Vis Niranjan, MD; and Brian Weaver, BS, RRT

Study objective: To determine whether spinal muscular atrophy (SMA) type 1 can be managed without tracheostomy and to compare extubation outcomes using a respiratory muscle aid protocol vs conventional management.

Design: A retrospective cohort study.

Methods: Eleven SMA type 1 children were studied during episodes of respiratory failure. Nine children required multiple intubations. Along with standard treatments, these children received manually and mechanically assisted coughing to reverse airway mucus-associated decreases in oxyhemoglobin saturation. Extubation was not attempted until, most importantly, there was no oxygen requirement to maintain oxyhemoglobin saturation greater than 94%. After extubation, all patients received nasal ventilation with positive end-expiratory pressure. Successful extubation was defined by no need to reintubate during the current hospitalization.

Results: Two children have survived for 37 and 66 months and have never been intubated despite requiring 24-h nasal ventilation since 5 and 7 months of age, respectively. One other child underwent tracheostomy for persistent left lung collapse and inadequate home care, another for need for frequent readmission and intubation, and one child was lost to follow-up 3 months after successful extubation. The other six children have been managed at home for 15 to 59 (mean 30.4) months using nocturnal nasal ventilation after an episode of respiratory failure. The nine children were successfully extubated by our protocol 23 of 28 times. The same children managed conventionally were successfully extubated 2 of 20 times when not using this protocol (p < 0.001 by the two-tailed Fisher’s Exact t Test).

Conclusion: Although intercurrent chest colds may necessitate periods of hospitalization and intubation, tracheostomy can be avoided throughout early childhood for some children with SMA type 1.

Key words: bilevel positive airway pressure; mechanical ventilation; noninvasive ventilation; pulmonary complications; respiratory failure; spinal muscular atrophy; survival

Abbreviations: EPAP = expiratory positive airway pressure; IPAP = inspiratory positive airway pressure; MI-E = mechanical insufflation-exsufflation; SaO₂ = arterial oxyhemoglobin saturation; SMA = spinal muscular atrophy.

Autosomal recessive spinal muscular atrophy (SMA) is the most common inherited neuromuscular disease of the hypotonic newborn and, along with Duchenne muscular dystrophy, is 1 of the 2 most commonly inherited neuromuscular diseases. It is caused by a chromosome 5 defect. About 1 in 40 people carry the defective gene, and the overall incidence has been reported to be 1 out of 5000. It has been categorized into 4 types according to severity. The SMA type 1 infant never attains the ability to sit independently. Less than 20% of these children survive 4 years, and then only with indwelling tracheostomy tubes. Virtually all die from respiratory complications. SMA type 2 children can temporarily sit independently but can never walk, and they too usually have periods of respiratory failure during early childhood. Other SMA types have milder courses.
The lungs of patients with neuromuscular disease can be ventilated noninvasively by intermittent positive pressure ventilation provided by volume-cycled ventilators or by pressure-cycled ventilators. However, with or without using ventilatory assistance, 3–5 SMA patients are usually stable until an intercurrent chest cold results in pneumonia and acute respiratory failure because of inability to cough effectively. 6

For SMA type 1 infants this usually occurs between birth and 2 1/2 years of age. Clinicians are often reluctant to intubate them because they often lose breathing autonomy with the correction of compensatory metabolic alkalosis that accompanies normalization of arterial carbon dioxide tensions.

