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ABOUT COVER

Editor-in-Chief of *World Journal of Clinical Cases*, Bao-Gan Peng, MD, PhD, is Professor and Director of the Department of Orthopedics at The Third Medical Center of PLA General Hospital. Professor Peng's research interest is spinal surgery. His career work has generated a multitude of new academic viewpoints and theories, and more than 200 academic papers, published both at home and abroad. In practice, he has systematically elucidated the pathogenesis of discogenic low back pain and established a new minimally invasive treatment method: The intradiscal methylene blue injection. He also revealed and characterized a new pathogenesis of Schmorl's nodes, which is a now a famous concept. Finally, he was the first to discover that ingrowth of Ruffini corpuscles into degenerative cervical disc is related to dizziness of cervical origin. (L-Editor: Filipodia)

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The primary aim of *World Journal of Clinical Cases* (WJCC, *World J Clin Cases*) is to provide scholars and readers from various fields of clinical medicine with a platform to publish high-quality clinical research articles and communicate their research findings online.

WJCC mainly publishes articles reporting research results and findings obtained in the field of clinical medicine and covering a wide range of topics, including case control studies, retrospective cohort studies, retrospective studies, clinical trials studies, observational studies, prospective studies, randomized controlled trials, randomized clinical trials, systematic reviews, meta-analysis, and case reports.

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Cervical intervertebral disc degeneration and dizziness

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Abstract

Clinical studies have found that patients with cervical degenerative disease are usually accompanied by dizziness. Anterior cervical surgery can eliminate not only chronic neck pain, cervical radiculopathy or myelopathy, but also dizziness. Immunohistochemical studies show that a large number of mechanoreceptors, especially Ruffini corpuscles, are present in degenerated cervical discs. The available evidence suggests a key role of Ruffini corpuscles in the pathogenesis of dizziness caused by cervical degenerative disease (*i.e.* cervical discogenic dizziness). Disc degeneration is characterized by an elevation of inflammatory cytokines, which stimulates the mechanoreceptors in degenerated discs and results in peripheral sensitization. Abnormal cervical proprioceptive inputs from the mechanoreceptors are transmitted to the central nervous system, resulting in sensory mismatches with vestibular and visual information and leads to dizziness. In addition, neck pain caused by cervical disc degeneration can play a key role in cervical discogenic dizziness by increasing the sensitivity of muscle spindles. Like cervical discogenic pain, the diagnosis of cervical discogenic dizziness can be challenging and can be made only after other potential causes of dizziness have been ruled out. Conservative treatment is effective for the majority of patients. Existing basic and clinical studies have shown that cervical intervertebral disc degeneration can lead to dizziness.

Key Words: Cervical intervertebral disc degeneration; Cervicogenic dizziness; Cervical discogenic dizziness; Cervical spondylosis; Neck pain; Mechanoreceptors

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Core Tip: Cervical discogenic dizziness is an emerging and very attractive concept. Degenerative cervical discs are rich in Ruffini corpuscles and prone to inflammatory reactions resulting in dizziness that can be eliminated by intradiscal analgesic block. Based on basic and clinical findings, degenerated cervical discs can be thought as an important source of dizziness.

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INTRODUCTION

Dizziness is a common complaint encountered in clinical practice^[1]. Cervicogenic dizziness, which occurs in the cervical spine, is considered to be one of the most common etiologies^[2]. It is generally described as "a nonspecific sensation of altered orientation in space, and disequilibrium originating from abnormal afferent activity arising in the neck"^[3]. Cervical degenerative disease, or cervical spondylosis, is currently considered to be the most common cause of cervicogenic dizziness^[4]. The major pathological feature of cervical spondylosis is cervical disc degeneration. Patients with chronic neck pain often suffer from dizziness^[5]. Neck pain and dizziness are two common concomitant symptoms of cervical degenerative disease. When these two complaints present at the same time, do they have any relationship? Can degeneration of cervical intervertebral discs cause dizziness? If so, what are the pathophysiological mechanisms of this dizziness? This narrative review will scientifically answer these topical clinical issues based on existing basic and clinical studiesevidence.

