*The Laryngoscope*


# Treatment of Chronic Neurogenic Cough With In-Office Superior Laryngeal Nerve Block

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**Objectives:** Neurogenic cough is believed to result from a sensory neuropathy involving the internal branch of the superior laryngeal nerve (SLN). We present our outcomes for the treatment of neurogenic cough with localized blockade of the internal branch of the SLN.

**Methods:** A retrospective chart review of patients who underwent in-office percutaneous SLN block for treatment of neurogenic cough between 2015 and 2017 was conducted. Patient demographics, indications for injection, and response to treatment were recorded and analyzed. Cough severity index (CSI) scores before and after treatment were compared.

**Results:** Twenty-three patients underwent percutaneous blockade of the internal branch of the SLN in the clinic setting, and five patients were excluded for incomplete records. The indication was neurogenic cough as a diagnosis of exclusion. The injectable substance used was a 1:1 mixture of a long-acting particulate corticosteroid and a local anesthetic. Unilateral injections were performed in 13 patients, and five patients underwent bilateral injections. Of the unilateral injections, 10 were left-sided. Patients underwent an average of 2.4 SLN block procedures (range 1–7). Mean follow-up time postinjection was 85.4 days (7–450 days). Cough severity index scores decreased significantly from an average of 26.8 pretreatment to 14.6 posttreatment ($P < 0.0001$).

**Conclusion:** The SLN block is an effective treatment for neurogenic cough, with average CSI scores significantly improved following injection. Further study is necessary to determine the characteristics of patients' responses to treatment, long-term outcomes, and efficacy of the procedure when compared to placebo and other accepted treatments for neurogenic cough.

**Key Words:** Chronic cough, neurogenic cough, peripheral neuropathy, outcomes, quality of life.

**Level of Evidence:** 4.

***Laryngoscope*, 128:1898–1903, 2018**

## INTRODUCTION

Cough is one of the most common reasons that patients seek medical attention in the United States, accounting for more than 30 million physician visits each year.[1] A chronic cough is defined as a cough that persists for more than 8 weeks; it has a world-wide prevalence of 9.5% in the adult population.[2] The three most common causes of persistent cough in the adult population are cough-variant asthma, gastroesophageal reflux disease (GERD), and upper airway cough syndrome.[3] These etiologies are typically explored and empirically treated in patients with chronic cough.

Neurogenic cough is a diagnosis of exclusion applied to persistent cough with a negative workup for other common causes, including upper airway cough syndrome, cough-variant asthma, and GERD. Neurogenic cough has been attributed to a laryngeal hypersensitivity resulting from postviral neural damage to the internal branch of the superior laryngeal nerve (SLN).[4,5] The internal branch of the SLN enters the thyrohyoid membrane just superior to the superior laryngeal artery. It divides into an upper and lower branch and provides general sensation (pain, touch, temperature) above the level of the true vocal folds. The upper branch supplies the inferior pharynx, epiglottis, vallecula, and laryngeal vestibule. The lower branch supplies the aryepiglottic folds and the false vocal folds.[6] The cough is typical triggered by activities or actions that stimulate the larynx, such as talking, laughing, singing, swallowing, temperature changes, position changes, or external stimulation of the neck.[7] Patients may describe a foreign body sensation or irritation in the throat that precedes or accompanies the cough. Objectively, videostroboscopy may demonstrate vocal fold paresis if the motor branch of the recurrent laryngeal nerve is involved.[8]

The mainstays of treatment for neurogenic cough are respiratory retraining therapy and neuromodulating

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Editor's Note: This Manuscript was accepted for publication on March 5, 2018.

A portion of this data was presented as an oral presentation at the Fall Voice Conference in Scottsdale, Arizona, U.S.A., in October 2016.

Financial Disclosure: The authors have no funding, financial relationships, or conflicts of interest to disclose.

