Medications and Adverse Voice Effects

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Summary: Objectives. To identify the medications used by patients with dysphonia, describe the voice symptoms reported on initial speech-language pathology (SLP) examination, evaluate the possible direct and indirect effects of medications on voice production, and determine the association between direct and indirect adverse voice effects and self-reported voice symptoms, hydration and smoking habits, comorbidities, vocal assessment, and type and degree of dysphonia.

Study design. This is a retrospective cross-sectional study.

Methods. Fifty-five patients were evaluated and the vocal signs and symptoms indicated in the Dysphonia Risk Protocol were considered, as well as data on hydration, smoking and medication use. We analyzed the associations between type of side effect and self-reported vocal signs/symptoms, hydration, smoking, comorbidities, type of dysphonia, and auditory-perceptual and acoustic parameters.

Results. Sixty percent were women, the mean age was 51.8 years, 29 symptoms were reported on the screening, and 73 active ingredients were identified with 8.2% directly and 91.8% indirectly affecting vocal function. There were associations between the use of drugs with direct adverse voice effects, self-reported symptoms, general degree of vocal deviation, and pitch deviation.

Conclusions. The symptoms of dry throat and shortness of breath were associated with the direct vocal side effect of the medicine, as well as the general degree of vocal deviation and the greater pitch deviation. Shortness of breath when speaking was also associated with the greatest degree of vocal deviation.

Key Words: Medications–Voice–Voice disorders–Speech-language pathology–Voice symptoms.

INTRODUCTION

Several studies have reported the use of specific drugs for the control of voice alterations.[1,2] However, in standard clinical voice practice, speech pathologists and otolaryngologists often treat patients with medications whose adverse effects on the voice are not completely elucidated. Importantly, these adverse effects may affect the proposed treatment plan for a patient, highlighting the need to understand the relationship between medications and voice.

In the specific literature of the field, we did not find studies that have been published on the direct relationship between medications and adverse voice effects. However, the indirect relationship of possible secondary effects of certain types of drugs or active ingredients (AIs) on the voice, larynx, and vocal tract has been examined in several studies. Some drugs have been described as affecting the fluid balance of mucous membranes[3–5] and causing hydric deficit, which can alter the viscoelastic properties of laryngeal mucosa, thereby affecting the aerodynamic and acoustic measurements of voice production.[6,7]

It is also important to consider the use of nonprescription medications, the so-called over-the-counter (OTC) medicines, which are sold directly to consumers in pharmacies.[8,9] Because of the free availability of OTCs and the lack of knowledge of their composition and possible side effects, many patients do not consider this information relevant and therefore do not report their use.

Advances in pharmacovigilance highlight the need for continued research on drug effects on vocal function, which can have a significant impact on voice/speech therapy strategies.

The investigation regarding the use of medication use must include all medicine taken by the patient, in addition to time of use, type of use—continuous or sporadic—, diagnosis that resulted in the prescription, and the prognosis that motivated the use of such medications. This investigation should provide valuable information to help determine both the therapeutic success and the limits of any vocal intervention. Moreover, due to the fact that some medications may consist of long-term or continuous-use drugs, treating voice symptoms does not necessarily ensure the effectiveness of treatment. Weighing the risks and benefits of any therapy together with the multidisciplinary team should be part of the speech-language-therapy routine. Additionally, such research may help guide health promotion efforts that educate the population about medication effects on voice function, especially in cases of self-medication and indiscriminate use of over-the-counter medications.

To our knowledge, no studies have been published correlating adverse medication effects and self-reported voice symptoms to data from the speech-language pathology (SLP) assessment in people with dysphonia. Therefore, this study aimed to identify the medications used by patients with dysphonia, describe the voice symptoms reported on initial SLP examination, evaluate the possible direct and indirect effects of medications on voice production, and determine the association between direct and indirect adverse voice effects and self-reported voice symptoms, hydration and smoking habits, comorbidities, vocal assessment, and type and degree of dysphonia.

METHODS

In this cross-sectional study, we retrospectively analyzed the medical records of patients who received specialist care at the Speech-Language Pathology Clinic of the University of São Paulo

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Medical School (FMUSP), São Paulo, Brazil, between 2007 and 2015. The study was approved by the FMUSP Research Ethics Committee (protocol 194/15).

Patients, regardless of gender, age, or diagnosis, who completed the Dysphonia Risk Screening Protocol (DRSP-general)[10] and reported using medications with package inserts listing possible adverse voice effects were included in the analysis. Patients who did not report using continuous-use medication or who were not taking medications on a date close to the clinic visit and patients who reported using medications with package inserts not listing adverse voice effects were excluded from the analysis.

Of 106 medical records examined, 55 included medications with possible adverse voice effects and were included in the analysis. In total, 73 AIs were identified in the DRSP-general, which was cited in the initial SLP investigation, and some patients used more than one medication. The self-reported voice symptoms and data regarding hydration and smoking/contact with smokers and associated diseases were collected from the DRSP-general.

