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Miguel R. Gonçalves and John R. Bach wrote all the drafts of the article and gathered and analyzed all the data regarding the reviews and consensus. Alice Hon, Eduardo Luis De Vito, Yuka Ishikawa, Francisco Prado, and Marie Eugenia Dominguez gathered information from all the reviews and consensuses and added material to the text of the article. All authors read and approved the final article.
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REVIEW & ANALYSIS

Changing Trends in the Management of End-Stage Neuromuscular Respiratory Muscle Failure

Recommendations of an International Consensus

ABSTRACT

Bach JR, Gonçalves MR, Hon A, Ishikawa Y, De Vito EL, Prado F, Dominguez ME: Changing trends in the management of end-stage neuromuscular respiratory muscle failure. Am J Phys Med Rehabil 2012;91:00–00.

Objectives: Respiratory management of patients with end-stage respiratory muscle failure of neuromuscular disease has evolved from no treatment and inevitable respiratory failure to the use of up to continuous noninvasive intermittent positive pressure ventilatory support (CNVS) to avert respiratory failure and to permit the extubation of "unweanable" patients without tracheostomy. An international panel experienced in CNVS was charged by the 69th Congress of the Mexican Society of Pulmonologists and Thoracic Surgeons to analyze changing respiratory management trends and to make recommendations.

Design: Neuromuscular disease respiratory consensuses and reviews were identified from PubMed. Individual respiratory interventions were identified; their importance was established by assessing the quality of evidence-based literature for each one and their patterns of use over time. The panel then determined the evidence-based strength for the efficacy of each intervention and made recommendations for achieving prolonged survival by CNVS.

Results: Fifty publications since 1993 were identified. Continuous positive airway pressure, oxygen therapy, bilevel positive airway pressure used at both low and high spans, "air stacking," manually assisted coughing, low pressure (<35 cm H_2O) and high pressure (≥40 cm H_2O) mechanically assisted coughing, noninvasive positive pressure ventilation part time (<23 hrs per day) and full time (>23 hrs per day; CNVS), extubation and decannulation of ventilator-dependent patients to CNVS, and oximetry feedback for noninvasive positive pressure ventilation and mechanically assisted coughing were identified. All noted interventions are being used with increasing frequency and were unanimously recommended to achieve prolonged survival by CNVS, with the exception of supplemental oxygen and continuous positive airway pressure, which are being used less and were not recommended for this population.

Conclusions: CNVS and extubation of unweanable patients to CNVS are increasingly being used to prolong life while avoiding invasive interfaces.

KeyWords: Neuromuscular Disease, Pulmonary, Respiratory Muscle Failure, Ventilation

Before 1953, *noninvasive ventilation* referred to the use of body ventilators such as the iron lung.[1] Despite their success for continuous ventilatory support, tracheostomy mechanical ventilation (TMV) became the standard for ventilatory support after the 1952 Danish polio epidemic, for which few iron lungs were available.[2] Because TMV freed patients from iron lungs to be mobilized in wheelchairs and facilitated airway secretion management for many, this spread to the United States.

Then, in 1953, Dr John Affeldt wrote, "… some of our physical therapists, in struggling with [iron lung] patients, noticed that they could simply take the positive pressure attachment, apply a small plastic mouthpiece …, and allow that to hang in the patient's mouth …. We even had one patient who has no breathing ability who has fallen asleep and been adequately ventilated by this procedure, so that it appears to work very well, and I think does away with a lot of complications of difficulty of using [invasive] positive pressure. You just hang it by the patients and they grip it with their lips, when they want it, and when they don't want it, they let go of it. It is just too simple."[3]

Patients who were using body ventilators around the clock began using mouthpiece noninvasive intermittent positive pressure ventilation (NIV) during daytime hours (Fig. 1). Many then used mouthpiece NIV around the clock, refusing to return to body ventilators for sleep. Losing the mouthpiece during sleep could have meant death. The advent of the Bennett Lipseal (Philips-Respironics International Inc, Murrysville, PA) in 1968 prevented this by securing the mouthpiece and diminishing oral air leakage (Fig. 2). This permitted the use of NIV for up to full continuous noninvasive ventilatory support (CNVS) as an alternative to TMV.[4]

In 1956, the Harris Thompson portable 28-lb Bantam positive pressure ventilator became available. The next year, it was noted, "If a patient is going to be left a respirator cripple with a very low VC, a tracheotomy may be a great disadvantage. It is very difficult to get rid of a tracheotomy tube when the VC is only 500 or 600 ml and there is no power of coughing, whereas, as we all know, a patient who has been treated in a respirator (body ventilator) from the first can survive and get out of all mechanical devices with a VC of that figure."[5] Thus, it was recognized that TMV could result in greater ventilator dependence because of deconditioning, tube-induced secretions, hyperventilation by bypassing upper airway afferents, and, possibly, other factors.[6]

Mouthpiece/lip seal NIV was reported to have been used for up to CNVS by 257 patients, most of whom were cared for by Goldwater Memorial Hospital[7] from 1968 through 1987. In 1987, nasal NIV was first used for CNVS for a patient with multiple sclerosis with 100 ml of vital capacity (VC) and no autonomous breathing ability by the same author.[8] This led to a case series[9] reported in 1990 in which nasal NIV was used as part of CNVS. Despite this 1990 publication, no other centers reported using CNVS until Servera et al.[10] did to avert intubations in 2005 and Toussaint et al.[11] did for patients with Duchenne muscular dystrophy (DMD) in 2006. Available since 1984, continuous positive airway pressure (PAP) "masks" were adapted for use with ventilator circuits.[12,13] However, in most centers, patients with progressive neuromuscular respiratory muscle failure continued to be treated with continuous PAP and low spans of bilevel PAP during