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**DOI: 10.1002/lary.27201**

medications.[4] Respiratory retraining therapy is noninvasive and has been shown to be an effective treatment modality for chronic cough in a placebo-controlled study.[9] However, patients may be unable to pursue therapy due to cost, time constraints, or distance to an appropriate speech language pathologist. Multiple neuromodulating medications have been shown to be beneficial in the treatment of neurogenic cough, including amitriptyline, $\gamma$-aminobutyric acid (GABA) analogs (gabapentin and pregabalin), and the GABA agonist baclofen.[4] Although these medications may be effective in controlling neurogenic cough, they often require titration and some patients are unable to tolerate their side effects. The cost of these medications may be prohibitive as well.

Therapeutic nerve blocks with corticosteroid or local anesthetic are a well-established treatment for peripheral neuropathies.[10] The SLN entry point in the thyrohyoid membrane is easily identified and accessed in most patients. We describe our technique and outcomes in patients treated with SLN block with local anesthetic and long-acting particulate corticosteroid for chronic cough. We hypothesize that chronic cough in a subset of patients represents a hypersensitivity or neuropathy of the SLN, and that targeted blockade of the nerve will result in an improvement in symptoms.

## MATERIALS AND METHODS

### Patient Cohort and Procedure

Under an institutional review board-approved protocol, the medical records of adult patients treated at our institution with SLN block for chronic cough between 2015 and 2017 were reviewed. Patients were identified via a search of electronic medical records for the Current Procedural Terminology code for vagal nerve block (64408). Patients included in the study had complete medical records, including follow-up after the procedure and pre- and posttreatment cough severity index (CSI) questionnaire scores. Patients excluded had incomplete medical records and/or additional medical comorbidities that could potentially account for their cough. Patients previously started on and concurrently taking neuromodulating medications (amitriptyline, gabapentin, pregabalin, and baclofen) as treatment for their cough were not excluded.

The SLN block was performed in the clinic setting with the patient seated upright in the examination chair. Two milliliters of a 50:50 solution of a long-acting particulate steroid (triamcinolone acetonide 200 mg/5 mL or methylprednisolone 80 mg/1 mL) and a local anesthetic (1% lidocaine with 1:100,000 epinephrine or 0.5% bupivacaine) were injected at the entry point of the internal branch of the SLN in the posterior thyrohyoid membrane via a 27-gauge needle. The volume of injectable material was chosen based on volume used for nerve blocks elsewhere in the body, as described in the pain management literature.[11,12] The choice of particulate steroids was also based on existing literature assessing their efficacy when used for nerve blocks.[13] The superior thyroid tubercle and the greater horn of the hyoid bone were used as landmarks to identify the entry point. Some patients were found to have a trigger point over the thyrohyoid space, palpation of which triggered discomfort or cough. The injection was directed toward this trigger point in those patients. In patients without a trigger point, the injection was directed toward the posterior thyrohyoid (TH) membrane. This location was chosen in order to expose the nerve to the injectable material along its entire course over the TH membrane as it runs from the posterior aspect of the membrane toward its slightly more anterior entry point. Staged bilateral injections were performed if the patient had trigger points bilaterally. If no trigger point or laterality of symptoms was detected, one side was arbitrarily chosen for the block. In patients who did not respond to the initial block, a contralateral SLN block was offered at the return visit 2 weeks later. Concurrent bilateral blocks were not performed in order to prevent dysphagia and/or aspiration due to the potential for sensory alteration of the pharynx and larynx. Superior laryngeal nerve blocks were repeated as needed in patients who had improvement in their cough but experienced only transient relief.

### Data Collected, Outcomes Measured, and Statistical Analysis

Existing medical records were reviewed, along with data pertaining to patient demographics, previous or concurrent treatment for chronic cough, indications for SLN block procedure, and CSI scores before and after treatment. The number of SLN block procedures, laterality, and injectable substances used were recorded as well. Prism 7.0 (GraphPad Software, La Jolla, CA) was used for statistical analysis, with parametric values analyzed using the paired Student $t$ test.