LITERATURE SEARCH

A comprehensive literature search of PubMed and MEDLINE from the inception of the database to February 2020 was performed. The search terms included "cervicogenic dizziness", "cervical dizziness", "cervical vertigo", "cervical disc innervation", and "cervical disc degeneration". References for this review were also identified from the personal libraries of the authors and supplemented by the reference lists of recent reviews and book chapters. Publications relevant to cervical intervertebral disc degeneration and dizziness were selected based on author expertise to summarize our current understanding of the impact of cervical disc degeneration on dizziness.

DISTRIBUTION OF MECHANORECEPTORS IN CERVICAL DISC

Strasmann *et al*^[6] found a great number of Pacinian corpuscles in the longitudinal ligaments and intervertebral discs of the cervical spine of small laboratory marsupials. The large number of mechanoreceptors suggests their importance for the detection of changes in position of the cervical spine and head. Mendel *et al*^[7] first found mechanoreceptors similar to Pacinian corpuscles and Golgi organs in the annulus fibrosus of human cervical discs obtained at autopsy, which may indicate that the mechanical status of cervical discs is monitored by the central nervous system. Recently, an immunohistochemical study published by Yang *et al*^[8] found Ruffini corpuscles in the anterior longitudinal ligaments and outer annulus fibrosus of human normal cervical discs. Ruffini corpuscles were significantly increased in number in the deep tissues of the inner annulus fibrosus and the nucleus pulposus of degenerating cervical discs from cervical spondylosis patients with dizziness compared with cervical discs from patients without dizziness. A small number of Golgi organs were seen in disc tissue samples from patients with dizziness, suggesting that these mechanoreceptors are involved in the development of dizziness. No Pacinian

corpuscles were found in any samples of cervical discs. According to the basic principles of neurobiology, abnormal ingrowth of nerve endings must be associated with abnormal nerve function. It is well known that Ruffini corpuscles normally distribute around joints and sense movement and direction and Golgi tendon organs sense muscle tension. A positive correlation of the increase of Ruffini corpuscles and the occurrence of dizziness in patients with cervical spondylosis has been shown, suggesting involvement of Ruffini corpuscles in the pathogenesis of dizziness caused by cervical spondylosis.

Yang *et al*^[9] collected cervical intervertebral disc specimens from patients with chronic neck pain and dizziness for immunohistochemical study. Those patients showed degeneration of the cervical disc on imaging, without cervical disc herniation or nerve root compression, and an increased number of Ruffini corpuscles and substance P-positive free nerve fibers in the degenerative cervical discs compared with normal controls. The distribution of the free nerve fibers was highly consistent with that of Ruffini corpuscles.

DISC DEGENERATION, INFLAMMATION, AND NERVE INGROWTH

Disc degeneration is characterized by elevation of inflammatory cytokines such as tumor necrosis factor (TNF)- α , interleukin (IL)-1 β , IL-6, and IL-17 secreted by the disc cells themselves^[10]. These cytokines promote matrix degradation in degenerative discs by producing and activating degradative enzymes, chemokine production, and changes in cell phenotype. Release of chemokines from degenerative discs promotes infiltration and activation of T and B cells, macrophages, and mast cells, further amplifying the inflammatory cascade and release of neurotrophins, nerve growth factor (NGF) in particular^[11]. It is now considered that the innervation characteristic of intervertebral disc degeneration is related to the role of NGF^[10,11].

Normal intervertebral discs are poorly innervated by only sensory and sympathetic peripheral nerve fibers. Physiologically, proteoglycans in the matrix of the intervertebral disc, especially aggrecans, provide interstitial hydrostatic pressure to counteract nerve and vascular ingrowth into disc^[12]. In addition, aggrecan chondroitin sulfate components in normal intervertebral discs inhibit nerve formation. In human degenerative discs as well as in animal models of disc degeneration, the increased expression of NGF in the disc and the breakdown of aggrecans lead to the ingrowth of sensory nerve fibers^[12].