FIGURE 1 *A 66-yr-old woman with no ventilator-free breathing ability and using a 15-mm angled mouthpiece for intermittent positive pressure ventilation, seen here with the mouthpiece in her mouth adjacent to sip-and-puff wheelchair controls, since 1954. She has used a Bennett Lipseal interface (Philips-Respironics International Inc, Murrysville, PA) for nocturnal ventilatory support since 1968.*

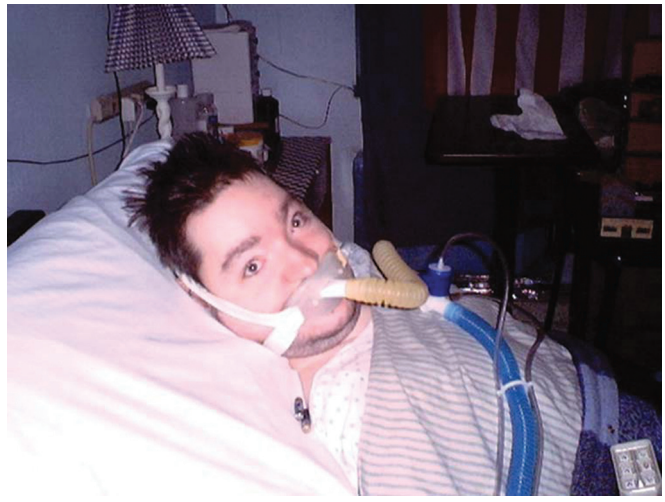

FIGURE 2 *A 41-yr-old with Duchenne muscular dystrophy using the Lipseal for nocturnal ventilatory support since the age of 12 yrs and using a 15-mm angled mouthpiece for daytime support since the age of 14 yrs.*

sleep rather than with ventilators that facilitate extending NIV use to CNVS as needed.[14,15] This continues to result in preventable episodes of ventilatory/respiratory failure (RF).[16–18]

Airway secretion congestion, especially during intercurrent respiratory tract infections, can result in acute RF and intubation.[19] With failure to pass spontaneous breathing trials (SBTs), tracheotomy is conventionally indicated.[20] The ability to increase cough flows by mechanically assisted coughing (MAC), available since 1993, has been reported to help to avoid acute RF[19,21,22] and facilitate successful extubation[23,24] and CNVS. The purpose of this study was to identify the changing trends in the respiratory management of neuromuscular disease (NMD) and to identify and analyze facilitative interventions.

METHODS

Clinicians who had published or presented CNVS outcomes were invited to take part in an expert panel at the 69th Congress of the Mexican Society of Pulmonologists and Thoracic Surgeons, charged with considering the evolution of NMD respiratory management. Respiratory management reviews and consensus articles were identified from MEDLINE. The key words used were *neuromuscular disease*, *Duchenne muscular dystrophy (DMD)*, *amyotrophic lateral sclerosis (ALS)*, *spinal muscular atrophy type 1 (SMA 1)*, *noninvasive ventilation*, *respiratory management*, *respiratory care*, *long term ventilation*, and *acute respiratory failure*. Exclusion criteria were non-English language, editorials, animal subjects, and studies not relevant to the topic. The key interventions associated with achieving CNVS were identified as well as trends in their use over time. Current recommendations were formulated.

Each included publication was read and appraised for methodological rigor according to American College of Chest Physicians task force criteria.[25] Levels of evidence were assigned to each intervention, and ensuing recommendations were graded according to the following: 1A/strong recommendation, high-quality evidence; 1B/strong recommendation, moderate-quality evidence; 1C/strong recommendation, low-quality evidence; 2A/weak recommendation, high-quality evidence; 2B/weak recommendation, moderate-quality evidence; and 2C/weak recommendation, low-quality evidence.[25]

RESULTS

Fifty relevant references were identified including 34 on various NMDs: five on DMD, six on SMA 1, and six on ALS.[17,20,26–73] Ten references were from the decade of the 1990s and 40 were from the subsequent decades. The following interventions were identified: oxygen therapy, cough peak flow (CPF) evaluation and augmentation, "air stacking," low pressure (≤35 cm H_2O) and high pressure (≥40 cm H_2O) MAC, bilevel PAP used at both low and high spans, NIV that includes nasal and mouthpiece NIV part time (<23 hrs per day) and full time (>23 hrs per day), oximetry feedback for NIV and MAC, elective tracheotomy without meeting the described criteria for tracheotomy,[74–76] and extubation and decannulation of patients unable to pass SBTs to CNVS.[23]

Oxygen Therapy Avoidance

Supplemental oxygen therapy for hypercapnic patients with respiratory muscle weakness can

decrease ventilatory drive; exacerbate hypercapnia and its symptoms and result in CO_2 narcosis[77]; render nocturnal bilevel PAP and NIV less effective[78]; and render oximetry ineffective as a gauge of hypoventilation, airway mucus congestion, atelectasis, and pneumonia.[6,19,79] Oxygen supplementation was reported to result in significantly more pneumonias, hospitalizations, and hospitalization days than does NIV or no treatment at all.[77]

History

Avoidance of supplemental oxygen was recommended by 24 of the 50 early articles, and its use was ignored by the rest except for a 2004 consensus[27] and a 2010 consensus[28] in which it was strongly discouraged despite the absence of randomized controlled trials.

Recommendation

The panel unanimously recommended that oxygen be administered only for acute resuscitation, for hospitalized patients when CNVS and MAC cannot normalize (≥95%) oxyhemoglobin saturation (SpO_2) and the patient can readily be intubated, and for euthanasia along with morphine for patients with advanced bulbar ALS who satisfy criteria for but refuse tracheotomy[80] (grade of recommendation: 1C).

Lung Volume Recruitment Techniques: Air Stacking

Air stacking involves the glottis holding consecutively delivered air volumes from a volume-cycled ventilator or a manual resuscitator until no more can be held (maximal insufflation capacity).[81] Controlled trials demonstrated significant increases in lung volume recruitment by air stacking.[76] Lung volume recruitment, whether by glottis air stacking or by passive lung insufflations,[82] limits chest wall contractures and lung restriction, increases CPF[83] and voice volume, and promotes lung growth and impedes chest deformity for children with NMD.[6] For small children with paradoxical breathing who cannot air stack, nocturnal NIV has been reported to accomplish this.[84,85]

History

Air stacking was cited in 21 of the 50 articles, in only 2 articles before 2002 but in 6 of 12 articles since 2009.

