Surface-Evoked Laryngeal Sensory Action Potential Evaluation in Neurogenic Chronic Cough

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Summary: Objectives. Neurogenic chronic cough is currently a diagnosis of exclusion. We hypothesized that surface-evoked laryngeal sensory action potential (SELSAP) testing could be used to help establish a diagnosis of laryngeal sensory neuropathy as a cause of chronic cough, based on altered SELSAP waveform morphology.

Study Design. Retrospective cohort study.

Methods. Laryngeal electromyographic (EMG) data including SELSAP waveform testing from patients with chronic cough were directly compared with a control population without significant laryngeal symptoms, and statistical analysis of unilateral and bilateral neuropathy injury subgroups was performed.

Results. Thirty patients with a chief complaint of chronic cough underwent laryngeal EMG testing since January 2000 with needle EMG and surface nerve conduction studies. SELSAP waveform analysis of unilateral and bilateral laryngeal neuropathy demonstrated significantly lowered median SELSAP peak amplitude compared with controls ($P < 0.01$).

Conclusions. Patients with suspected neurogenic chronic cough demonstrate statistically significant alterations in SELSAP waveform that can support a diagnosis of laryngeal sensory neuropathy.

Key Words: Laryngeal EMG–Chronic cough–SELSAP–Neuropathy–Evoked potential–Neurogenic.

INTRODUCTION

Patients with chronic cough present a diagnostic and therapeutic challenge to the otolaryngologist.[1] Chronic cough is defined as a cough with a duration of greater than 8 weeks, and it is one of the most common reasons for specialist referral in current medical practice.[2,3] Chronic cough can be induced by a wide variety of causes affecting multiple different physiological and sensory pathways including upper airway cough syndrome, cough-variant asthma, gastroesophageal reflux disease (GERD), or laryngopharyngeal reflux.[2,4] Published guidelines exist that delineate possible approaches for the management of these challenging patients.[2,3,5] Proper diagnosis is crucial in developing an effective treatment protocol for chronic cough.[6] Studies have shown that up to 42% of patients with chronic cough will not improve despite extensive workup and directed therapy.[1] These patients often undergo frequent radiologic examinations, receive numerous pharmacologic interventions, and endure multiple specialist referrals without successful diagnosis and treatment of their cough.[7] Treatment failure for patients with chronic cough is associated with a significantly impaired health-related quality of life,[8] and many of these patients suffer from chest wall pain, stress-related urine incontinence, sore throat, dysphonia, and social embarrassment. It also has an adverse impact on their family and partners.[1] It is therefore imperative that better directed therapies and testing for various cough etiologies be developed.

Neurogenic chronic cough (NCC) has emerged as a possible diagnosis for this challenging population.[7,9,10] Cranial neuropathies are known to lead to deranged motor and sensory function in multiple head and neck disease states such as Bell's palsy, trigeminal neuralgia, and glossopharyngeal neuralgia.[11] Similar involvement of the internal branch of the superior laryngeal nerve (SLN) may lead to laryngeal sensory neuropathy and subsequent induction of NCC.[10] NCC is typically suspected in patients with chronic cough after multiple common etiologies of cough have been excluded including lack of tobacco use history and a negative chest X-ray. Diagnosis of NCC is supported by a thorough history and careful physical examination.[12] Laryngeal sensory neuropathy may occur after viral infection, chemical inhalation, or after sources of mechanical trauma to the vagus or SLN.[13] It is often accompanied by motor neuropathy as evidenced by subtle vocal fold paresis, but determination of altered SLN function on videostroboscopy remains challenging.[14,15] Many patients with NCC will respond to neuromodulatory medications, drawing parallels between chronic cough and other chronic neuropathies such as chronic pain syndromes.[13] Despite increasing evidence of NCC in clinical practice and published literature, few modalities for diagnosing NCC beyond physical examination exist.[16] NCC continues to be a diagnosis of exclusion,[14] and treatment is empiric.[2,3,5,17]

Laryngeal sensory nerve function can be tested using laryngeal surface-evoked potentials to detect conduction along the internal branch of the SLN, termed surface-evoked laryngeal sensory action potential (SELSAP) testing.[18] The SELSAP technique involves transcutaneous stimulation of the SLN through noninvasive surface cathodes placed adjacent to the mastoid prominence, with evoked potential measurement

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at test electrodes placed at the level of the cricothyroid membrane, following the path of the internal branch of the SLN. Previous work has shown that patients with documented videostroboscopic and needle electromyographic (EMG) evidence of laryngeal motor neuropathy had statistically significant and reproducible differences in SELSAP waveform parameters, including baseline-to-peak amplitude, conduction velocity, and intrasubject side-to-side amplitude ratio.[18] We hypothesize that SELSAP testing will demonstrate altered sensory-evoked potential waveform morphology in patients with NCC compared with normal controls, enabling objective confirmation of this challenging diagnosis. In this study, we present a series of patients who were referred for EMG testing for chronic cough to evaluate the role of SELSAP testing in diagnosis of NCC.