Further, once a patient is intubated, tracheostomy is thought to be mandatory when ventilator weaning is delayed or thought to be impossible. Because it is considered inevitable, tracheostomy is often recommended during the initial episode of respiratory failure. 5 If these infants wean from ventilator use, are extubated, and the parents persist in refusing tracheostomy, the parents are often advised to avoid future intubations and to simply let the children die. 3

Because we have succeeded in using continuous noninvasive ventilation long-term as an alternative to tracheostomy, 6–8 and because we have used a home respiratory muscle aid protocol to avoid pneumonias and hospitalizations for older patients who can cooperate, 9 when parents refused tracheostomies for their infants, we attempted to modify this protocol for their children. We hypothesized that we could use these principles for hospitalized SMA type 1 children who require endotracheal intubation for episodes of respiratory failure and thereby maintain the children free of tracheostomy until they are old enough to cooperate fully with the home protocol. In this way it may be possible to avert tracheostomy indefinitely. 9

We also hypothesized that extubation would more likely be successful for patients managed by our protocol than for patients managed conventionally.

### MATERIALS AND METHODS

Eleven consecutively referred SMA type 1 children in respiratory failure were managed as per a protocol (Table 1) that was approved by our Institutional Review Board. All 11 patients had severe skeletal and bulbar muscle weakness to the extent that none had functional extremity movements or ability to take any nutrition by mouth. Three have not developed the ability to verbalize. All of the parents of the 11 had refused tracheostomies on multiple occasions.

Nine of the 11 patients have required one or more intubations. All were intubated in respiratory failure with oxygen requirement and were managed conventionally with respect to hydration and nutrition via feeding tubes, but not with respect to respiratory care (Table 1). Because oxygen administration can mask oxyhemoglobin desaturations that would otherwise signal airway mucous accumulation or hyperventilation, its use was restricted to patients who were acutely ill and intubated or who required emergency resuscitation.

Immediately upon extubation the patients received nasal ventilation with positive end-expiratory pressure at a rate slightly greater than the patients’ spontaneous breathing rate. This was provided by a ventilator support system (BiPAP-ST; Respironics Inc; Murrysville, PA) for 10 children, and by volume-cycled ventilator (Bird VIP; Exeter, UK) on assist/control for one patient who breathed more rapidly than the maximum rate of the BiPAP device. Initially, an inspiratory positive airway pressure (IPAP) of 10 cm H2O was used, but the IPAP was quickly increased to 20 cm H2O or to the point that the patient demonstrated good chest expansion and the spontaneous respiratory rate slowed. Thus, although the small infants could not trigger the BiPAP-ST, provided that IPAP/EPAP (expiratory positive airway pressure) spans were adequate, they breathed in synchrony with it unless their spontaneous rate exceeded the...
machine’s capabilities. The EPAP was 3 cm H2O. An EPAP of 3 cm H2O was used to prevent excessive CO2 rebreathing, while minimizing any decrease in the IPAP/EPAP span.10

All patients were eventually weaned to nocturnal only nasal ventilation and were discharged using a BiPAP-ST. After discharge, daytime end-tidal CO2 remained normal for all patients. Bilevel spans were adjusted during sleep to achieve good chest expansion during inspiration and an SaO2 level of 94% without supplemental oxygen, and to better rest inspiratory muscles. All children received IPAP > 14 cm H2O.

We often used modified Hudson size 4 or 5 infant nasal continuous positive airway pressure cannulas (Hudson Respiratory Care; Temecula, CA) as nasal interfaces (Fig 1). The nasal seal had to be adequate for the infants to trigger or synchronize with the ventilator; otherwise, they often experienced precipitous oxyhemoglobin desaturations that necessitated brief manual resuscitation. The nasal interface was connected to the ventilator circuit using intervening tubing adapters. The restraints for these prongs were originally designed for infants weighing 2 kg; therefore, they had to be improvised (Fig 1). For our children between 6 months and 5 years of age, when tolerated and effective (with minimal leak), we used the Respironics (Murrysville, PA) pediatric nasal mask.

While nasal ventilation aided inspiratory muscle function, expiratory aid was provided by manual abdominal compressions during the exsufflation phase of mechanical insufflation-exsufflation (MI-E). MI-E was used via indwelling tubes or, after extubation, was provided via oral-nasal interfaces.11 Manual thrusts were not performed or were performed gingerly for 2 h after meals.