Recommendation

The panel unanimously recommended daily air stacking once the VC is lower than 80% of normal, and, if ineffective because of severe glottic impairment, then passive deep lung insufflations will be used[82] (grade of recommendation for air stacking: 1B). Evaluation of the maximal insufflation capacity–VC difference was also unanimously recommended as an objective, reproducible, quantitative measure of glottic (bulbar-innervated muscle) integrity[86] (grade of recommendation: 1B).

Evaluation and Augmentation of CPF

Manually assisted coughing consists of maximal air stacking followed by a cough-timed abdominal thrust. In controlled trials, it was demonstrated to significantly increase CPF. The CPF, when less than 4.5–5 liters/sec, indicates the need for manually assisted coughing during periods of airway congestion.[87,88] Cough flows were increased from 2.5 ± 2.0 liters/sec to 4.3 ± 1.7 liters/sec by manually assisted coughing.[81]

History

Evaluation and augmentation of CPF were cited in 25 of the 50 articles, only one article before 2000 but in all but five since 2009.

Recommendation

The panel unanimously recommended routine measurement and augmentation of CPF (grade of recommendation: 1A) when it is less than 4.5 liters/sec (grade of recommendation: 1C).

NIV and Bilevel PAP

Bilevel PAP is conventionally prescribed for patients with NMD whose VCs have decreased lower than 50% and whose bilevel PAP settings were titrated to eliminate "apneas" and "hypopneas" by polysomnography. When patients deteriorate to require CNVS, however, bilevel PAP becomes inadequate.[26,89] Most of these devices do not function with direct current and thus cannot be used on a wheelchair, these cannot always be triggered by infants and others with little VC, air stacking to increase cough flows is not possible,[6] and inspiratory muscle rest is suboptimal at less than full support settings, so these patients eventually develop RF and undergo tracheotomy rather than be managed by CNVS.[90,91]

History

Three reviews and consensuses of respiratory management of NMD did not mention NIV or bilevel PAP. The remaining 47 suggested a variety of indications for introducing nocturnal bilevel PAP, with 11 recommending high-span PAP (inspiratory PAP minus expiratory PAP spans >10 cm H_2O), and 29,

only nocturnal low-span PAP. Controlled studies demonstrated a statistically significant prolongation of survival for several months using nocturnal bilevel PAP, but none reported extending the use of bilevel PAP to CNVS.

Recommendation

Because bilevel PAP cannot be used for air stacking, expiratory PAP is counterproductive for assisting weak respiratory muscles, and, because portable ventilators eventually become necessary for CNVS, the panel recommended that all patients with the ability to air stack use nocturnal NIV rather than bilevel PAP (grade of recommendation: 1C).

Continuous Noninvasive Intermittent Positive Pressure Ventilatory Support

This can be provided during sleep via nasal or oronasal interface and during daytime hours via mouthpiece except for those whose lips are too weak to grab it, in which case, nasal prongs are used.[6,92] CNVS has been reported to have been used successfully as an alternative to TMV for 760 patients from 21 centers[93] and for patients for up to 58 yrs (Fig. 1).

History

The use of some daytime mouthpiece NIV was recommended in 16 of 47 articles and, for up to CNVS, in 10 articles, but none noted that tracheostomy could be avoided by CNVS, especially when the patients are intubated. Extubation of "unweanable" patients to CNVS has thus far only been reported in four centers.[7,10,11,26]

Recommendation

Because of the limitations of bilevel PAP and the eventual need for CNVS, the panel unanimously recommended that assist-control volume-cycling NIV be used for patients capable of air stacking and that pressure-cycling NIV be used otherwise. The grade of recommendation is 1A for using ventilators for CNVS because of the extremely large and consistent magnitude of the treatment effect,[25] that is, no randomized controlled trials are possible to demonstrate prolonged survival because discontinuance of CNVS can only result in death for patients without the autonomous ability to breathe.[94,95] However, the panel unanimously recommended the use of nocturnal bilevel PAP or pressure-cycling NIV for patients with bulbar ALS who hypoventilate during sleep but cannot air stack (grade of recommendation: 1A).[75]

Mechanically Assisted Coughing

MAC is defined as mechanical insufflation-exsufflation (e.g., Cough Assist; Philips-Respironics Inc, Murraysville, PA) with an exsufflation-timed abdominal thrust. The mechanical in-exsufflator delivers positive pressure to full clinical chest expansion then negative pressure to maximal lung emptying via an oronasal interface or an invasive airway tube.[96] Like withdrawal of CNVS for patients with 0 ml of VC, withdrawal of MAC from patients with productive airways but who are unable to cough necessarily results in RF, most often from pneumonia in the left lung fields because airway suctioning misses the left mainstem bronchus more than 90% of the time.[97] The only randomized controlled trial of MAC *vs.* invasive airway suctioning significantly favored the former.[98] The use of MAC has been reported to be critical to avoid RF, hospitalization, and intubation for patients with chest infections[21,74,99,100] and to permit extubation/decannulation of patients failing SBTs.[23] The patients who benefit the most from MAC are those whose bulbar muscle function is insufficient to permit optimal air stacking for assisted CPF (>4.5–5 liters/min) but is adequate to maintain airway patency.[76]

History

Only 12 articles mentioned in-exsufflation use at the insufflation and exsufflation pressures considered effective by this panel (>35 cm H_2O).[101–103] Nineteen articles recommended low pressures, 3 noted no settings, and 15 did not mention it. No articles cited the use of MAC via invasive airway tubes.