MATERIALS AND METHODS

Patient selection

The institutional review board of the Medical College of Wisconsin approved this research protocol. All patients from our institution who were referred for neurologic examination and laryngeal EMG specifically for chronic cough were identified between January 2000 and December 2009. All patients received both SELSAP and bipolar concentric needle laryngeal EMG testing using standard techniques. Inclusion criteria included patients older than 18 years, cough of at least 8 weeks' duration, and completed EMG evaluation done explicitly for cough of unknown etiology. Patients with a previously identified nonneurogenic etiology for their cough and those with a primary lung or head and neck malignancy were excluded. Patient medical records were reviewed for demographic information, disease presentation and duration, medical history, medications, videostroboscopy examination results, imaging, and treatment when available. Videostroboscopy information was obtained from review of medical records (KayPENTAX VNL-1170K and digital videostroboscopy system 9295; Kay Elemetrics Corp, Montvale, NJ). Control population data for the SELSAP waveform morphology were taken from previous works.[18] Control patients were selected for these studies without significant history of laryngeal symptoms, denying dysphonia, dysphagia, cough, throat clearing, or globus, and videostroboscopy showed no evidence of apparent vocal fold paralysis or paresis.

Electrophysiologic technique

All patients underwent bipolar concentric needle EMG via standard technique. SELSAP testing techniques were presented in detail previously.[18] Briefly, surface stimulation of the vagus nerve was performed over the mastoid tip, 7–10 cm proximal to paired surface electrodes placed over the cricothyroid membrane 1.5 cm off midline using bipolar stimulation with current duration of 0.01–0.02 milliseconds (Figure 1). An averaging technique was used when necessary, incorporating between six and 10 tracings. All electrophysiologic studies were performed using a Nicolet Viking IV EMG machine (Nicolet Biomedical, Inc, Madison, WI). Control values for SELSAP waveform morphology comparison of patients with chronic cough were used from the previously published and established normal ranges.[18]

Statistics

Stata software (StataCorp LP, College Station, TX) was used for all statistical analysis. SELSAP waveform amplitudes and amplitude ratios were reviewed with scatter plots and paired coordinate plots before any statistical tests were performed. Patients with bilateral injury patterns had an averaged value determined for peak amplitude by taking a mean value between both sides of the neck and then taking a group mean value for pooled data. Values for control, unilateral, and bilateral injury patients are presented as mean values ± standard deviation. Differences between the involved and uninvolved sides in the unilateral injury patient group were evaluated by a paired t test. Group differences in mean amplitude ratios were evaluated by a t test with unequal variances. Statistical significance between experimental groups was set at $P < 0.01$ unless otherwise stated.

RESULTS

Thirty patients were identified with chronic cough who were referred for laryngeal EMG testing since January 1, 2000 (Table 1). There were nine male and 21 female patients, with an average age of 56.3 years and an age range from 18 to 78 years. All patients had chronic cough with the duration of cough greater than 8 weeks. Eighteen patients had concurrent laryngeal symptoms including hoarseness, throat pain, throat clearing, dysphonia, or dysphagia. Thirteen of 30 patients (43%) had a prior clinical diagnosis of GERD, and 19 patients (61.3%) were either currently taking or had failed a trial of

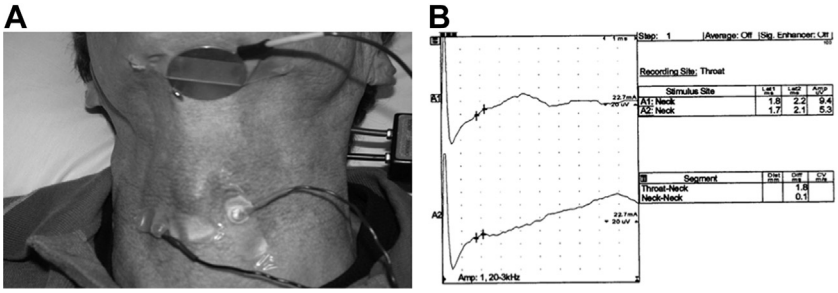

FIGURE 1. Demonstration of SELSAP testing. (**A**) Surface electrode placement and stimulus localization for eliciting SELSAP response. (**B**) Representative SELSAP tracing showing normal range peak amplitude in upper (A1) tracing and flattened peak amplitude in lower (A2) tracing.[18]