The type of dysphonia was classified as behavioral and/or organic on the basis of the medical diagnosis.[11]

In order to define the degree of dysphonia, we considered the auditory-perceptual analysis of voices previously defined by the team that attended the patient and later confirmed for this research by a specialized speech-language therapist with more than 10 years of experience in this type of assessment and great reliability[10] by means of CAPE-V parameters adapted to Brazilian Portuguese.[12]

The acoustic analysis was performed for this study using Praat software (www.praat.org) and Voxmetria (CTS Informática, Paraná, Brazil). We extracted the following automatic measurements: fundamental frequency, jitter, shimmer, irregularity, glottal-to-noise excitation, and noise. The phonatory deviation diagram was considered deviated when it was in quadrants 2, 3 4, and normal in quadrant 1. The outcome of the acoustic analysis was considered for statistical analysis purposes, and those in which at least two of the measurements were outside of the stated standards were classified as deviated.

The vocal records were performed in an acoustically treated room, and we used a desktop computer (Hewlett-Packard, Palo Alto, California, United States), the Audacity program (Audacity®, General Public License), the Edirol UA-101 interface (Roland, Swansea, UK) and a unidirectional/condensed headset microphone (model 520; AKG, Hofgeismar, Germany) positioned between 3 and 5 cm from the individual's mouth on an axis from 45 to 90 degrees.

Regarding the medicine, all information was obtained from the package inserts, which are regulated by the National Health Surveillance Agency of Brazil's Ministry of Health.[13] AIs were classified according to their possible adverse voice effects into direct adverse voice effects and indirect adverse voice effects: 1) direct adverse voice effects, including those that made explicit reference to the voice such as hoarseness, aphonia, dysphonia, and their synonyms; 2) indirect adverse voice effects classified in this category reactions that may predispose to voice alterations including dehydration, xerostomia, dry mouth, sweating, diarrhea, vomiting, dyspepsia, gastrointestinal disturbances, and gastroesophageal reflux; 3) risk of laryngeal or vocal tract bleeding, pharyngitis, sinusitis, and rhinitis per drug, laryngopharyngeal irritation or pain, laryngopharyngeal edema, fungal infections of the mouth and throat, respiratory effects including dry cough, dyspnea, and shortness of breath, and neurological symptoms such as dyskinesia and muscle rigidity, among others.[3–5,14–17]

The AIs and their direct adverse voice effects and indirect adverse voice effects are described in Figure 1.

In the item hydration, we considered for the purposes of statistical analysis ideal/sufficient self-reported consumption of six or more glasses of water per day and insufficient consumption of less than six glasses of water per day. For smoking/contact with smokers, we considered presence and absence. For self-reported comorbidities, we considered constant colds, allergic processes, and gastroesophageal reflux.

We performed chi-square or Fischer's exact tests for comparison of the qualitative variables (self-reported vocal signals and symptoms, comorbidities, type of dysphonia, acoustic outcome) and the variables of interest (type of medication effect, self-reported vocal signs and symptoms, type of dysphonia). For the comparisons among the quantitative variables (aspects related to the general degree of vocal deviation) and the variables of interest (self-reported vocal signals and symptoms and medication effect), the Student *t* test and the Wilcoxon test were used. The statistical program used was R-Project version 3.3.3 (R Foundation for Statistical Computing, Vienna, Austria). The level of significance considered in this study was 5%.

RESULTS

Of 106 patients, 55 (51.8%) reported using medications that may directly or indirectly affect the voice. Of the 55 medical charts included in the study, 60% were from women (n = 33) and 40% from men (n = 22); the mean age was 51.8 years, and different laryngeal conditions were diagnosed. Of the 55 patients included, 18.2% (n = 10) reported using AIs that directly affect vocal function, and 81.8% (n = 45) reported using AIs that indirectly affect vocal function. The mean number of self-reported medications used was 3.6.

In total, 73 AIs were identified, and the mean number of AIs (prescribed or nonprescribed) used per patient was 1.32.

Of the 73 AIs that may cause some adverse voice effects, 8.2% (n = 6) directly affect and 91.8% (n = 67) indirectly affect vocal function. In addition, most medications can cause more than one direct and/or indirect adverse effect (Figure 1).

The most frequent self-reported voice symptoms were dry throat (69.1%), hoarseness (67.3%), speech failures/breaks (67.3%), vocal fatigue (65.5%), throat clearing (65.5%), weak voice (50.9%), and shortness of breath (47.3%) (Table 1). Regarding the presence of associated diseases, 40.0% reported allergic processes, 25.4% gastroesophageal reflux, and 10.9% constant colds. In relation to the type of dysphonia, the sample was steady with 28 (50.9%) behavioral dysphonia and 27 (49.1%) organic dysphonia.

There was an association between medication with direct vocal adverse side effect and the self-reported symptoms dry throat