Recommendation

The panel unanimously recommended that MAC be used, whether noninvasively or via invasive airway tube, for all NMD patients with CPF less than 5 liters/sec[21] to treat airway congestion (grade of recommendation: 1A).

Extubation and Decannulation

Despite CNVS and MAC, aspiration and intercurrent respiratory tract infections can result in pneumonia and RF, and early tracheotomy has been proposed to "minimize respiratory complications."[104–106] Conventionally, ventilator weaning is considered necessary for extubation. Tracheostomy for end-stage respiratory management and extubation failure was cited in 46 of the 50 articles, and none described the extubation or the decannulation of patients who could not pass SBTs. However, a 2010 publication reported successful extubation

of 155 of 157 unweanable patients with NMD to CNVS and MAC in two centers using a NMD-specific protocol.[23] Decannulation of unweanable patients to CNVS and MAC has also been described for more than 100 patients with NMD and spinal cord injury (SCI).[24,107,108]

History

Only one consensus article in 2010 recommended three extubation attempts to CNVS before resorting to tracheostomy but implied that the latter would eventually become necessary.[28]

Recommendation

The panel unanimously recommended that all patients with NMD and SCI meeting the criteria, whether weanable or not, be offered extubation or decannulation to CNVS and MAC as described[24,107] (grade of recommendation: 1A). Likewise, the panel unanimously recommended tracheotomy only for patients who cannot maintain an SpO_2 of greater than or equal to 95% despite CNVS and MAC,[74] that is, essentially, only for bulbar ALS (grade of recommendation: 1C).

Oximetry Feedback Protocol

The protocol consists of using an oximeter for feedback to maintain an SpO_2 of greater than or equal to 95% by using ambient air CNVS and MAC as needed, for example, during intercurrent respiratory tract infections and after extubation/decannulation.[19,23] No randomized controlled trials were done, but patients requiring CNVS during respiratory tract infections and having oxyhemoglobin desaturations because of airway congestion have never been previously reported to have been managed at home and to have no invasive cannulation.

History

The protocol was recommended in 8 of the 50 articles but in only 1 article before 2003.[74,109]

Recommendation

The panel unanimously agreed that, because it is impossible to develop RF with an SpO_2 of greater than or equal to 95% in ambient air, patients with ineffective CPF be taught the protocol to avoid RF[21,22] (grade of recommendation: 1C).

DISCUSSION

Mechanisms by which the recommended interventions can improve the clinical picture include relieving symptoms; resting the respiratory muscles and decreasing metabolic demand; increasing tidal volumes and relieving hypercapnia; resetting chemoreceptors; opening atelectatic areas; maintaining airway patency; improving ventilation/perfusion matching; maintaining lung and chest wall range of motion and compliance; improving cough flows and airway clearance; and, most importantly, assisting, supporting, and substituting for respiratory muscle function.[6,79] Bilevel PAP use at spans of less than 10 cm H_2O may not adequately achieve these goals and cannot provide CNVS. Nocturnal NIV at full ventilatory support settings is typically spontaneously extended into daytime hours and eventually around the clock, thereby averting hospitalizations for RF and tracheostomy tubes, and has been used by some patients for up to 58 yrs (Fig. 1).

In 1993, indication for tracheotomy was described as the need for NIV more than 15 hrs a day.[29] That consensus had only one dissenting voice who argued for CNVS (the first author of this article). Now, however, others from that group are using CNVS rather than tracheostomy for patients with NMD.[104] None of the five centers that extubate unweanable patients had any of their 385 patients with DMD on CNVS undergo tracheotomy except when they required critical care and were lost to the expert center.[110–113]

Noninvasive management is invariably preferred more than tracheostomy by patients for safety, convenience, appearance, comfort, speech, sleep, swallowing, and general acceptability,[114] and a recent controlled trial demonstrated significantly longer survival by CNVS than by TMV for DMD.[113] Long-term complications of tracheostomy include greater ventilator dependence,[107] ineffective cough, and more frequent pneumonias and hospitalizations than with CNVS.[115,116] Whereas some recent consensuses recommended most of the cited interventions, all gave rationales to resort to tracheotomy. Indeed, a 2010 DMD consensus group[28] was the first to make all of the important recommendations but concluded that tracheostomy was indicated when preferred by the patient and clinician, when NIV was unsuccessful, when there was inability of "the local medical infrastructure to support NIV," for three extubation failures despite optimal use of NIV or bilevel PAP and MAC, and for aspiration of airway secretion to the extent that the SpO_2 remains less than 95% despite optimal use of NIV and MAC. However, that panel of 11 experts had only 1 who came from a center where patients with NMD who failed SBTs are extubated without tracheotomy and who did not agree that tracheostomy would become necessary, except for the latter two scenarios.

FIGURE 3 *Brothers with SMA type 1 aged 17 and 15 yrs old, continuously dependent on noninvasive ventilatory support since the age of 4 mos. SMA indicates spinal muscular atrophy.*

In this panel, every member has long-term CNVS users and at least five members are from centers that routinely extubate and decannulate unweanable patients with NMD.[23] None of the 760 properly trained and equipped CNVS-dependent patients reported by this panel ever opted for or "preferred" elective tracheotomy without meeting the ALS criteria for it.[74] The authors suggest that only patients not offered with CNVS and MAC at optimal settings prefer tracheostomy. Other than for patients with severe mental impairment, no one on this panel has encountered a patient with DMD who could "not successfully use or tolerate CNVS." The authors are also unaware of the inability of local medical infrastructure to support NIV except in countries where ventilator use is not funded. Five of 101 patients with DMD in one center have been dependent on CNVS for more than 20 yrs, with none of 40 intercurrent extubation attempts on them having failed.[93,113] None, therefore, have failed three extubation attempts.[74] Unfortunately, the tracheotomy recommendations of the 2010 consensus can be used by any clinician to justify tracheostomy rather than organize a support system of comprehensive instruction, equipping, and training in noninvasive management.[99] Such a premise perpetuates expensive, invasive care, with need for higher technology and skilled nursing and more institutionalization that diminishes quality-of-life and that is rarely, if ever, preferred by patients.