CERVICAL SPONDYLOSIS AND DIZZINESS

Clinical studies have found that patients with cervical degenerative disease tend to have concomitant dizziness^[13-15]. Cervical degenerative disease is the most common cervical spine disorder in humans^[5]. The incidence of complaints of dizziness is 50%-65% in patients with cervical spondylosis^[16,17]. Using vibration- and galvanically-induced body-sway posturography assessment, Karlberg *et al*^[16] found that patients with cervical spondylosis had poor postural control. The objective findings indicated that balance function was impaired in those patients compared with healthy subjects. Persson *et al*^[18] assessed postural performance using posturography in 71 consecutive patients with cervical spondylotic radiculopathy who were randomized to three treatment groups. Surgery (anterior cervical decompression and fusion) achieved significantly improved postural performance and reduced neck pain scores compared with two conservative treatments (physiotherapy and cervical collar). Many clinical studies have shown that anterior cervical decompression and fusion can effectively treat cervical spondylosis patients with cervicogenic dizziness^[13-15]. The main indications for surgical treatment of cervical spondylosis are cervical radiculopathy or myelopathy; and after decompression, cervical nerve root and cervical spinal cord conduction are improved. Proprioception is also improved, which may be one of the reasons that anterior cervical decompression improves dizziness^[16,18]. Recently, Peng *et al*^[15] performed a prospective cohort study to compare the effectiveness of anterior cervical surgery and conservative treatment for cervicogenic dizziness. They found that anterior cervical decompression surgery had a significantly greater effect on dizziness during 12 mo of follow-up than conservative treatment. Because cervical spondylosis is characterized by cervical intervertebral disc degeneration, evidence from the studies described above suggests that cervicogenic dizziness is caused by cervical disc degeneration. Yang *et al*^[9] performed a clinical and immunohistochemical

study of patients with chronic cervical pain and refractory dizziness and cervical disc degeneration without disc herniation or radiculopathy on imaging. Resolution or improvement of neck pain and dizziness following bupivacaine injection indicated a symptomatic disc. were significantly reduced or resolved, indicating that the disc was symptomatic. They then performed anterior cervical fusion in those patients. After surgery, the patients experienced a significant reduction in neck pain and dizziness. Thus, it has been proved theoretically and clinically that cervical discogenic dizziness does exist.

PATHOGENESIS OF CERVICAL DISCOGENIC DIZZINESS

The mechanism of cervical discogenic dizziness is not clear. With disc degeneration, there is a net loss of proteoglycans and water from the nucleus, leading to loss of normal structure and to abnormal motion, which can provoke mechanical stimulation. Abnormal stimulation of the mechanoreceptors in degenerated discs can, in certain circumstances, such as inflammation, result in an amplified response called peripheral sensitization. That may explain why some degenerative discs produce dizziness, and others do not^[8]. Some mechanoreceptors are more sensitive to mechanical stimuli in inflamed joints than in normal joints^[19]. If the discharging characteristics of the mechanoreceptors in a degenerative cervical disc are altered by inflammation and an increase in their number, erroneous signals will be produced^[8]. Abnormal cervical proprioceptive inputs are transmitted to the central nervous system, resulting in a sensory mismatch of vestibular and visual information that leads to dizziness and instability^[8]. It is because of the strong connection between cervical dorsal roots and vestibular nuclei *via* cervical proprioceptors that the pathology of degenerative cervical disc can be related to dizziness or imbalance^[8,9,15,20].

Cervical intervertebral discs have long been considered as a major source of neck pain. Degenerative cervical discs have a rich supply of nerve fibers, are prone to inflammatory reactions, and are susceptible to pain that can be provoked by disc stimulation and can be eliminated by analgesic injection^[8,9,21]. A recent review has summarized the evidence that cervical intervertebral disc degeneration can lead to neck pain^[22].

Electric stimulation of group III muscle afferents and intramuscular injection of hypertonic saline have been shown to result in significant changes in the activity of γ -fusimotor afferents in leg muscles^[23,24]. These observations led Johansson *et al.*^[25] to propose a pathophysiological model based on nociceptive regulation of the fusimotor system. According to their hypothesis, thin myelinated (group III) and unmyelinated (group IV) muscle afferents can be sensitized by increased concentrations of interstitial potassium, lactic acid, or arachidonic acid caused by static muscle contractions secondary to pain. Both static and dynamic γ -motoneurons are excited by group III and IV muscle afferents, which were strong enough to increase the sensitivity of muscle spindles. This may serve as a positive feedback loop to increase reflex-mediated muscle tension and stiffness. In addition, the connection between second pain neurons and spinal motoneurons can also help increase muscle tension. Increasing sensitivity of muscle spindles can lead to erroneous proprioceptive signals, especially when muscle spindles in different cervical muscles or on different sides of the neck are unevenly sensitized.