The caregivers were trained in all aspects of noninvasive support as well as in chest percussion and postural drainage. They provided the bulk of the care within hours of extubation and through discharge. The children were discharged home with pulse oximeters, in-exsufflators (J.H. Emerson Co; Cambridge, MA), and BiPAP-ST machines. After initial hospitalization, arrangements were made for 24-h nursing for 1 week. The home nurses were trained by specifically trained respiratory therapists and ultimately by the parents. Patients were considered able to cooperate successfully with the protocol when they could avoid hospitalizations despite requiring continuous nasal ventilation and despite having airway mucus-associated oxyhemoglobin desaturations reversed by using respiratory muscle aids.9 This was usually the case by 4 years of age. The patients presented for physician evaluation when SaO2 decreased < 95% despite use of nasal ventilation and expiratory support, when fever persisted, or when dehydration was suspected.

We defined a failed extubation as that resulting in reintubation during the same hospitalization. We used a contingency table with Instat Software (Graphpad; San Diego, CA) and developed an odds-for-success ratio for protocol vs nonprotocol extubations using the Woolf approximation.12 The two-tailed Fisher’s Exact t Test for unpaired data was used to determine significance. A p value 0.05 was considered significant.

**Results**

In all, 11 consecutively referred patients were treated by the respiratory aid protocol. The demographic data and the results of management are summarized in Table 2. They had 28 distinct episodes of respiratory compromise necessitating hospitalizations: 2 postoperative, 2 associated with insidiously progressive inspiratory muscle dysfunction, and 24 sudden episodes mostly due to chest colds. These resulted in a total of 48 intubations. Nonprotocol therapy and extubation were attempted 20 times, including 8 times at our institution by nonparticipating physicians. Protocol therapy was used 28 times. On 9 occasions children were extubated to continuous nasal ventilation despite having no autonomous breathing capability. These patients weaned to nocturnal-only nasal ventilation up to 3 weeks after extubation. In three cases, the infants weaned to nocturnal-only nasal ventilation after discharge home. Two patients (Table 2, patients 10 and 11) remained 24-h ventilator dependent.

Protocol care was generally well tolerated, although two children had periods of abdominal distention while using nasal ventilation and required frequent burping of gastrostomy tubes. MI-E expelled the secretions into the endotracheal tube or adapter or the mouth, from where they were suctioned, and oxyhemoglobin desaturations were reversed. Two patients received IM glycopyrrolate to decrease secretions before extubation.

Comparing the success of protocol vs nonprotocol extubations, the two-tailed Fisher’s Exact t Test p value of 0.001 was very significant. The odds ratio was 18.72, with a confidence interval from 2.85 to 92.56.12

One child (patient 6) succeeded in being extubated and discharged home with normal SaO2 and using only nocturnal nasal ventilation but was rehospitalized in respiratory failure three times in 5 months because of persistent left lung collapse. She underwent tracheostomy and used nocturnal tracheostomy ventilation but died suddenly, at home, 3 months later. Another patient who developed respiratory failure at only 3 months of age (Table 2, patient 8) underwent tracheostomy at 7 months of age, after six intubations during 3 months of almost continuous hospitalization. Another patient (patient 2) was lost to follow-up subsequent to relocation 3

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**Figure 1.** Modified infant nasal cannula used as nasal interface.
months after successful extubation. The other seven patients are alive a mean of 34.7 months since their first episodes of respiratory failure. This includes one 6-year-old boy who has been hospitalized and intubated six times during intercurrent chest colds. Over the last 2 years, however, he has required continuous nasal ventilation and has successfully reversed airway mucus-associated oxyhemoglobin desaturations during four chest colds, thereby avoiding several hospitalizations. Two children have required continuous nasal ventilation and have had no autonomous breathing ability for 59 and 32 months, respectively, without ever being intubated. Although we do not have the hospital length of stay data for the patients managed at other institutions, the mean number of days our protocol patients were intubated was 8.2 ± 3.2, and the mean hospital stay was 16.6 ± 7.8 days.