## RESULTS

A total of 23 patients underwent SLN block for treatment of chronic cough at our institution between 2015 and 2017. Eighteen patients had complete medical records and were included in the analysis. Table I displays the demographics, procedure details, pre- and posttreatment CSI scores, and length of follow-up for these patients. The indication for all injection was chronic cough, deemed to be neurogenic based on previous negative workup. The mean age of the patient population was 60 years (range 29–86 years), and 15 patients were female (83%). The mean duration of cough prior to initial SLN block procedure was 84.5 months (range 3–240 months). Two patients had a relatively short duration of symptoms prior to presentation at our institution (3 and 4 months), but they had failed other empiric therapies and had histories and symptoms consistent with a neurogenic etiology of cough. The remainder of patients who underwent SLN block for treatment of their cough reported symptoms for at least 60 months. The vast majority of patients (16 of 18) had previously been treated for all three of the typical contributors to chronic cough: atopic disease, asthma, and GERD. This included failed empiric trials of steroid inhalers, prolonged (greater than 2 months) acid suppression with proton pump inhibitors ± blockers, fundoplication for treatment of GERD, immunotherapy, and antihistamines/nasal steroids. Six patients had been treated previously with neuromodulating medications without benefit (gabapentin, pregabalin, amitriptyline, baclofen). Four patients were taking neuromodulating medications prior to the SLN block and continued this treatment (amitriptyline: 3 patients; amitriptyline and gabapentin: 1 patient) during the postprocedure period. The dosages of these medications were not altered immediately prior to or after the

TABLE I.
Patients Who Underwent SLN Block for Treatment of Chronic Cough

| Patient No. | Sex | Age (Years) | Steroid/ Anesthetic Injected | Number of Blocks | Unilateral/ Bilateral | Cough Improved (Y/N) | Pre-CSI | Post-CSI | Neuromodulator (Y/N) | Follow-up (days) |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | F | 57 | TA/LE | 2 | Bilateral | N | 22 | 21 | N | 86 |
| 2 | F | 56 | TA/LE | 1 | Unilateral | N | 33 | 32 | N | 46 |
| 3 | F | 86 | TA/B | 1 | Unilateral | N | 16 | 15 | N | 14 |
| 4 | F | 29 | TA/LE | 1 | Unilateral | Y | 29 | 8 | N | 23 |
| 5 | M | 75 | TA/LE | 1 | Unilateral | Y | 25 | 17 | N | 21 |
| 6 | F | 55 | TA/B | 1 | Unilateral | Y | 19 | 0 | N | 7 |
| 7 | F | 71 | TA/LE | 1 | Unilateral | Y | 36 | 31 | N | 139 |
| 8 | M | 68 | TA/LE | 1 | Unilateral | Y | 38 | 34 | N | 35 |
| 9 | F | 59 | TA/LE | 1 | Unilateral | Y | 30 | 27 | N | 35 |
| 10 | F | 70 | TA/B | 1 | Unilateral | Y | 27 | 24 | N | 21 |
| 11 | F | 68 | TA/B | 1 | Unilateral | Y | 27 | 6 | N | 14 |
| 12 | F | 48 | TA/LE<br>MP/B<br>MP/B<br>TA/B × 3 | 6 | Unilateral | Y | 34 | 15 | Y | 450 |
| 13 | F | 37 | TA/B | 7 | Bilateral | Y | 40 | 13 | N | 103 |
| 14 | F | 66 | TA/LE TA/ B × 5 | 6 | Bilateral | Y | 26 | 0 | N | 178 |
| 15 | F | 63 | TA/LE | 2 | Bilateral | Y | 10 | 0 | N | 85 |
| 16 | F | 53 | TA/B × 2<br>TA/LE | 3 | Bilateral | Y | 17 | 0 | Y | 60 |
| 17 | F | 72 | TA/B | 6 | Unilateral | Y | 23 | 16 | Y | 150 |
| 18 | M | 45 | TA/B | 2 | Unilateral | Y | 30 | 3 | Y | 70 |
| | | Mean 60 | | Mean 2.4 | | | Mean 26.8 | Mean 14.6 | | Mean 85.4 |

Patients 1–3 were nonresponders who reported no improvement with SLN block; patients 4–11 reported lasting improvement after a single SLN block; and patients 12–18 reported transient improvement after SLN block and underwent multiple blocks for management of their cough. For patients who underwent multiple injections, the CSI score at the most recent follow-up visit was used in the analysis.

