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Vertigo and its clinical management: a brief overview

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ABSTRACT

Vertigo, one of the most common vestibular complaints presented in otolaryngology clinics, has diverse origin and etiology. Pathophysiology of vertigo thus plays a major role in determining its pharmacotherapy. Vertigo is mainly a multisensory syndrome in which three sensory systems plays a key role- the vestibular system, visual system, and somatosensory system; however the vestibular system is most commonly implicated. Depending on their etiology though, vestibular diseases can be treated with drugs, physical therapy, psychotherapeutic measures and rarely surgery.

INTRODUCTION

Dizziness and vertigo are common medical issues affecting approximately 20-30% of the general population accounting for about 2-3% of all consultations in general practice and emergency departments. [1,2] Dizziness is a symptom which describes sensations like vertigo, light-headedness, faintness, and imbalance. Vertigo is a subtype of dizziness in which a patient inappropriately experiences an illusory or hallucinatory sense of movement of the body or environment, most often a feeling of spinning, the illusion of motion due to dysfunction of the vestibular system. Vertigo presents a challenge to diagnosis as the words used by the patients are diverse and non-specific that is inadequate to establish the etiology. Vertigo is one of the 10 most common symptoms for which patients seek medical advice. Vertigo can occur in people of all ages. The prevalence of vertigo rises with age and is about two to three times higher in females compared to males. [3] It is often associated with nausea, emesis, and diaphoresis as well as a balance disorder, causing difficulties with standing or walking.

Owing to its diverse etiopathology, treatment modalities with a conventional, single-target, single-molecule approach seems restricted. With different parts of the peripheral and central nervous systems being involved in the etiology, no specific treatment approach from conventional medicine has been absolutely effective. Moreover in patients with chronic vertigo, long term use of these conventional medications has been prohibited due to the adverse effects laid down by them. Thus a multitargeted, multicomponent approach might be an efficient therapeutic option, such as those delivered by bioregulatory therapy with low-dose/ultralow dose medications. Treatment goals are mainly symptomatic, specific, or rehabilitative. Acute vertigo is often self limiting. However, the severity of the illness can substantially diminish the quality of life. In acute care settings, the most relevant decision to be made by the health care practitioner is if vertigo is accompanied by symptoms like new/severe headache or neck pain, blurred vision, hearing loss, difficulties speaking, unconsciousness, falling or problems walking, ataxia, parasthesias, bradycardia/tachycardia, angina pectoris. Further emergency measures, including prompt referral to any specialist or emergency wing, needs to be undertaken. Careful history taking and a proper clinical evaluation are an essential component in guiding diagnosis and treatment initiation in patients without these symptoms. [4] Depending on their etiology though, vestibular diseases can be treated with drugs, physical therapy, psychotherapeutic measures and rarely surgery. Understanding pathophysiology hence plays an important role in deciding the proper pharmacotherapy.

Pathophysiology

Under normal circumstances, the brain relies on three sensory systems to maintain the spatial orientation namely the vestibular system, visual system, and somatosensory system. These systems overlap thereby allowing the brain to assemble an accurate sense of spatial orientation. However, a compromised system or conflicting signals can lead to conditions usually referred as vertigo. Vertigo is due to a disturbance in the vestibular system. The sensory organs for the vestibular system are located in the

bony labyrinths of the inner ear including three semicircular canals which transduce angular acceleration; an otolithic apparatus on each side which transduce linear acceleration; and the static gravitational forces providing a sense of head position in space. The otolithic apparatus consists of tiny particles of calcium carbonate suspended in a gelatinous matrix in two structures called the utricle and saccule. These particles shift in response to movement in a straight line thus stimulating cilia that are embedded in the gel. Movement at an angle is detected by the semicircular canals. [5]

The neural output of the end organs is conveyed to the vestibular nuclei in the brainstem via the eighth cranial nerves. The principal projections from the vestibular nuclei are to the nuclei of cranial nerves III, IV, and VI; spinal cord; cerebral cortex; and cerebellum. The vestibuloocular reflex (VOR) serves to maintain visual stability during head movement and depends on direct projections from the vestibular nuclei to the sixth cranial nerve nuclei in the pons and, via the medial longitudinal fasciculus, to the third and fourth cranial nerve nuclei in the midbrain. These connections account for the nystagmus. The vestibular nerves and nuclei project to areas of the cerebellum that modulate VOR. Glutamate is the major excitatory neurotransmitter acting through the N-methyl D- aspartate (NMDA) receptors in the vestibular nerve fibers. In the vestibular nuclei, cholinergic and H1 histaminergic receptors are the main receptor types. The cholinergic system accounts for neural storage while the histaminergic system is responsible for stimulation of vomiting centre. The GABA-ergic system inhibits signals from the cerebellar Purkinje cells, while the noradrenergic system projecting from the brainstem to the vestibular nuclei inhibits vestibular activity. Stimuli from the gastrointestinal tract are transmitted to the vomiting centre through the serotonergic pathway. The chemoreceptor trigger zone in the area postrema acts on the vomiting centre and can be blocked by D2 dopamine agonists, while the vestibular nuclei act on the vomiting centre through the H1 histaminergic system. The vestibulospinal pathways assist in the maintenance of postural stability. Projections to the cerebral cortex, via the thalamus, provide conscious awareness of head position and movement.[6] Vertigo may represent either physiologic stimulation or pathologic dysfunction in any of the three sensory systems.

