ORIGINAL ARTICLE

Lower Thoracic Spinal Cord Stimulation to Restore Cough in Patients With Spinal Cord Injury: Results of a National Institutes of Health–Sponsored Clinical Trial. Part I: Methodology and Effectiveness of Expiratory Muscle Activation

Anthony F. DiMarco, MD, Krzysztof E. Kowalski, PhD, Robert T. Geertman, MD, PhD, Dana R. Hromyak, BS

ABSTRACT. DiMarco AF, Kowalski KE, Geertman RT, Hromyak DR. Lower thoracic spinal cord stimulation to restore cough in patients with spinal cord injury: results of a National Institutes of Health–sponsored clinical trial. Part I: methodology and effectiveness of expiratory muscle activation. Arch Phys Med Rehabil 2009;90:717-25.

Objective: Evaluation of the capacity of lower thoracic spinal cord stimulation (SCS) to activate the expiratory muscles and generate large airway pressures and high peak airflows characteristic of cough, in subjects with tetraplegia.

Design: Clinical trial.

Setting: Inpatient hospital setting for electrode insertion; outpatient setting for measurement of respiratory pressures; home setting for application of SCS.

Participants: Subjects (N=9; 8 men, 1 woman) with cervical spinal cord injury and weak cough.

Interventions: A fully implantable electrical stimulation system was surgically placed in each subject. Partial hemilaminectomies were made to place single-disk electrodes in the epidural space at the T9, T11, and L1 spinal levels. A radiofrequency receiver was placed in a subcutaneous pocket over the anterior portion of the chest wall. Electrode wires were tunneled subcutaneously and connected to the receiver. Stimulation was applied by activating a small portable external stimulus controller box powered by a rechargeable battery to each electrode lead alone and in combination.

Main Outcome Measures: Peak airflow and airway pressure generation achieved with SCS.

Results: Supramaximal SCS resulted in high peak airflow rates and large airway pressures during stimulation at each electrode lead. Maximum peak airflow rates and airway pressures were achieved with combined stimulation of any 2 leads. At total lung capacity, mean maximum peak airflow rates and airway pressure generation were 8.6±1.8 (mean ± SE) L/s and 137±30 cmH_2O (mean ± SE), respectively.

Conclusions: Lower thoracic SCS results in near maximum activation of the expiratory muscles and the generation of high peak airflow rates and positive airway pressures in the range of those observed with maximum cough efforts in healthy persons.

Key Words: Cough; Electric stimulation; Quadriplegia; Rehabilitation; Respiratory muscles; Spinal cord injuries.

CERVICAL AND HIGH THORACIC spinal cord injury results in paralysis of the expiratory intercostal and abdominal muscles, the major muscle groups responsible for generating the high positive airway pressures characteristic of a normal cough.[1-3] The ability of patients with SCI to clear airway secretions therefore is markedly impaired, resulting in physical discomfort, inconvenience, and the development of atelectasis and recurrent respiratory tract infections.[4-8] Consequently, these patients are dependent on caregiver assistance for the application of manual suctioning, assisted coughing maneuvers, or other methods of airway management.[9-12] These techniques are generally uncomfortable and cumbersome and often restrict patient mobility. Moreover, despite their use, respiratory tract infections remain a major cause of morbidity and mortality in this patient population.[13-16]

In theory, restoration of expiratory muscle function and thereby an effective cough mechanism would improve life quality, enhance mobility, eliminate the need for artificial methods of secretion clearance, and potentially reduce the incidence of respiratory complications in SCI. Because the neuromuscular apparatus below the level of injury is generally intact, the expiratory muscles are amenable to a variety of

List of Abbreviations

FRC	functional residual capacity
IC	inspiratory capacity
SCI	spinal cord injury
SCS	spinal cord stimulation
TLC	total lung capacity

From the Departments of Physiology and Biophysics (DiMarco, Kowalski, Hromyak) and Neurological Surgery (Geertman), Case Western Reserve University, Cleveland, OH; Division of Neurological Surgery, MetroHealth Medical Center, Cleveland, OH (Geertman).