For typical SMA 1, survival has thus far been extended to up to 18½ yrs by up to CNVS from as early as 4 mos of age for 60 patients with SMA 1 (Fig. 3).[117,118] Despite these outcomes, consensuses of experts as recent as 2009 report that 95% of children with SMA 1 die before 18 mos of age, with a mean age of death at 25 wks, and none reported using CNVS.[34,35]

Many articles continue to be published on palliative care for ALS, with none thus far referring to prolonging life by CNVS.[36,80,119–124] Because about 40% of patients with ALS, or 335 reported by this panel, can survive using CNVS for a mean of 11 mos,[93,109] palliative care precepts are inappropriate for properly equipped and trained patients with adequate personal care before they meet the criteria for tracheostomy.[74] For most non-ALS NMD diagnoses, palliative care interventions are distinctly inappropriate because oxygen therapy and narcotics hasten death. Thus, "palliative respiratory care" for patients with NMD perpetuates the misconception that NIV is only for symptom relief and not for CNVS to prolong survival.

REFERENCES

1. Bach J: The history of mechanical ventilation and respiratory muscle aids, in Bach JR (ed): *Noninvasive Mechanical Ventilation*. Philadephia, PA, Hanley & Belfus, 2002, pp. 45–72
2. Bach J: A historical perspective on the use of noninvasive ventilatory support alternatives. *Respir Care Clin N Am* 1996;2:161–81
3. *Round Table Conference on Poliomyelitis Equipment*. National Foundation for Infantile Paralysis–March of Dimes, Inc. Roosevelt Hotel, White Plaines, New York City, May 1953
4. Bach JR, Alba AS: Sleep and nocturnal mouthpiece IPPV efficiency in postpoliomyelitis ventilator users. *Chest* 1994;106:1705–10
5. Hodes H: Treatment of respiratory difficulty in poliomyelitis, in: *Poliomyelitis: Papers and Discussion: Presented at the Third International Poliomyelitis Conference*. Philadelphia, PA, Lippincott, 1955, pp 91–113
6. Bach JR: Update and perspectives on noninvasive respiratory muscle aids. Part 1: The inspiratory aids. *Chest* 1994;105:1230–40

7. Bach JR, Alba AS, Saporito LR: Intermittent positive pressure ventilation via the mouth as an alternative to tracheostomy for 257 ventilator users. *Chest* 1993;103:174–82

8. Bach JR, Alba A, Mosher R, et al: Intermittent positive pressure ventilation via nasal access in the management of respiratory insufficiency. *Chest* 1987;92: 168–70

9. Bach JR, Alba AS: Management of chronic alveolar hypoventilation by nasal ventilation. *Chest* 1990; 97:52–7

10. Servera E, Sancho J, Zafra MJ, et al: Alternatives to endotracheal intubation for patients with neuromuscular diseases. *Am J Phys Med Rehabil* 2005;84:851–7

11. Toussaint M, Steens M, Wasteels G, et al: Diurnal ventilation via mouthpiece: Survival in end-stage Duchenne patients. *Eur Respir J* 2006;28:549–55

12. Brochard L, Isabey D, Piquet J, et al: Reversal of acute exacerbations of chronic obstructive lung disease by inspiratory assistance with a face mask. *N Engl J Med* 1990;323:1523–30

13. Carrey Z, Gottfried SB, Levy RD: Ventilatory muscle support in respiratory failure with nasal positive pressure ventilation. *Chest* 1990;97:150–8

14. Ellis ER, Bye PT, Bruderer JW, et al: Treatment of respiratory failure during sleep in patients with neuromuscular disease, positive pressure ventilation through a nose mask. *Am Rev Respir Dis* 1987; 135:148–52

15. Kerby G, Mayer L, Pingleton SK: Nocturnal positive pressure ventilation via nasal mask. *Am Rev Respir Dis* 1987;135:738–40

16. Bach JR, O'Brien J, Krotenberg R, et al: Management of end stage respiratory failure in Duchenne muscular dystrophy. *Muscle Nerve* 1987;10:177–82

17. Hotes LS, Johnson JA, Sicilian L: Long-term care, rehabilitation, and legal and ethical considerations in the management of neuromuscular disease with respiratory dysfunction. *Clin Chest Med* 1994;15: 783–95

18. Wallgren-Pettersson C, Laing NG: 109th ENMC International Workshop: 5th workshop on nemaline myopathy, 11th–13th October 2002, Naarden, The Netherlands. *Neuromuscul Disord* 2003;13:501–7

19. Tzeng AC, Bach JR: Prevention of pulmonary morbidity for patients with neuromuscular disease. *Chest* 2000;118:1390–6

20. Make BJ, Hill NS, Goldberg AI, et al: Mechanical ventilation beyond the intensive care unit. Report of a consensus conference of the American College of Chest Physicians. *Chest* 1998;113:289S–344S

21. Gomez-Merino E, Bach JR: Duchenne muscular dystrophy: Prolongation of life by noninvasive ventilation and mechanically assisted coughing. *Am J Phys Med Rehabil* 2002;81:411–5

22. Vitacca M, Paneroni M, Trainini D, et al: At home and on demand mechanical cough assistance program for patients with amyotrophic lateral sclerosis. *Am J Phys Med Rehabil* 2010;89:401–6

23. Bach JR, Goncalves MR, Hamdani I, et al: Extubation of patients with neuromuscular weakness: A new management paradigm. *Chest* 2010;137:1033–9

24. Bach JR, Saporito LR: Criteria for extubation and tracheostomy tube removal for patients with ventilatory failure. A different approach to weaning. *Chest* 1996;110:1566–71

25. Guyatt G, Gutterman D, Baumann M, et al: Grading strength of recommendations and quality of evidence in clinical guidelines: Report from an American College of Chest Physicians Task Force. *Chest* 2006;129:174–81