B = 0.5% bupivacaine; CSI = cough severity index; F = female; LE = 1% lidocaine with 1:100,000 epinephrine; M = male; MP = methylprednisolone 80 mg/cc; N = no; SLN = superior laryngeal nerve; TA = triamcinolone acetonide 200 mg/5 mL; Y = yes.

SLN block procedure, making the procedure the only new addition to their treatment for chronic cough.

Fifteen patients (83.3%) reported an improvement in their cough with the SLN block procedure. The patients who reported benefit with the injection noticed improvement in their cough approximately 2 to 4 days after the procedure. Unilateral injections were performed in 13 patients, and five patients underwent bilateral injections. Of the unilateral injections, 10 were left-sided. Eight patients underwent a single block with improvement in symptoms and did not pursue further injections. Seven patients who noted improvement in their cough underwent multiple blocks, and four of these patients underwent staged bilateral procedures. Overall, patients underwent an average of 2.4 SLN block procedures (range 1–7). Those who pursued multiple blocks underwent a mean of 4.6 procedures (range 2–7) at mean intervals of 41.5 days. Mean follow-up time after the initial procedure was 85.4 days (7–450 days). The injectable substance used was a 1:1 mixture of a long-acting corticosteroid (triamcinolone acetonide 200 mg/5 mL or methylprednisolone 80 mg/1 mL) and a local anesthetic (1% lidocaine with 1:100,000 epinephrine or 0.5% bupivacaine). Cough severity index questionnaire scores were obtained for all patients at initial presentation and at the most recent follow-up visit. There was a statistically significant decrease in CSI scores after treatment, with a mean of 26.8 at presentation decreasing to 14.6 at follow-up (mean improvement 12.22; 95% confidence interval (CI), 7.38–17.07; $P < 0.0001$). When controlling for those patients who concurrently took a neuromodulating medication to help manage their cough by excluding them from the statistical analysis, the CSI improvement remained significant (mean improvement in CSI of 10.71; 95% CI, 5.02–16.41; $P = 0.0013$). Figure 1 depicts the changes in pre- and posttreatment CSI scores. One patient experienced a brief self-limited episode of laryngospasm immediately after injection, and two patients noted transient throat anesthesia or paresthesia; otherwise, there were no complications. No patients developed clinical symptoms or signs of dysphagia or aspiration, and none developed swelling or fluctuance in the location of injection.

## DISCUSSION

Chronic cough is a complaint commonly encountered by general otolaryngologists, laryngologists, and