PHYSIOLOGIC VERTIGO

This condition is experienced in normal individuals when the brain is confronted with a conflict among the three stabilizing sensory systems or the vestibular system is subjected to unfamiliar head or neck movements to which it is previously unadapted.

Motion sickness is attributed to incongruence in the sensory input from the vestibular, visual, and somatosensory systems. Space sickness, a frequent transient effect of active head movement in the weightless zero-gravity environment, is another example of physiologic vertigo. Height vertigo is instability subjective, from postural and locomotor balance induced by visual, accompanied by the fear of falling, and vegetative symptoms. Physiologic vertigo is usually easily corrected, either by moving the head and neck into a more normal position or focusing on an external reference point to give the vestibular system an opportunity to stabilize.

PATHOLOGIC VERTIGO

Pathologic vertigo results from any lesion or disorders in the visual, somatosensory, or vestibular systems. Visual vertigo is caused by new or incorrect spectacles or by the sudden onset of an extraocular muscle paresis with diplopia; in either instance, CNS compensation rapidly counteracts the vertigo. Somatosensory vertigo is usually due to a peripheral neuropathy or myelopathy that reduces the sensory input necessary for central compensation when there is dysfunction of the vestibular or visual systems. The most common cause of pathologic vertigo is vestibular dysfunction involving labyrinth, nerve, or central connections. The vertigo is frequently accompanied by nausea, jerk nystagmus, postural unsteadiness, and gait ataxia. Since vertigo increases with rapid head movements, patients tend to hold their heads still.[5]

LABYRINTHINE DYSFUNCTION

Under normal circumstances, when the head is straight and immobile, the vestibular end organs generate a tonic resting firing frequency that is equal from the two sides. With any rotational acceleration, the anatomic positions of the semicircular canals on each side necessitate an increased firing rate from one and an equal decrease from the other. This change in neural activity is finally projected to the cerebral cortex, where it is summed with inputs from the visual and somatosensory systems to produce the appropriate conscious sense of rotational movement. After cessation of this movement, the firing frequencies of the two end organs reverse. A sense of rotation in the opposite direction is thus experienced. As there is no actual head movement, this hallucinatory sensation is referred to as **physiologic post rotational vertigo**. Transient abnormalities produce short-lived symptoms. With a fixed unilateral deficit, central compensatory mechanisms ultimately diminish the vertigo. Since compensation depends on the plasticity of connections between the vestibular nuclei and the cerebellum, patients with brainstem or cerebellar disease have reduced adaptive capacity, with symptoms persisting indefinitely. Compensation is always inadequate for severe fixed bilateral lesions despite normal cerebellar connections. These patients are permanently symptomatic.

Acute unilateral labyrinthine dysfunction is caused by infection, trauma, and ischemia. Being mostly idiopathic, nonspecific terms such as acute labyrinthitis, acute peripheral vestibulopathy, or vestibular neuritis are often used to describe the event. The vertiginous attacks are brief and leave the patient with mild vertigo for several days. Infection with herpes simplex virus type 1 has also been implicated. Acute inflammation of the vestibular nerve is a common cause of acute, prolonged vertigo. Associated hearing loss occurs if the labyrinth is involved. The vertigo usually lasts a few days and resolves within several weeks. Many cases of vestibular neuronitis or labyrinthitis are attributed to self-limited viral infections, although specific proof of a viral etiology rarely is identified. Treatment focuses on symptom relief using vestibular suppressant medications, followed by vestibular rehabilitation exercises.[7] Vestibular compensation occurs more rapidly and more completely if the patient begins twice-daily vestibular rehabilitation exercises as soon as tolerated after the acute vertigo has been alleviated with medications. Labyrinthine ischemia occurring due to occlusion of the labyrinthine branch of the internal auditory artery may be the sole manifestation of vertebrobasilar insufficiency. Patients with this syndrome present with the abrupt onset of severe vertigo, nausea, and vomiting, but without tinnitus or hearing loss. Piracetam is a nootropic drug that is a cyclic derivative of GABA. It alleviates vertigo after a head injury or vertigo of central origin, especially in conditions of vertebrobasilar insufficiency by decreasing the frequency and the

severity of exacerbations in patients with chronic or recurrent vertigo. [8]

Acute bilateral labyrinthine dysfunction is usually caused due to toxins such as drugs or alcohol. The most common offending drugs are the aminoglycoside antibiotics that damage the hair cells of the vestibular end organs causing a permanent disorder of equilibrium. Studies have reported positive effects using vitamin B6 on drug-induced vertigo and nausea, suggesting that vitamin B6 appears to offer protection against this form of vertigo. [9]