Untreated SMA type 1 children have paradoxical breathing and develop pectus excavatum that worsens with time. Pectus excavatum disappeared with institution of nocturnal nasal ventilation for all 11 children.

**DISCUSSION**

This study suggests that it may be possible for infants with SMA type 1 to avoid tracheostomy long enough to be able to cooperate with the use of respiratory muscle aids and possibly safely avoid tracheostomy indefinitely. This is important because the parents of children with neuromuscular disease often refuse tracheostomy but want their children to survive.

Hypercapnia can cause oxyhemoglobin desaturation. We have noted that patients with neuromuscular disease tend to become symptomatic for hypercapnia only when it causes $\text{SaO}_2$ to decrease < 95%. Likewise, desaturation can be caused by accumulating airway mucus. Thus, oxygen administration can eliminate oximetry as an important monitor of airway plugging and clinically significant alveolar hypventilation, and it can result in exacerbation of hypercapnia. It was only used after extubation in conjunction with manual resuscitation to treat precipitous desaturations as nasal interfaces were being fit, ventilator synchronization achieved, and airway secretions exsufflated and suctioned. Its avoidance played an important role in the success of this protocol.

The use of nasal ventilation was reported to have failed to prolong life for children with SMA type 1. However, in this latter attempt, the low bilevel spans used may not have been adequate, and MI-E was not used. All four patients who died did so from inadequate ventilatory assistance or from failure to intubate or use expiratory aids during chest colds once the parents were resigned to let their children die. Indeed, MI-E via an indwelling tube has never before been reported. However, whether via a tube or via the upper airway, its use succeeded in eliminating airway mucus, and the children showed neither discomfort nor any evidence of barotrauma. It is also appropriate for SMA type 1 children to nocturnally use high span bilevel positive airway pressure to prevent pectus excavatum and to promote more normal lung growth.

Shortcomings of this study include the small number of patients due to the rarity of this condition, and the lack of controls. However, performing a random-

### Table 2—SMA 1: Noninvasive Management Outcomes

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Sex</th>
<th>Age (months)</th>
<th>Conventional Outcomes</th>
<th>Protocol Outcomes</th>
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<tr>
<td></td>
<td></td>
<td>a  b  c</td>
<td>Success  Failure</td>
<td>Success  Failure</td>
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<tr>
<td>1</td>
<td>F</td>
<td>6  21 44</td>
<td>0  0</td>
<td>2  0</td>
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<tr>
<td>2</td>
<td>M</td>
<td>6  28 311</td>
<td>0  3</td>
<td>2  0</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>6  26 81</td>
<td>2  5</td>
<td>4  0</td>
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<tr>
<td>4</td>
<td>F</td>
<td>4  11 42</td>
<td>0  0</td>
<td>3  1</td>
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<td>5</td>
<td>F</td>
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<tr>
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<td>F</td>
<td>6  7 151</td>
<td>0  3</td>
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<tr>
<td>7</td>
<td>F</td>
<td>11 12 27</td>
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<tr>
<td>8</td>
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<td>0  4</td>
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<td>10</td>
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<td>2  5 37</td>
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<tr>
<td>11</td>
<td>M</td>
<td>4  7 66</td>
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*Age a = first diagnosed; age b = first intubation or episode requiring ventilatory support; age c = last follow up; ages c–b = except for patient nos. 6 and 8, months of use of nocturnal nasal ventilation. M = male; F = female.
†Lost to follow-up.
‡Deceased suddenly after 3 months of tracheostomy ventilation.
§Underwent tracheostomy following an unsuccessful extubation using the protocol.
ized, controlled trial in adequate numbers would be extremely difficult, if not impossible, considering the sporadic occurrence of the disease, and the ethical issues involved in getting parents to permit such a trial. We excluded SMA type 2 patients to maintain sample homogeneity and because SMA type 2 patients are much easier to manage by this protocol. Despite the small population, however, these 11 children had 48 interventions.