Presented in part to the Congress of Neurological Surgeons, October 7–12, 2006, Chicago, IL; the American Spinal Injury Association, May 30–June 2, 2007, Tampa, FL; the International Spinal Cord Society, June 27–July 1, 2007, Reykjavik, Iceland; the American Paraplegia Society, August 27–29, 2007, Orlando, FL; the American Academy of Physical Medicine and Rehabilitation, September 27–30, 2007, Boston, MA; the American Thoracic Society, May 16–21, 2008, Toronto, ON, Canada; and the American Spinal Injury Association, August 8–11, 2008, Orlando, FL.

Supported by the National Institute of Neurological Disorders and Stroke (grant no. R01 NS049516) and the National Center for Research Resources (grant no. M01 RR 00080 and UL1 RR024989). **Clinical Trial Registration Number:** NCT00116337.

We certify that we have affiliations with or financial involvement (eg, employment, consultancies, honoraria, stock ownership or options, expert testimony, grants and patents received or pending, royalties) with an organization or entity with a financial interest in, or financial conflict with, the subject matter or materials discussed in the article. Dr. DiMarco is a founder of and has a significant financial interest in Synapse BioMedical, Inc, a manufacturer of diaphragm pacing systems.

Correspondence to Anthony F. DiMarco, MD, MetroHealth Medical Center, Rammelkamp Center for Education and Research, 2500 MetroHealth Dr, Cleveland, OH 44109, email: *afd3@case.edu*. Reprints are not available from the author.

0003-9993/09/9005-00625$36.00/0
doi:10.1016/j.apmr.2008.11.013

stimulation techniques.[3,17-21] Based on previous investigations in animals,[18,22,23] we hypothesized that lower thoracic SCS would result in the generation of high peak airflow rates and large airway pressures in SCI, characteristic of a normal cough.

In this study, we present the results of a clinical trial in which lower thoracic SCS was applied to activate the expiratory muscles in SCI. By this technique, single-disk electrodes are positioned in the dorsal epidural space at the lower thoracic and upper lumbar spinal levels. In this article, the capacity of this technique to activate the expiratory muscles and generate large positive airway pressures and high peak airflow rates is presented. The stimulus-output relationships and effects of stimulation of different electrode combinations are also described. In a companion article,[24] we report the clinical effects of lower thoracic SCS in terms of benefits, risks, and side effects. Preliminary results of this technique were described previously in a case report.[25]

METHODS

This investigation was approved by the Institutional Review Board, the National Institute of Neurological Disorders and Stroke, and the Food and Drug Administration. Informed consent was obtained from each subject before enrollment in the study.

All research subjects had some form of traumatic injury to the cervical spinal cord and were in stable condition at the time of study entrance. None of the subjects had significant lung, cardiac, or brain disease, which represent exclusion criteria. Among the inclusion criteria for study subjects were objective evidence of expiratory muscle weakness and symptoms of an inadequate cough. Each subject had significant paresis of their expiratory muscles as evidenced by markedly reduced peak expiratory airflow rates and maximum expiratory pressures less than 2.5 L/s and 30 cmH_2O, respectively, measured at TLC. In addition, all subjects complained of difficulty coughing and mobilizing secretions.

Electrical Stimulation System

In a single procedure, a fully implantable electrical stimulation system was surgically placed in each subject to activate the expiratory muscles. Each subject underwent partial hemilaminotomies to place three, 4-mm single-lead, platinum-iridium disk electrodes[a] at the T9, T11, and L1 spinal levels (fig 1). Electrodes were positioned in the midline in the epidural space overlying the thecal sac using fluoroscopic guidance. A single-disk, ground electrode (30mm) was placed under the surface of the thoracolumbar fascia. A radiofrequency receiver (7.6×4.6×0.85cm; 12g)[b] was placed in a subcutaneous pocket over the anterior portion of the chest wall, over either the lower rib cage or the upper abdominal wall. The electrode wires were tunneled subcutaneously and connected to the receiver. During electrical stimulation applied in the operating room, contraction of the expiratory muscles was confirmed by visual inspection and palpation of the chest wall.

