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Co-Prevalence of Tremor with Spasmodic Dysphonia: A Case-Control Study:

Co-morbid tremor in Spasmodic Dysphonia

Laura White[1], **Adam Klein, MD**[2], **Edie Hapner, PhD**[2], **John Delgaudio, MD**[2], **John Hanfelt, PhD**[3], **H. A. Jinnah, MD, PhD**[4], and **Michael Johns III, MD**[5]

[1] Emory University School of Medicine, 1648 Pierce Drive, Atlanta, GA 30322

[2] Emory University Department of Otolaryngology, The Emory Voice Center, Medical Office Tower, 9th Floor, 550 Peachtree Street, Atlanta, GA 30308

[3] Rollins School of Public Health, Department of Biostatistics, 1518 Clifton Road NE, Room 314, Atlanta, GA 30322

[4] Emory University Departments of Neurology, Human Genetics & Pediatrics, Woodruff Memorial Building Suite 6305, 101 Woodruff Circle, Atlanta, GA 30322

Abstract

OBJECTIVES/HYPOTHESIS—The aim of this study was to define the co-prevalence of tremor with spasmodic dysphonia (SD).

STUDY DESIGN—A single institution prospective, case-control study was performed from May 2010 to July 2010.

METHODS—Consecutive patients with SD (cases) and other voice disorders (controls) were enrolled prospectively. Each participant underwent a voice evaluation and an evaluation for tremor.

RESULTS—146 voice disorder controls and 128 patients with SD were enrolled. 26% of patients with SD had vocal tremor, 21% had non-vocal tremor. Patients with SD were 2.8 times more likely to have co-prevalent tremor than the control group (OR = 2.81; 95% CI, 1.55 to 5.08) and only 35% of patients with SD had been seen by a neurologist for the evaluation of dystonia and tremor.

CONCLUSIONS—Tremor is highly prevalent in patients with SD. It is important for each patient diagnosed with SD to undergo an evaluation for tremor, this is especially important in patients diagnosed with vocal tremor. Level of evidence 3b.

Keywords

Spasmodic dysphonia; vocal tremor; tremor

[5]Corresponding Author. Emory University Department of Otolaryngology, The Emory Voice Center, Medical Office Tower, 9th Floor, 550 Peachtree Street, Atlanta, GA 30308. Michael.m.johns@emoryhealthcare.org. P: 404-686-1859, F: 404-686-4699.

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Introduction

Spasmodic dysphonia (SD) is a rare phonatory disorder of unknown pathogenesis. It is a type of dystonia that affects the laryngeal muscles causing involuntary and sustained muscle contractions. Patients suffer from voice breaks and a strained/strangulated voice. Other actions such as swallowing and singing are usually unimpeded. Current treatments provide only temporary relief of symptoms.

Patients with SD are at approximately a 7% risk of spread of dystonia to another body part.[1] Additionally, the co-prevalence of clinically significant vocal tremor in patients with SD has been reported to be approximately 25%, which is significantly higher than in the general population. [2,3,4] Several recent studies have described mild attentional defects and executive dysfunction accompanying essential tremor. [5] Although there is no cure for tremor, pharmacologic therapy is available and patients often show significant functional improvement. [6] Neurologists most commonly provide this evaluation and pharmacologic treatment. Therefore, recognition of co-morbid tremor and additional dystonias and subsequent referral to a neurologist for further management is warranted.

Materials and Methods

The study employed a case-control design. Between May and July 2010, 130 consecutive patients with SD and 157 consecutive patients with voice disorders were enrolled prospectively from a referral academic laryngology practice. Both new and returning patients were included. Emory University Institutional Review Board approval was obtained. Volunteers signed a written consent form prior to study participation. All patients were diagnosed with primary SD (with or without vocal tremor) after a comprehensive speech and voice evaluation, including standardized vocal tasks (running speech and sustained vowels) and videolaryngostroboscopy by both a fellowship trained laryngologist and a speech-language pathologist who specialized in voice disorders and have experience in voice disorder assessment and management.

Vocal tremor and non-vocal palatal and pharyngeal wall tremor were documented at the time of diagnosis. Exclusion criteria for the patients with voice disorders included: voice disorder due to malignancy, voice disorder due to a neurological condition, or chief complaint other than voice disorder. Exclusion criteria for the patients with SD included generalized dystonia and any secondary forms of dystonia that may have included SD.

