REVIEW

Vocal Cord Dysfunction: Current Understanding and Approach to Disease

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ABSTRACT

Vocal Cord Dysfunction (VCD) is a serious disorder of the vocal cords and laryngeal muscles that mimics asthma and can seriously affect the patient, both physically and emotionally. Patients with this condition are often misdiagnosed and treated inappropriately due to lack of systematic knowledge concerning diagnosis and therapy. The aetiology remains a topic of research; in fact, most experts now agree that vocal cord dysfunction is a group of conditions, or that it has multiple aetiologies. This is appreciated by the extensive number of terms that have been used to describe it. Epidemiological data is also limited, but preliminary investigations suggest that its incidence is higher than initially appreciated. This review summarizes the current existing knowledge and aims to help the reader recognize and develop a management approach to vocal cord dysfunction.

INTRODUCTION

Located in the center of the voice-production apparatus, in the gateway to the lungs, the vocal cords are critical in two fundamental aspects of human physiology: breathing and speech. First described in 1842 by Dunglison,[1] visualized by Mackenzie in 1869[2] and later described clinically by Sir William Osler in 1902,[3] aetiologies of disorders of the vocal cord and associated laryngeal muscles remain an active topic of research. Vocal Cord Dysfunction (VCD) is a disorder that has been described under many names including "Paradoxical Vocal Cord Motion (PVCM)", "Episodic Laryngospasms", "Functional Upper Airway Obstruction", and more recently, "Irritable Larynx Syndrome (ILS)".[4,5] Historically, psychiatric conditions, such as hysteria and Munchausen's stridor, have dominated the aetiological explanations.[1] The term 'Vocal Cord Dysfunction' emerged in the 1980s as an umbrella term to describe a group of ill-defined abnormalities of the vocal cords.[6] The symptoms caused by these conditions include inspiratory stridor or wheeze, dysphonia, globus, chronic cough, laryngeal spasms, and in some cases, severe airway obstruction (Table 1).[4] Given these symptoms, many of these patients are diagnosed with asthma and treated with high dose steroids while their symptoms persist.[5,6] In many patients, this has led to unnecessary hospitalization and tracheostomy.[7] Despite this, asthma is still an important differential diagnosis that must be ruled out.

Despite research efforts, the epidemiology of VCD remains poorly understood. Various investigations reported incidence rates that vary widely between 2% and 30% in patients with asthma[8,9] to 15% in the general population.[10] However, the incidence is estimated to be higher than generally expected.

The term VCD is thought to be too broad by some experts and terms such as ILS and PVCM, which are more descriptive of the underlying pathology, are preferred.[4,11] ILS, proposed by Morrison and colleagues, is used particularly when the causative trigger or stimulus is known.[4] This review will employ the term VCD to refer to all forms described, as the purpose is to provide an overview to non-expert health care professionals and medical students who may encounter patients with the described symptoms in primary care or hospital settings.

Table 1. Symptoms of VCD and differential diagnosis

Symptoms
• Inspiratory stridor/wheeze
• Tightness of throat
• Shortness of breath/dyspnea
• Laryngeal spasm
• Dysphonia
• Cough
• Choking sensations

Differential Diagnosis
CONGENITAL
• Subglottic stenosis
• Laryngeal web
ACQUIRED
• Asthma
• Foreign body
• GERD
• Infection
• Neoplasm
• Trauma
• Munchausen's/Anxiety

GERD = Gastroesophageal Reflux Disease

ANATOMY AND PHYSIOLOGY OF THE VOCAL CORDS

The vocal cords are located in the larynx. The false vocal cords are located superior to the true vocal cords and it is the dynamic true vocal cords or simply "vocal cords" which play a role in phonation, since the false cords are fixed. Abduction and adduction of the vocal cords are controlled by contraction of the posterior cricoarytenoid (PCA) and lateral cricoarytenoid (LCA) muscles, respectively.[11] The recurrent laryngeal nerve, a branch of the vagus nerve, innervates these muscles to control the space between the vocal cords referred to as the rima glottidis (Figure 1).[12] The width of this space regulates the amount of air flowing into and out of the lungs.[10] The tone of these muscles is rhythmic with the respiratory cycle as it is driven by the respiration center in the medulla.[10,11]