26. Benditt JO: Full-time noninvasive ventilation: Possible and desirable. *Respir Care* 2006;51:1005–12. discussion 1012–5

27. Finder JD, Birnkrant D, Carl J, et al: Respiratory care of the patient with Duchenne muscular dystrophy: ATS consensus statement. *Am J Respir Crit Care Med* 2004;170:456–65

28. Birnkrant DJ, Bushby KM, Amin RS, et al: The respiratory management of patients with Duchenne muscular dystrophy: A DMD care considerations working group specialty article. *Pediatr Pulmonol* 2010;45:739–48

29. Robert D, Willig TN, Leger P, et al: Long-term nasal ventilation in neuromuscular disorders: Report of a consensus conference. *Eur Respir J* 1993;6:599–606

30. Boitano LJ: Equipment options for cough augmentation, ventilation, and noninvasive interfaces in neuromuscular respiratory management. *Pediatrics* 2009;123(suppl 4):S226–30

31. Dean S, Bach JR: The use of noninvasive respiratory muscle aids in the management of patients with progressive neuromuscular diseases. *Respir Care Clin N Am* 1996;2:223–40

32. Shneerson JM, Simonds AK: Noninvasive ventilation for chest wall and neuromuscular disorders. *Eur Respir J* 2002;20:480–7

33. Mehta S: Neuromuscular disease causing acute respiratory failure. *Respir Care* 2006;51:1016–21. discussion 1021–3

34. Roper H, Quinlivan R: Implementation of "the consensus statement for the standard of care in spinal muscular atrophy" when applied to infants with severe type 1 SMA in the UK. *Arch Dis Child* 2010;95:845–9

35. Wang CH, Finkel RS, Bertini ES, et al: Consensus statement for standard of care in spinal muscular atrophy. *J Child Neurol* 2007;22:1027–49

36. Hughes RA, Bihari D: Acute neuromuscular respiratory paralysis. *J Neurol Neurosurg Psychiatry* 1993;56:334–43

37. Corrado A, Gorini M, De Paola E: Alternative techniques for managing acute neuromuscular respiratory failure. *Semin Neurol* 1995;15:84–9

38. Statements AC: Noninvasive positive pressure ventilation. *Respir Care* 1997;42:365–9

39. Teener JW, Raps EC: Evaluation and treatment of respiratory failure in neuromuscular disease. *Rheum Dis Clin North Am* 1997;23:277–92

40. Barthlen GM: Nocturnal respiratory failure as an indication of noninvasive ventilation in the patient with neuromuscular disease. *Respiration* 1997;64 (suppl 1):35–8

41. Bella I, Chad DA: Neuromuscular disorders and acute respiratory failure. *Neurol Clin* 1998;16:391–417

42. Gozal D: Pulmonary manifestations of neuromuscular disease with special reference to Duchenne muscular dystrophy and spinal muscular atrophy. *Pediatr Pulmonol* 2000;29:141–50

43. Birnkrant DJ: The assessment and management of the respiratory complications of pediatric neuromuscular diseases. *Clin Pediatr (Phila)* 2002;41:301–8

44. Howard RS, Davidson C: Long term ventilation in neurogenic respiratory failure. *J Neurol Neurosurg Psychiatry* 2003;74(suppl 3):iii24–30

45. Farrero E, Prats E, Escarrabill J: [Series 4: Respiratory muscles in neuromuscular diseases and the chest cavity. Decision making in the clinical management of patients with lateral amyotrophic sclerosis]. *Arch Bronconeumol* 2003;39:226–32

46. Perrin C, Unterborn JN, Ambrosio CD, et al: Pulmonary complications of chronic neuromuscular diseases and their management. *Muscle Nerve* 2004;29:5–27

47. Wallgren-Pettersson C, Bushby K, Mellies U, et al: 117th ENMC workshop: Ventilatory support in congenital neuromuscular disorders—Congenital myopathies, congenital muscular dystrophies, congenital myotonic dystrophy and SMA (II) 4–6 April 2003, Naarden, The Netherlands. *Neuromuscul Disord* 2004;14:56–69

48. Simmons Z: Management strategies for patients with amyotrophic lateral sclerosis from diagnosis through death. *Neurologist* 2005;11:257–70

49. Mellies U, Dohna-Schwake C, Voit T: Respiratory function assessment and intervention in neuromuscular disorders. *Curr Opin Neurol* 2005;18:543–7

50. Simonds AK: Ethical aspects of home long term ventilation in children with neuromuscular disease. *Paediatr Respir Rev* 2005;6:209–14

51. Kang SW: Pulmonary rehabilitation in patients with neuromuscular disease. *Yonsei Med J* 2006;47: 307–14

52. Hess DR: Noninvasive ventilation in neuromuscular disease: Equipment and application. *Respir Care* 2006;51:896–911. discussion 911–2

53. Simonds AK: Recent advances in respiratory care for neuromuscular disease. *Chest* 2006;130:1879–86

54. Panitch HB: Respiratory issues in the management of children with neuromuscular disease. *Respir Care* 2006;51:885–93. discussion 894–5

55. Giannini A, Pinto AM, Rossetti G, et al: Respiratory failure in infants due to spinal muscular atrophy with respiratory distress type 1. *Intensive Care Med* 2006;32:1851–5

56. Kirk VG: Pulmonary complications of neuromuscular disease. *Paediatr Respir Rev* 2006;7(suppl 1): S232–4

57. Gregory SA: Evaluation and management of respiratory muscle dysfunction in ALS. *NeuroRehabilitation* 2007;22:435–43

58. Simonds AK: Respiratory support for the severely handicapped child with neuromuscular disease: Ethics and practicality. *Semin Respir Crit Care Med* 2007;28:342–54

59. Birnkrant DJ, Panitch HB, Benditt JO, et al: American College of Chest Physicians consensus statement on the respiratory and related management of patients with Duchenne muscular dystrophy undergoing anesthesia or sedation. *Chest* 2007;132:1977–86