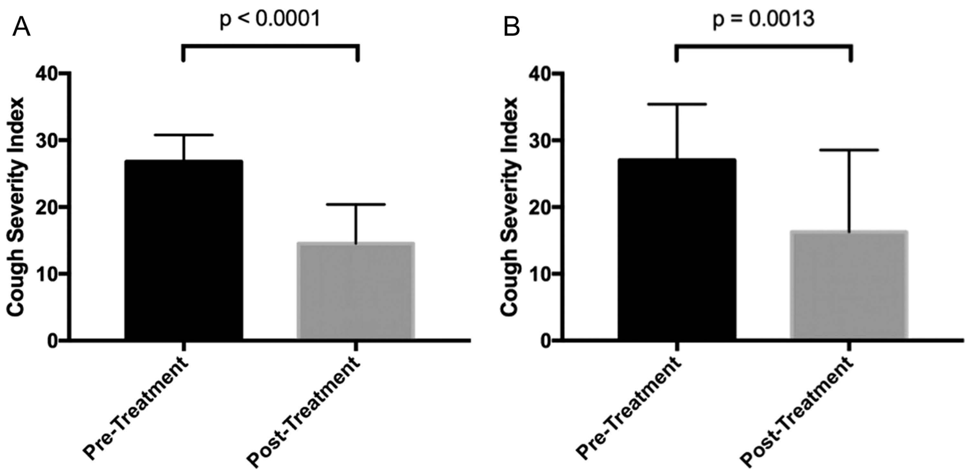


Fig. 1. (A) Bar graph depicting pre- and posttreatment CSI scores for patients who underwent superior laryngeal nerve block for treatment of chronic cough. (B) Pre- and post-treatment CSI scores with patients concurrently taking neuromodulating medications excluded from the analysis.
CSI = cough severity index.

speech language pathologists. It may be frustrating to both patients and clinicians in that many patients have seen multiple physicians and attempted various treatments without improvement in their symptoms. Many patients find their cough debilitating, and it significantly impacts their quality of life. Neurogenic cough may be suspected when the most common etiologies of chronic cough have been ruled out and conventional treatments fail to provide relief. Current accepted treatments for neurogenic cough attempt to target the sensory input involved in triggering cough. Respiratory muscle retraining therapy aims to reduce the force of oropharyngeal musculature during inspiration by increasing abdominal muscle involvement.[14] This has been shown to normalize aberrant laryngeal sensation in patients with chronic cough and paradoxical vocal fold mobility disorder.[15] Neuromodulating medications likely improve cough symptoms by acting on aspects of the neural cough pathway as well. Amitriptyline inhibits norepinephrine and serotonin reuptake, which is thought to reduce the cough reflex by reducing the sensory threshold of afferent nerve fibers.[16,17] GABA analogs (gabapentin and pregabalin) inhibit voltage-gated calcium channel release of excitatory neurotransmitters. These medications are typically used to treat neuropathic pain,[18] and their effect on neurogenic cough is presumably mediated through the same mechanism. Baclofen, a GABA agonist, presumably inhibits cough through the same mechanism[19] and has also been shown to inhibit the cough reflex in animals via a central pathway.[20]

We hypothesize that the SLN block alters sensory feedback via the SLN, resulting in a disruption of the cough signaling pathway. In the pain management literature, localized nerve blocks are a well-established treatment for peripheral neuropathies.[10,21] The SLN entry point in the thyrohyoid membrane is easily identified and accessed in the majority of patients, making it ideal for localized blockade. Data from this study demonstrate a high success rate for the procedure, with a statistically significant improvement in CSI being observed for the population after treatment. Although some patients were concurrently taking neuromodulating medications, the improvement in CSI scores was still statistically significant when controlling for this. The preexisting dosages of these medications were not altered prior to the SLN block procedure or in the postprocedure period, making the SLN block the only new treatment modality introduced for these patients. The fact that the patients who remained on neuromodulators responded to the SLN block suggests that this is a viable treatment in patients who are currently taking these medications. From this preliminary study, there appear to be three major categories of patient responses to the SLN block (Table I): 1) nonresponders who receive no benefit (3 of 18, 17%) after one or two procedures and who did not wish to pursue additional blocks, 2) initial complete responders who have lasting improvement after one SLN block (8 of 18, 44%), 3) and temporary responders who experience an improvement in cough but require periodic repeat injections (39%, 7 of 18). The temporary responders who underwent multiple SLN blocks did so at mean intervals of 41.5 days. Patients who required repeat injections typically reported a return of cough at intervals ranging from 2 weeks to 3 months. Given that some planned staged injections were given and that patients did not keep daily diaries of their cough symptoms, we are not able to give an exact range of the length of efficacy of the injections. Further study may help elucidate other characteristics or predictive factors pertaining to these groups of responders, but current data will help guide the expectations of patients undergoing the procedure.