During inspiration, contraction of the PCA muscle leads to

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abduction of the vocal cords and opening of the glottidis. During expiration, the glottidis narrows partially.[10] Thus, the glottidis is usually open during breathing and changes width during speech to produce phonation (Figure 1).[11,13] The glottis also plays an important role in protecting the airways against noxious stimuli, through the mechanism of coughing.[10]

THE VOCAL CORDS IN VCD

In VCD, the vocal cords paradoxically close during inspiration. The posterior diamond-shaped gap, referred to as the 'glottis chink', represents a characteristic pattern seen in laryngoscopy during an acute attack (Figure 2).[10,14] This is considered the gold standard diagnostic criterion and causes extrathoracic upper airway obstruction leading to potentially severe dyspnea and wheezing. Episodic closure, which takes place during speech, can also result in dysphonia. Some patients may also experience cough and the sensation of choking.[10]

DIAGNOSIS OF VCD

The presenting symptoms of patients with VCD, as well as any existing co-morbidities, have helped to shed some light on the possible causes. Many criteria have been proposed in the diagnosis of VCD. It is important to start with a thorough history to illicit the symptoms, triggers and co-existing risk factors, such as reflux disease or emotional distress (Table 1). The role of a physical exam is limited to noting any spasm or tension in the laryngeal muscles or signs that suggest an alternative diagnosis, such as cyanosis and eczema in asthma. Pulmonary function tests and oxygen status, along with visualizing the paradoxical closure, are recommended as gold standards.[10,11,14] Spirometry typically exhibits a pattern of extrathoracic airway obstruction during inspiration.[5,10,13] Three criteria seem to be emphasized in the diagnosis of VCD: 1) adduction of the true vocal cords during inspiration or during both inspiration and expiration; 2) presence of posterior open glottis chink during adduction (Figure 2), and; 3) absense of gagging or coughing during laryngoscopy, since these cause closure of the cords even in absence of VCD.[15] Palpable or visualized laryngeal tension in the presence of a known stimulus, ranging from odours to psychogenic phenomena, are emphasized in the diagnosis of ILS.[4] Other helpful indicators include a lack of significant improvement in response to bronchodilators or corticosteroids, which is usually observed in asthma. In reality, all of these steps are important to rule out other causes and better characterize the diagnosis (Table 2).[5,11] Due to the lack of systematic diagnostic and interventional protocols, a patient with high suspicion of having VCD should be referred to a specialist such as a laryngologist or respirologist. This also highlights the importance of educating primary health care professionals and trainees about VCD because it is often misdiagnosed as asthma due to their similar clinical presentations. In complex cases, VCD can co-exist with asthma, therefore a detailed multi-disciplinary assessment and supervision of therapy must be present.[15]

Table 2. Recommended elements in diagnosing VCD

Diagnostic Approach
History
• Triggers (e.g. GERD, allergy, anxiety)
• Episode duration
• Symptoms (e.g. dysphonia, feeling of choking, cough)
• Medical and psychiatric conditions
Physical
• Laryngeal tension
• Signs of asthma (e.g. cyanosis, eczema)
Tests
• Oxygen saturation
• Laryngoscopy during attack (posterior chink visualization)
• Pulmonary function test (noting inspiratory extrathoracic obstruction)

AETIOLOGY

Although the definite pathophysiology of VCD remains unknown, theories that explain both the presenting complaints and the success of certain interventions have been proposed. Psychogenic conditions were dominant explanations when the symptoms of VCD were first described. Cases of 'hysteric croup', 'Munchausen's stridor', and conversion disorders have all been reported.[1,7,16] Although these have not been proven, psychogenic and emotional disturbances seem to act as triggers in some patients.[15,17] More recent investigations found the aetiology of this group of syndromes to be more complex. Bucca and colleagues