60. Annane D, Orlikowski D, Chevret S, et al: Nocturnal mechanical ventilation for chronic hypoventilation in patients with neuromuscular and chest wall disorders. *Cochrane Database Syst Rev* 2007;CD001941

61. Manzur AY, Kinali M, Muntoni F: Update on the management of Duchenne muscular dystrophy. *Arch Dis Child* 2008;93:986–90

62. Hutchinson D, Whyte K: Neuromuscular disease and respiratory failure. *Pract Neurol* 2008;8:229–37

63. Weber M: Meeting report of European ALS Consortium (EALSC): 6th European ALS congress research workshop and young investigators' meeting. *Amyotroph Lateral Scler* 2008;9:318–20

64. Ozsancak A, D'Ambrosio C, Hill NS: Nocturnal noninvasive ventilation. *Chest* 2008;133:1275–86

65. Ambrosino N, Carpene N, Gherardi M: Chronic respiratory care for neuromuscular diseases in adults. *Eur Respir J* 2009;34:444–51

66. Benditt JO: Initiating noninvasive management of respiratory insufficiency in neuromuscular disease. *Pediatrics* 2009;123(suppl 4):S236–8

67. Radunovic A, Annane D, Jewitt K, et al: Mechanical ventilation for amyotrophic lateral sclerosis/motor neuron disease. *Cochrane Database Syst Rev* 2009; 4:CD004427

68. Schroth MK: Special considerations in the respiratory management of spinal muscular atrophy. *Pediatrics* 2009;123 (suppl 4):S245–9

69. Racca F, Del Sorbo L, Mongini T, et al: Respiratory management of acute respiratory failure in neuromuscular diseases. *Minerva Anestesiol* 2010; 76:51–62

70. Miller RG, Jackson CE, Kasarskis EJ, et al: Practice parameter update: The care of the patient with amyotrophic lateral sclerosis: Multidisciplinary care, symptom management, and cognitive/behavioral impairment (an evidence-based review): Report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology* 2009;73:1227–33

71. Panitch HB: The pathophysiology of respiratory impairment in pediatric neuromuscular diseases. *Pediatrics* 2009;123(suppl 4):S215–8

72. Vazquez-Sandoval A, Huang EJ, Jones SF: Hypoventilation in neuromuscular disease. *Semin Respir Crit Care Med* 2009;30:348–58

73. Kennedy JD, Martin AJ: Chronic respiratory failure and neuromuscular disease. *Pediatr Clin North Am* 2009;56:261–73. xii

74. Bach JR, Bianchi C, Aufiero E: Oximetry and indications for tracheotomy for amyotrophic lateral sclerosis. *Chest* 2004;126:1502–7

75. Farrero E, Prats E, Povedano M, et al: Survival in amyotrophic lateral sclerosis with home mechanical ventilation: The impact of systematic respiratory assessment and bulbar involvement. *Chest* 2005;127: 2132–8

76. Sancho J, Servera E, Diaz J, et al: Efficacy of mechanical insufflation-exsufflation in medically stable patients with amyotrophic lateral sclerosis. *Chest* 2004;125:1400–5

77. Bach JR, Rajaraman R, Ballanger F, et al: Neuromuscular ventilatory insufficiency: Effect of home mechanical ventilator use vs. oxygen therapy on pneumonia and hospitalization rates. *Am J Phys Med Rehabil* 1998;77:8–19

78. Bach J, Robert D, Leger P, et al: Sleep fragmentation in Kyphoscoliotic individuals with alveolar hypoventilation treated by NIPPV. *Chest* 1995;107:1552–8

79. Bach JR: Update and perspective on noninvasive respiratory muscle aids. Part 2: The expiratory aids. *Chest* 1994;105:1538–44

80. Maessen M, Veldink JH, van den Berg LH, et al: Requests for euthanasia: Origin of suffering in ALS, heart failure, and cancer patients. *J Neurol* 2010;257:1192–8

81. Kang SW, Bach JR: Maximum insufflation capacity. *Chest* 2000;118:61–5

82. Bach JR, Mahajan K, Lipa B, et al: Lung insufflation capacity in neuromuscular disease. *Am J Phys Med Rehabil* 2008;87:720–5

83. Kang SW, Bach JR: Maximum insufflation capacity: Vital capacity and cough flows in neuromuscular disease. *Am J Phys Med Rehabil* 2000;79:222–7

84. Bach JR, Bianchi C: Prevention of pectus excavatum for children with spinal muscular atrophy type 1. *Am J Phys Med Rehabil* 2003;82:815–9

85. Chatwin M, Bush A, Simonds AK: Outcome of goal-directed non-invasive ventilation and mechanical insufflation/exsufflation in spinal muscular atrophy type I. *Arch Dis Child* 2011;96:426–32

86. Bach JR: Amyotrophic lateral sclerosis: Predictors for prolongation of life by noninvasive respiratory aids. *Arch Phys Med Rehabil* 1995;76:828–32

87. Bach JR, Goncalves MR, Paez S: Expiratory flow maneuvers in patients with neuromuscular diseases. *Am J Phys Med Rehabil* 2006;85:105–11

88. Bach JR: Mechanical insufflation-exsufflation. Comparison of peak expiratory flows with manually assisted and unassisted coughing techniques. *Chest* 1993; 104:1553–62

89. Bach JR: Continuous noninvasive ventilation for patients with neuromuscular disease and spinal cord injury. *Semin Respir Crit Care Med* 2002;23: 283–92

90. Schonhofer B, Sortor-Leger S: Equipment needs for noninvasive mechanical ventilation. *Eur Respir J* 2002; 20:1029–36

91. Fauroux B, Leroux K, Desmarais G, et al: Performance of ventilators for noninvasive positive-pressure ventilation in children. *Eur Respir J* 2008;31:1300–7