On enrollment, patients were asked to fill out a questionnaire that reviewed the duration of their voice disorder, past diagnosis of tremor, and if they had ever been evaluated by a neurologist. Each participant was evaluated for tremor in other body parts including the head/neck, tongue, arms, hands, trunk, and legs. Tremor in any of these body parts was categorized as non-vocal tremor. Our goal was to determine the co-prevalence of vocal and non-vocal tremor in patients with SD as compared to patients with other voice disorders in a treatment-seeking population from the same clinic. An additional goal was to determine the percentage of patients with SD who had been evaluated by a neurologist. To compare the two groups, t-tests for the quantitative outcome variables and Pearson chi-square tests for the binary and categorical variables were used. If any expected table entries were less than 5, then Fisher's exact test instead of the Pearson chi-square test was used. All tests were 2-sided and p-values less than 0.05 were regarded as significant.

Results

Two hundred and eighty-five patients were enrolled. Of these, 11 patients were excluded: 3 patients with a diagnosis other than a voice disorder; 3 patients with generalized dystonia; 3

patients with a voice disorder secondary to a different neurological condition; 1 patient with a voice disorder secondary to a malignancy, and 1 patient with a missing diagnosis. Of the included patients, 146 were in the control group and 128 were diagnosed with SD. 95% of patients with SD had Adductor type, 4% had Abductor type, and 1% had Atypical SD.

In both the SD and control groups, the majority of patients were women (79% and 66%, respectively) and white/Caucasian (80% and 70%, respectively). As expected, patients with associated tremor were older than the patients without tremor in both the control and the SD group. The difference in age between the two groups was not significant; therefore, it was not controlled for in this study. Of note, only 35% of patients with SD had been seen by a neurologist as part of the evaluation and work-up of SD. Additional demographic and clinical characteristics are displayed in Table I.

Analysis was then performed to determine the rates of co-morbid vocal tremor and non-vocal tremor in SD and controls (Table II). Patients with SD were 2.8 times more likely to have tremor than the control group ($P < 0.001$). When separating vocal and non-vocal tremor, patients with SD were 12.81 times more likely to have vocal tremor than the control group ($P < 0.001$). However, patients with SD were no more likely than controls to have non-vocal tremor (OR = 1.59, $P = 0.14$).

Further analysis was performed to determine the co-prevalence of additional non-vocal tremor within the sub-population of patients with vocal tremor (Table III). In the control group, 5/5 (100%) of these patients also had non-vocal tremor, whereas in the SD group, 19/33 (58%) of these patients also had non-vocal tremor. The prevalence rate of non-vocal tremor, among patients with evocal tremor, was not significantly different between groups (Fisher's exact test, $P = 0.14$).

Discussion

Complicating the diagnosis of spasmodic dysphonia is its co-prevalence and occasional similar presentation to vocal tremor. Severe cases of vocal tremor may cause voice breaks similar to those of SD, and co-morbid vocal tremor is common in patients with SD. [7] Additionally, there are currently no standardized methods for diagnosing or separating SD from isolated vocal tremor, which can lead to improper and delayed diagnosis by inexperienced clinicians.

Proper treatment for both essential tremor and SD are contingent on a correct diagnosis. Therefore, a comprehensive speech and voice evaluation by both an otolaryngologist and a speech-language pathologist who specialize in voice disorders and have significant experience in voice disorder assessment and management is needed to accurately diagnose and distinguish SD and vocal tremor. Similarly, to properly evaluate patients for body tremor and other dystonias, an evaluation by an experienced neurologist is necessary.

The diagnosis of tremor is made clinically. [8] In a recent large, population-based study, the prevalence of tremors in the general population was 14.5%.[9] According to this study, 60% of tremors are actually enhanced physiologic tremor, and 40% is essential tremor. However, quantitative tremor analyses using accelerometry is needed to distinguish these tremors, as they are clinically indistinguishable.

In this study, patients with SD had significantly higher rates of co-morbid tremor than controls, when combining vocal and non-vocal tremor, and the prevalence of co-morbid vocal tremor was significantly higher in patients with SD ($p <0.001$). The prevalence of co-morbid non-vocal tremor in SD (21%) was higher than controls (14%); however, this difference was not significant ($P = 0.14$). In controls, the prevalence of co-morbid non-vocal

tremors was consistent with reported rates of prevalence in the general population. Although the odds ratio for being diagnosed co-morbid body tremor was not statistically significant between groups, patients with SD were 50% more likely to be diagnosed with non-vocal tremor, which is likely clinically significant for patients.

Additionally, 58% of the patients with SD and vocal tremor had an associated non-vocal tremor and 100% of controls with vocal tremor had an associated non-vocal tremor. This establishes the presence of co-morbid non-vocal tremor in all patients with vocal tremor, both in patients with SD and in controls.