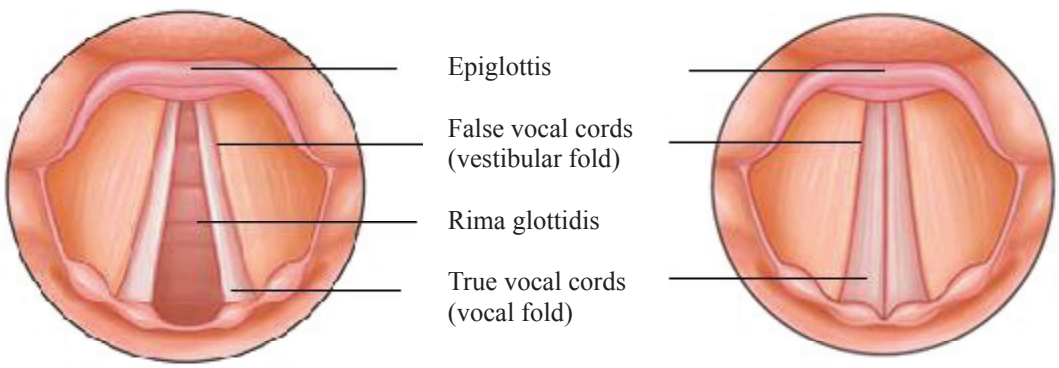

Figure 1. Vocal cords during: inspiration (left) and phonation (speaking) (right).

Adapted from Drake R, Vogl, W Mitchell AWM. Gray's anatomy for students. 1st ed. Philadelphia: Elsevier; 2005: 960; with permission.

hypothesize that laryngeal hyper-responsiveness and bronchial hypersensitivity are due to local inflammatory processes that lead to enhanced reflexes and glottis closure.[18] Ayers and Gabbott put forward the 'altered autonomic response' hypothesis in 2002, which states that areas of the brain with autonomic functions, such as the midbrain, the medulla and prefrontal cortex, have polysynaptic connections with the larynx.[19] They propose that in VCD, an initial inflammatory episode results in adaptation of the local irritant receptors in the larynx, leading to an exaggerated protective reflex by the pharynx at the central level.[19]

Morrison and colleagues (1999), who cointed the term ILS, also suggested a hypothesis that encompasses hypersensitivity and some form of altered central nervous system circuitry.[4] Therefore, their theory will be elaborated upon here. Because a known stimulus is an important criterion in ILS, they studied various triggers in 39 VCD patients. Their neural plasticity hypothesis explains that these stimuli alter the way the central nervous system (CNS) responds to sensory afferent input, which can be a range of sensations or psychogenic thoughts. There are two proposed mechanisms for how this happens: 1) death of original connections leading to sprouting of other adjacent connections to the laryngeal motor system or 2) continuous noxious stimulation leading to enhanced neurotransmitter release and altered genetic expression in the neuron.[4] This altered neuronal physiology leads to a hypersensitive response in the case of ILS. This theory is consistent with the physiological changes that take place in chronic pain, which include decreased action potential firing threshold of the neurons and central sensitization. Furthermore, they suggest an area in the brain might be responsible called the periaquaductal gray (PAG). Plasticity occurs here since this area receives both sensory and emotional input and is involved in vocal and laryngeal motor output.[4,20]

The co-morbidities that tend to exist in VCD patients point towards a common underlying mechanism consistent with a continuous trigger leading to central sensitization. Andrianopoulos and colleagues showed that after asthma symptoms, gastrointestinal (GI) symptoms and conditions, including GERD (gastroesophageal reflux disease), were the most common medical complaints in patients with VCD.[21] Amongst the rest were various other inflammatory and psychogenic conditions such as allergies and anxiety. GERD is an important trigger being further investigated since GI secretions seem to provoke laryngospasm in canine models and lead to sensitization of mucosal chemoreceptors and vagal-mediated neuronal networks.[22,23] When asked about triggers, reflux and emotions are highly reported by patients along with other various stimuli.[4]

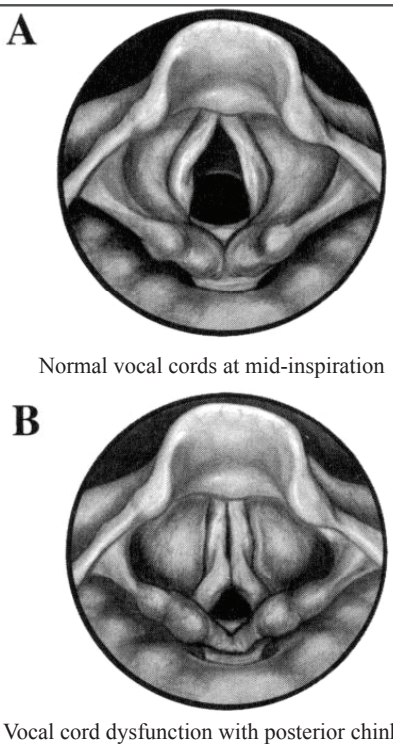

Figure 2. The appearance of the vocal cords during (A) inspiration in a healthy patient and (B) during inspiration in a patient with VCD, showing the adduction of the vocal cords with the characteristic posterior "chink" opening.