92. Bach JR, Martinez D: Duchenne muscular dystrophy: Continuous noninvasive ventilatory support prolongs survival. *Respir Care* 2011;56:744–50

93. Goncalves MR: *Noninvasive ventilation and mechanical assisted cough: Efficacy from acute to chronic care* [PhD thesis in BioMedicine]. Porto, Portugal, Faculty of Medicine, University of Porto, 2010

94. Boitano LJ, Benditt JO: An evaluation of home volume ventilators that support open-circuit mouthpiece ventilation. *Respir Care* 2005;50:1457–61

95. Bach JR: Bilevel pressure vs volume ventilators for amyotrophic lateral sclerosis patients. *Chest* 2006;130:1949. author reply 1949–50

96. Chatwin M: How to use a mechanical insufflator-exsufflator "cough assist machine". *Breathe* 2008; 4:321–5

97. Fishburn MJ, Marino RJ, Ditunno JF Jr: Atelectasis and pneumonia in acute spinal cord injury. *Arch Phys Med Rehabil* 1990;71:197–200

98. Goncalves MR, Honrado T, Winck JC, et al: Effects of mechanical insufflation-exsufflation in preventing respiratory failure after extubation: A randomized controlled trial. *Crit Care* 2012;16:R48

99. Bach JR, Intintola P, Alba AS, Holland I: The ventilator-assisted individual. Cost analysis of institutionalization vs rehabilitation and in-home management. *Chest* 1992;101:26–30

100. Bach J, Gupta K, Reyna M, Hon A: Spinal muscular atrophy type 1: Prolongation of survival by noninvasive respiratory aids. *Pediatric Asthma Allergy Immunol* 2009;22:151–62

101. Winck JC, Goncalves MR, Lourenco C, et al: Effects of mechanical insufflation-exsufflation on respiratory parameters for patients with chronic airway secretion encumbrance. *Chest* 2004;126:774–80

102. Fauroux B, Guillemot N, Aubertin G, et al: Physiologic benefits of mechanical insufflation-exsufflation in children with neuromuscular diseases. *Chest* 2008;133:161–8

103. Sancho J, Servera E, Marin J, et al: Effect of lung mechanics on mechanically assisted flows and volumes. *Am J Phys Med Rehabil* 2004;83:698–703

104. Soudon P, Steens M, Toussaint M: A comparison of invasive versus noninvasive full-time mechanical

ventilation in Duchenne muscular dystrophy. *Chron Respir Dis* 2008;5:87–93

105. Vianello A, Bevilacqua M, Arcaro G, et al: Prevention of pulmonary morbidity in patients with neuromuscular disorders: A possible role for permanent cricothyroid minitracheostomy. *Chest* 1998;114:346–7
106. Bach JR: Tracheostomy for advanced neuromuscular disease. Con. *Chron Respir Dis* 2007;4:239–41
107. Bach JR, Goncalves M: Ventilator weaning by lung expansion and decannulation. *Am J Phys Med Rehabil* 2004;83:560–8
108. Bach JR, Alba AS: Noninvasive options for ventilatory support of the traumatic high level quadriplegic patient. *Chest* 1990;98:613–9
109. Bach JR: Amyotrophic lateral sclerosis: Prolongation of life by noninvasive respiratory AIDS. *Chest* 2002;122:92–8
110. Birnkrant DJ, Pope JF, Eiben RM: Management of the respiratory complications of neuromuscular diseases in the pediatric intensive care unit. *J Child Neurol* 1999;14:139–43
111. Baydur A, Kanel G: Tracheobronchomalacia and tracheal hemorrhage in patients with Duchenne muscular dystrophy receiving long-term ventilation with uncuffed tracheostomies. *Chest* 2003;123:1307–11
112. Biering-Sorensen M, Biering-Sorensen F: Tracheostomy in spinal cord injured: Frequency and follow up. *Paraplegia* 1992;30:656–60
113. Ishikawa Y, Miura T, Aoyagi T, et al: Duchenne muscular dystrophy: Survival by cardio-respiratory interventions. *Neuromuscul Disord* 2011;21:47–51
114. Bach JR: A comparison of long-term ventilatory support alternatives from the perspective of the patient and care giver. *Chest* 1993;104:1702–6
115. Epstein SK: Late complications of tracheostomy. *Respir Care* 2005;50:542–9
116. Sancho J, Servera E, Vergara P, et al: Mechanical insufflation-exsufflation vs. tracheal suctioning via tracheostomy tubes for patients with amyotrophic lateral sclerosis: A pilot study. *Am J Phys Med Rehabil* 2003;82:750–3
117. Bach JR, Niranjan V, Weaver B: Spinal muscular atrophy type 1: A noninvasive respiratory management approach. *Chest* 2000;117:1100–5
118. Bach JR, Saltstein K, Sinquée D, et al: Long-term survival in Werdnig-Hoffmann disease. *Am J Phys Med Rehabil* 2007;86:339–45. quiz 346–8, 379
119. Albert SM, Murphy PL, Del Bene ML, et al: Prospective study of palliative care in ALS: Choice, timing, outcomes. *J Neurol Sci* 1999;169:108–13
120. Kuhnlein P, Kubler A, Raubold S, et al: Palliative care and circumstances of dying in German ALS patients using non-invasive ventilation. *Amyotroph Lateral Scler* 2008;9:91–8
121. Kwiecinski H: [Symptomatic treatment and palliative care of ALS]. *Neurol Neurochir Pol* 2001;35:51–9
122. Laaksovirta H: [Palliative care tailored according to the symptoms of the ALS patient is an art form]. *Duodecim* 2005;121:220–4
123. Zimmerman EK, Eslinger PJ, Simmons Z, et al: Emotional perception deficits in amyotrophic lateral sclerosis. *Cogn Behav Neurol* 2007;20:79–82
124. Blackhall LJ: Amyotrophic lateral sclerosis and palliative care: Where we are, and the road ahead. *Muscle Nerve* 2012;45:311–8