It might also be argued that a selection bias existed. Patients who repeatedly succeed in being extubated with conventional care might not have been referred to us, and this might have resulted in children surviving without tracheostomy and without the use of our protocol. However, 3-year survival has not been reported for children with SMA type 1 without tracheostomy, and only one other center has reported 24-h ventilator users (none with SMA type 1), managed strictly noninvasively. Thus, most of the seven SMA type 1 infants known to be managed noninvasively and who now have a mean age of 43.4 months would have been expected to have died or undergone tracheostomy by this time.

Larger issues at hand are those of quality of life, cost, and survival comparisons with children ventilated via tracheostomies. Tracheostomy intermittent positive pressure ventilation has occasionally permitted children with SMA type 1 to survive more than 4 years. While “do not resuscitate” orders may be an acceptable alternative to tracheostomy for some parents, noninvasive ventilation can prolong life, is more desirable than tracheostomy, and in our experience has not been refused. Patients who have used both tracheostomy and noninvasive ventilatory support almost invariably prefer the latter for safety, convenience, and facilitation of speech, sleep, swallowing, appearance, comfort, and overall acceptability. Besides the disadvantages of tracheostomy ventilation, the imposition of a tube often results in the need for continuous, rather than nocturnal-only ventilator use. This, along with need for tracheal suctioning, has untoward consequences on quality of life. Further, considering the ethics of ventilator use, unlike for tracheostomy ventilation users, individuals using noninvasive aids can discontinue them on their own.

On the other hand, the introduction of noninvasive ventilation often requires effort intensive ventilator synchronization, interface preparation and fitting, and airway secretion management, especially when the patient cannot cooperate. Thus, after extubation, patients can require close surveillance and intensive intervention for days until they wean to nocturnal-only nasal ventilation and their airway secretions have dissipated. The first few hours after extubation can require the continuous presence and intense efforts of a highly skilled respiratory therapist to manage sudden, precipitous oxyhemoglobin desaturations. Because it can be virtually impossible to achieve this level of ongoing respiratory-nursing care for more than the initial few post-extubation hours in our understaffed intensive care units, we train the infants’ parents and rely heavily on them to eventually provide much if not most of the intensive care. Having a thoroughly trained and totally dedicated family member or care provider is critical for successful noninvasive home management. It must be emphasized that the parent must be comfortable managing sudden oxyhemoglobin desaturations by manually resuscitating the patient, using MI-E and oral suctioning, re-adjusting nasal interfaces, repositioning, and applying other therapies to facilitate lung ventilation and airway secretion elimination. It is unlikely that this approach can succeed long-term in the event that both parents work or have difficulty learning or performing the interventions required.

Both of our patients who underwent tracheostomy had suboptimal parent involvement.

Cost is a difficult issue. For patients with milder neuromuscular conditions, such as Duchenne muscular dystrophy, the avoidance of respiratory complications and hospitalizations with the use of noninvasive respiratory muscle aids create considerable cost savings by comparison with the multiple and often prolonged hospitalizations associated with conventional management and tracheostomy. However, at least until SMA patients are old enough to cooperate with the noninvasive protocol, essentially every chest cold must be treated by hospitalization and intubation. This may be more costly and effort-intensive than managing intercurrent chest colds via a tracheostomy tube. Cost, quality of life, and survival issues deserve further study.

In summary, the need to intubate an SMA type 1 infant does not mean that tracheostomy is inevitable. These patients have a better chance of successful extubation when they are extubated in the manner used in this study. Although intubation may be required during intercurrent chest colds, tracheostomy can usually be avoided if respiratory muscle aids are used by highly trained and dedicated parents in both the acute and home settings, as needed.

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