Illustration by Leigh Landskroner. Adapted from Perkner JJ, Fennelly KP, Balkissoon R, et al. Irritant-associated vocal cord dysfunction. J Occup Environ Med 1998; 40:136–43; with permission (Lic.:2158381124834).

TREATMENT

Chronic Management

The diversity of treatment options used in VCD reflects the multiple aetiologies and triggers potentially implicated. Education is an important step in teaching patients to recognize triggers and be aware of treatment options for this rare condition.[17,21] VCD is a good example to highlight the importance of a multidisciplinary approach, which is becoming increasingly favourable in medicine. In fact, much research and clinical interventions in VCD have been formulated by speech-language pathologists.[5,17,24] They can train patients to practice breathing exercises and cough suppressing techniques that have the potential to reverse the postulated CNS-mediated hypersensitivity in the long term, and abort acute attacks with techniques such as panting and sniffing.[11,21,25] Relationship-building with the patient is important as patients with VCD are known to use the health care system frequently prior to the proper diagnosis and management of symptoms.[26]

As psychiatric conditions have been postulated in the aetiology and provocation of VCD attacks, it is not surprising that psychotherapy, biofeedback, and hypnosis have been attempted as therapies. A review by Morris and colleagues found that 55.7% of treated patients received some form of psychotherapy.[10] Some patients seemed to benefit, particularly in the presence of psychological conditions such as anxiety, which may act as a trigger. However, the efficacy of these therapies have not been systematically evaluated. Essentially, speech-language pathology and psychotherapy are considered pillars of chronic management of vocal cord dysfunction, but systematic investigation of efficacy and long term data remain unavailable.

In terms of pharmacologic management, patients with VCD may benefit from maintenance therapy for co-existing conditions that may act as triggers, including GERD and allergies.[21] It is worth emphasizing that patients with VCD often have a history of unresponsiveness to asthma medications.[6,15] However, asthma may be concomitant, thus the decision to taper or start inhaled bronchodilators should be done cautiously.[14,15]

Acute management

VCD patients can also present with more severe attacks that require immediate management. In such settings, Heliox, an inhaled mixture of oxygen and helium has been commonly used.[27] Because of its low density, Heliox allows air to flow through and

Table 3. Treatment of acute and chronic VCD

Treatment options
Acute Attack
• Panting/ sniffing/ calming
• Heliox gas
• Benzodiazepine
• Botulinum toxin
Chronic
• Speech language pathology training
• Counselling/ psychotherapy

thus decrease the effort of breathing and consequently reduce the anxiety of the patient. Benzodiazepines have also been found to alleviate acute symptoms by acting as sedatives and reducing the associated anxiety.[4] Botulinum toxin injections have also been used for acute management. They work by paralyzing the muscles controlling the cords leaving them unable to adduct episodically.[11,21] This modality was first used in patients with laryngeal dysphonia[28,29] and later used in VCD.[31] The delay before onset of action and the need for continuous injections are two disadvantages to using this modality as maintenance therapy. Severe attacks requiring intubation, intermittent and continuous positive airway pressure, and tracheostomy have also been reported[6,21]. The main treatment goal is to avoid these invasive methods by recognizing the symptoms early and attempting the other options first (Table 3).

SUMMARY

Despite the availability of many reports and observational studies on this topic, there remains limited objective methods of diagnosis and treatment. Efforts have been directed towards understanding the pathophysiology, which suggest an irritant-mediated mechanism leading to altered central responses. This could aid in recognizing the symptoms and in better targeting the treatment at the dysfunctional pathways.[4,18,19] At this time, it remains the clinician's judgement to select a treatment modality that addresses the potential underlying defects suspected from the history, physical and other investigations, such as spirometry and laryngoscopy (Table 2). Ultimately, training by speech-language pathologists is recommended because it can be tailored to the patient to target the underlying defect.[5,17,24] Chronic episodic airway obstruction and accompanying wheeze can have an extensive burden on the functional and psychosocial aspects of the patient's life. A strong doctor-patient relationship and a multi-disciplinary approach are recommended to help educate patients, train them to control and abort these attacks, and to provide symptomatic relief. Future efforts should focus on well-designed randomized control trials and prospective observational studies to test treatment modalities objectively and to establish the epidemiology and risk factors of VCD, respectively.

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