Neck pain is reported to have an effect on an alteration of cervical proprioception from muscle spindles^[20,26]. A study by Malmström *et al.*^[27] showed that injecting hypertonic saline into deep cervical muscles of volunteers caused intense, radiating neck pain, resulting in disorientation. The proprioceptive system of the cervical spine, in particular, is extremely well developed, as reflected by an abundance of mechanoreceptors, especially from muscle spindles in the deep segmental upper cervical muscles^[28]. The mechanisms that control posture involve a wide variety of structures including peripheral afferents, the central nervous system, and the effector muscles^[29]. Integration of symmetrical inputs from these afferent systems is essential for normal orientation and balance, and any dysfunction or asymmetry of afferent inputs in these sensory organs can lead to imbalance or dizziness^[4]. Proprioceptive signals of the cervical muscles and cervical intervertebral discs play an important role in maintaining and adjusting a person's resting direction and balance during movement, and changes in the proprioceptive signals could cause cervicogenic dizziness^[4,9,20].

MANAGEMENT

Like cervical discogenic pain, the diagnosis of cervical discogenic dizziness can be challenging and can only be made after other potential causes of dizziness have been ruled out^[4]. Based on the mechanisms of cervical discogenic pain and dizziness described above, the symptom of neck pain for diagnosis of this dizziness is very important. If a patient has a chief complaint of dizziness that is not accompanied by neck pain, a diagnosis of cervical discogenic dizziness may be initially excluded. Similarly, the management of dizziness should be the same as this kind of neck pain^[1,5].

Conservative treatments such as nonsteroidal anti-inflammatory drugs, muscle relaxants, manual therapy, and physiotherapy, are effective for the majority of patients^[2,4]. Takahashi^[2] used muscle relaxants to treat patients with cervicogenic dizziness and stiffness of the neck and shoulders. After treatment, dizziness disappeared or improved significantly in 90% of the patients within 1 wk. Humphreys *et al*^[29] compared adult who presented for chiropractic treatment of neck pain with dizziness ($n = 177$) or without dizziness ($n = 228$). After 6 mo of follow-up, 80% of patients with dizziness and 78% of patients without dizziness reported clinically relevant improvement. In addition, there were no significant differences between patients with and without dizziness in any of the outcome measures. Reid *et al*^[30] assessed the effectiveness of a specific type of spinal mobilization known as sustained natural apophyseal glides for cervicogenic dizziness. They found significant improvement in the severity and frequency of dizziness and relief of neck pain at 6 and 12 wk after treatment.

Some authors encourage the implementation of vestibular rehabilitation for treatment of cervicogenic dizziness^[3,31]. It may be assumed that the vestibulo-cerebellar system is better able to compensate for changes in cervical sensory input in cases of cervicogenic dizziness. Therefore, it is believed that vestibular rehabilitation to strengthen the vestibulo-cerebellar system when normal cervical afferent inputs are impaired can improve the ability to adapt to that situation^[32]. Studies have reported positive results when combined with manual treatment and vestibular rehabilitation^[31].

If a patient with cervical radiculopathy or myelopathy accompanying dizziness does not respond to conservative treatment, anterior cervical surgery can guarantee the reduction of neurologic symptoms and signs and concomitant dizziness^[13-15]. If conservative treatment is not effective in a patient with dizziness and painful cervical disc degeneration confirmed by injection of intradiscal bupivacaine, and if cervical radiculopathy or myelopathy are absent, then anterior cervical fusion surgery can provide good therapeutic results^[9].

CONCLUSION

Degenerative cervical discs do not always cause dizziness, just as degenerative cervical discs do not always cause neck pain. If a degenerated cervical intervertebral disc does not contain a sufficient number of Ruffini corpuscles and does not have a strong inflammatory response, it may not produce a strong enough proprioceptive afferent impulse. Based on our basic and clinical findings, we have sufficient evidence that degenerated cervical discs are a source of dizziness. Of course, the best evidence we have is from patients who have recovered from dizziness and neck pain after treatment of cervical degenerative diseases. Further basic research is needed to elucidate the nerve conduction pathways in cervical discogenic dizziness and confirm this complex clinical mechanism and to improve diagnosis and treatment.

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