Postoperatively, stimulation was applied by activating a small portable external control box (9.5×6×2.5cm) connected to a rubberized transmitter, which was secured to the skin with tape directly over the implanted receiver. The stimulus controller box, which is powered by a rechargeable battery, delivers a radiofrequency signal to the implanted receiver, which is converted to an electrical signal that is transmitted to the electrodes (see fig 1). The stimulator provides a biphasic stimulus over a wide range of stimulus amplitudes (10–40V), stimulus frequencies (2–105Hz), and pulse widths (16–800μs). Stimulus on-time could be adjusted between 0.2 and 50s.

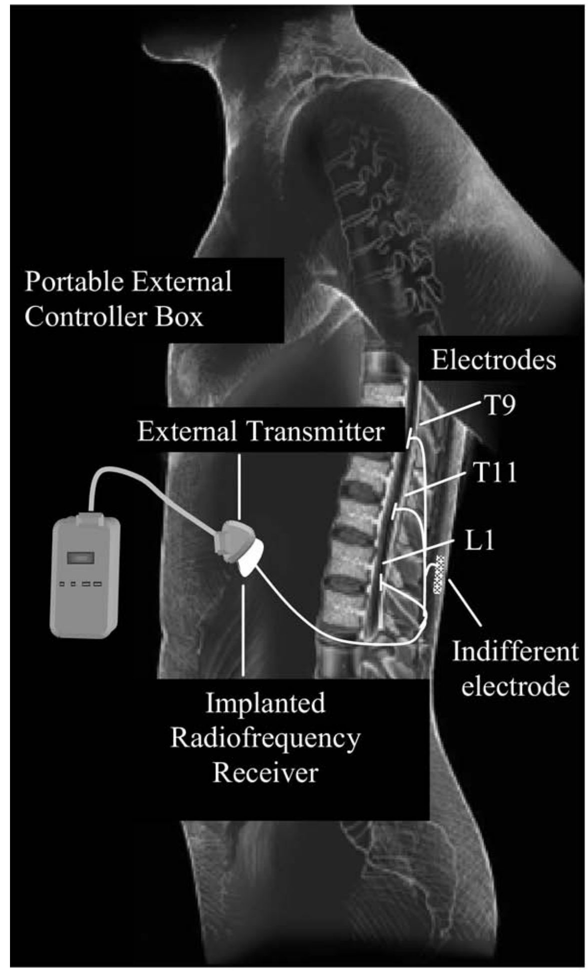

Fig 1. Electrical stimulation system.

Muscle Reconditioning

Prior to use of the cough system, 2 to 3 weeks were allowed to elapse to provide time for regression of edema and hemorrhage at the electrode and receiver sites and healing of all wounds. It was assumed that the expiratory muscles were significantly atrophied secondary to disuse and would require a period of repeated muscle stimulation to restore strength. After an initial evaluation session, subjects were instructed to apply stimulation every 30 seconds for 5 to 10 minutes, 2 or 3 times a day, in the home or nursing home setting. Stimulus parameters were set at values resulting in near maximal positive airway pressure generation, as tolerated, because high intensity force generation for short periods results in the greatest increases in muscle strength.[26-28] Subjects were also instructed to use the device for evacuation of secretions or pharyngeal clearance, as needed.

Measurements

Airway pressure was monitored with a pressure transducer[c] to assess the force of expiratory muscle contraction. Expiratory airflow rates were monitored by use of a heated pneumotachograph.[d] Measurements were made with use of a tight-fitting full face mask or through tracheostomy tube, when present. Subjects with tracheostomies all had cuffless tubes. Dressings