Predictive factors associated with increased tremor severity include older age, longer disease duration, presence of voice tremor, and a longer follow-up duration. [8] Additionally, tremor is a progressive disease and is associated with functional decline over time. It has been reported that up to 25% of people with tremor change jobs or retire early, and even the majority of persons with tremor that do not seek medical attention report disability. This highlights the importance of recognition of co-morbid vocal and non-vocal tremor.

First-line treatment of non-vocal tremor is with pharmacologic agents such as primidone and propranolol. For most patients, pharmacologic treatment of non-vocal tremor leads to significant improvements in symptoms. Botulinum toxin injections are considered first-line treatment for vocal tremor. [10] This is because medical management of vocal tremor has proven ineffective. [11,12] However, botulinum toxin injections often do not provide complete improvement in symptoms because of the multiple sites of tremor such as the pharynx, tongue base, and palate.

A neurologist who specializes in movement disorders should guide the management and treatment of non-vocal tremor and other dystonias. In our study population, the majority of patients (65%) with SD had not been evaluated by a neurologist at any point for the work-up of their disease. This demonstrates that patients with SD do not seek a neurological evaluation and the onus is on the treating clinician to make referrals for neurological evaluations for the evaluation of other neurologic disease and sites of dystonia and tremor involvement.

This study demonstrates that the presence of co-morbid non-vocal tremor in patients with vocal tremor is greater than 50% in both controls and patients with SD; therefore, the authors recommend referral of all patients with SD and/or vocal tremor to a neurologist for a thorough evaluation. Additionally, because incidence of tremor increases with age, otolaryngologists administering botulinum toxin injections to patients with SD should regularly evaluate patients for the development of vocal and body tremor and subsequently refer for re-evaluation as needed.

A limitation of this study is that it only determined the co-prevalence of vocal and body tremor in patients with SD and vocal controls, it did not demonstrate the prevalence of tremor at diagnosis or the risk of developing co-morbid tremor over time. An additional limitation is that electrophysiologic data demonstrating the muscle action potentials in spasmodic dysphonia and vocal cord tremors were not included. Therefore we were unable to comment on the specific muscle groups that were affected in vocal tremor.

Conclusion

Because of the benefit of pharmacologic therapy in treating tremor and the associated risks of tremor, it is important for each patient with SD to undergo a complete neurological evaluation for tremor and other dystonias. It is also important for otolaryngologists to assess for vocal tremor and counsel appropriately because often vocal tremor is not significantly

reduced by botulinum toxin injections. Additionally, otolaryngologists should inform patients that there is a potential risk of developing vocal and non-vocal tremor so that if a tremor develops the patient can seek a neurological evaluation.

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Table I

Demographic and clinical characteristics. Mean ± SD or frequency (%).

	Controls (n=146)	SD (n = 128)	
Gender			
Female	96 (66%)	101 (79%)	P = 0.02
Male	50 (34%)	27 (21%)	
Race			
White/Caucasian	102 (70%)	103 (80%)	P = 0.13
Black/African-American	36 (25%)	20 (16%)	
Other	8 (5%)	5 (4%)	
Age, years			
Overall	55.0 ± 14.9	59.3 ± 12.4	P = 0.009
Patients with vocal tremor	68.4 ± 14.7	66.6 ± 11.5	P = 0.76
Patients with body tremor	67.1 ± 13.3	64.3 ± 14.7	P = 0.50
Tremor (any)	21 (14%)	41 (32%)	P < 0.001
Vocal tremor	5 (3%)	33 (26%)	P < 0.001
Non-vocal tremor	21 (14%)	27 (21%)	P = 0.14
SD subtype			N/A
ADSD	-	122 (95%)	
ABSD	-	5 (4%)	
Atypical	-	1 (1%)	
Seen by neurologist for SD	-	45 (35%)	N/A

Table II

Prevalence of co-morbid vocal and non-vocal tremor; frequency (%).

	Controls (n = 146)	SD (n = 128)	P	Odds Ratio	95% Confidence Interval
Tremor, Any	21 (14%)	41 (32%)	<0.001	2.81	1.55 – 5.08
Vocal Tremor	5 (3%)	33 (26%)	< 0.001	12.81	4.12 – 39.77
Non-Vocal Tremor	21 (14%)	27 (21%)	0.14	1.59	0.85 – 3.1

Table III

Comorbid non-vocal tremor in patients with vocal tremor; frequency (%).

	Controls + Vocal Tremor (n = 5)	SD + Vocal Tremor (n = 33)	P	Odds Ratio	95% Confidence Interval
Non-vocal tremor	5 (100%)	19 (58%)	0.14	1.35	0.3 – 5.6