The SLN block procedure has several advantages: It is a low-cost procedure that requires materials readily available in most clinic settings. It is also noninvasive, takes only minutes to complete, and reported side effects were mild and transient. Our data suggest a high success rate, with only three of 18 patients reporting no improvement in their symptoms after the procedure. Many patients in this study noted lasting improvement after a single SLN block procedure. Perhaps most importantly, the SLN block avoids the potential side effects of neuromodulators. Commonly reported side effects of these medications include dry mouth, dizziness, somnolence, sedation, confusion, nausea, blurred vision, headache, and memory loss.[4] These may be intolerable for some patients and lead them to discontinue an otherwise effective therapy. The cost of these medications may be prohibitive as well. Given the ease of the procedure as well as the low cost and associated risk, there is very little downside to a trial SLN block in patients with neurogenic cough.

Disadvantages of the SLN block procedure include minor pain and discomfort during the injection, although most patients tolerated the procedure very well. Some patients, however, may not wish to undergo a procedure for treatment of a benign condition. The potential need for repetition in some patients is another drawback. There is also a theoretical risk of blindness or stroke due to embolization of particulate steroids into the arterial circulation. Although the authors have not encountered this complication with the SLN block, it has been reported with injection of both methylprednisolone and triamcinolone elsewhere in the head and neck.[22] The particles in these steroids range from 1 to 1,000 $\mu$m,[23] large enough to cause occlusion of cerebral vasculature. Sublingual nitroglycerin may be effective in treating this potential complication.[24] Drawing back on the syringe to ensure that the needle is not within a blood vessel and injecting slowly are techniques that may be used to prevent this complication. Slow injection is likely the most crucial because embolization into the cerebral or ophthalmic vasculature would require some force to result in retrograde flow from the external carotid system (superior thyroid artery and superior laryngeal artery, both located near the SLN entry point in the thyrohyoid membrane) into the internal carotid system via the common carotid.

Additional procedures for chronic cough that potentially target the sensory pathway have been described. Sasieta et al. treated 22 patients with chronic cough with laryngeal botulinum toxin A injections. Eleven patients reported greater than 50% improvement in their cough at follow-up. The authors hypothesized that the effect may be due to attenuation of capsaicin and C-fiber–mediated nociception (cough receptors), leading to desensitization of the cough pathway.[25] Crawley et al. performed injection augmentation of the vocal folds in patients with chronic cough. The authors reported an improvement in cough in five of six patients who underwent treatment and proposed that alteration of the laryngeal sensory signaling pathway may account for the improvement in symptoms. They also hypothesized that correction of glottic insufficiency and reduction in laryngeal trauma may also play a role.[26] Similar to these procedures, we hypothesize that the efficacy of the SLN block is due to alteration of the sensory input that leads to the cough reflex.

This study is limited primarily by its retrospective nature. Procedure protocols and follow-up were not standardized, and some patients had difficulty recalling the onset of and duration of symptom improvement. Because this study was not a prospective placebo-controlled trial, we cannot exclude the placebo effect as a cause of symptomatic improvement in patients who underwent SLN block. Future studies will address this potential influence. The small sample size is limiting as well. A larger study would better elucidate the onset and efficacy of the SLN block, as well as better define the characteristics of patients who do and do not respond to treatment. Future study is necessary to determine the efficacy of injection of a steroid or local anesthetic alone, as well as if there exists variability in response that is related to the amount of material injected. Two milliliters were chosen as the injection amount based on volumes used for nerve blocks elsewhere in the body.[11,12] Particulate steroids were chosen because they have been shown to be more effective than nonparticular steroids for transforaminal nerve root blocks,[13] but future studies could also investigate whether nonparticulate steroids might be effective when used for SLN blockade.

## CONCLUSION

The SLN block is an effective, low-risk, and low-cost in-office treatment for neurogenic cough. Eighty-three percent of patients reported subjective improvement in their cough, and average CSI scores were significantly improved following injection. Further study is necessary to determine the characteristics of patients' responses to treatment, long-term outcomes, and efficacy of the procedure when directly compared to placebo and other accepted treatments for neurogenic cough.


### Acknowledgment

The authors would like to acknowledge Jacob. B. Hunter, MD, for his assistance with the statistical analysis.


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