Recurrent unilateral labyrinthine dysfunction, in association with signs and symptoms of cochlear disease is usually due to Ménière's disease. The terms Ménière's disease and Ménière's syndrome are sometimes used interchangeably. Though both involve the inner ear apparatus, they are not the same disorder. While Ménière's disease develops due to idiopathic causes, Ménière's syndrome is however secondary to other diseases such as inner ear inflammation caused by syphilis, thyroid disease, or head trauma. Of the two, the most common is idiopathic Ménière's disease. Ménière's of either variety is characterized by a broad spectrum of symptoms ranging from vertigo, tinnitus, fluctuating low-frequency sensorineural hearing loss to a sense of fullness in the ear. The condition is also characterized by a condition known as endolymphatic hydrops, or increased hydraulic pressure in the inner ear's endolymphatic system. Impaired endolymphatic filtration and excretion in the inner ear leads to distention of the endolymphatic compartment. However recent researches reveals that endolymphatic hydrops in Ménière's disease may be caused by neurotoxicity and progressive damage to the cochlear nerve in the ear; the increased pressure is a result rather than a cause. [10] Some early research has suggested that nerve cell toxicity is mediated by nitric oxide, which is an important mediator in the inflammatory process. This suggests that agents that block nitric oxide may someday be important in the treatment of Ménière's. [10,11] People with Ménière's disease have been shown to have characteristic abnormalities in their inner ear and an elevated level of free radicals, free radical scavengers may be of benefit in treating Ménière's. Antioxidants mitigate the damaging effects of free radicals on tissues, cell membranes, and DNA. Vitamin C, vitamin E, lipoic acid, and glutathione are among the most important antioxidants. Studies have reported Vitamin C to have beneficial effects on patients with Ménière's disease when given in combination with glutathione, which is a powerful antioxidant. [11] People who have Ménière's may experience severe attacks of vertigo that last 1 to 8 hours. There may also be an aura (such as a sensation of seeing lights or smelling odors). These symptoms may last an indefinite period. In the worst cases, hearing loss is permanent. Treatment aims at lowering endolymphatic pressure. Although a low-salt diet (less than 1 to 2g of salt per day) and diuretics (most commonly the combination of hydrochlorothiazide and triamterene) often reduce the vertigo, these measures are less effective in treating hearing loss and tinnitus. Calcium channel blocker nimodipine was shown to be effective in Ménière's disease. In rare cases, surgical intervention, such as decompression with an endolymphatic shunt or cochleosacculotomy, may be required when Ménière's disease is resistant to treatment with low salt diet and diuretics. Ablation of the vestibular hair cells with intratympanic injection of gentamicin may also be effective.[12] However surgery is usually reserved for patients with severe, refractory Ménière's disease.

Positional vertigo is precipitated by a recumbent head position, either to the right or to the left. *Benign paroxysmal positional vertigo* (BPPV) of the posterior semicircular canal occurring after a sudden movement of the head is one of the most common types of vertigo .Women are affected twice as often as men, and the average age of onset is the mid-50s. BPPV is usually harmless and idiopathic, however, in some cases it is caused by age-related degeneration or head trauma. Patients with BPPV have short-lived episodes of temporary dizziness, lightheadedness, imbalance, and nausea generally abating spontaneously after weeks or months. Symptoms of BPPV, which usually develop suddenly after a change in head position, may be severe enough to cause vomiting. Typical motions that cause episodes of BPPV include getting out of bed, rolling over, bending down, and looking up while standing. One of the characteristic symptoms of BPPV is rapid movement of the eye in one direction followed by a slow drift back to its original position, commonly referred as a type of nystagmus having a distinct pattern of latency, fatigability, and habituation that differs from the less common central positional vertigo due to lesions in and around the fourth ventricle. When supine, with the head turned to the side of the offending ear, the lower eye displays a large-amplitude torsional nystagmus, and the upper eye has a lesser degree of torsion combined with upbeating nystagmus. If the eyes are directed to the upper ear, the vertical nystagmus in the upper eye increases in amplitude. Mild disequilibrium when upright may also be present. BPPV is caused by calcium debris in the semicircular canals (canalithiasis), usually the posterior semicircular canal. This renders the canal oversensitive to the pull of gravity, producing a constant sense of motion or falling. Medications generally are not recommended for the treatment of this condition. The vertigo improves with head rotation maneuvers that displace free-moving calcium deposits back to the vestibule. Maneuvers include the canalith repositioning procedure or Epley maneuver[13] and the modified Epley maneuver[14]. The modified Epley maneuver can be performed at home. Patients may need to remain upright for 24 hours after canalith repositioning to prevent calcium deposits from returning to the semicircular canals, although this measure is not universally recommended. Epley maneuver is concluded to be a safe treatment that is likely to result in improvement of symptoms and conversion from a positive to negative Dix-Hallpike maneuver. Contraindications to canalith repositioning procedures include severe carotid stenosis, unstable heart disease, and severe neck disease, such as cervical spondylosis with myelopathy or advanced rheumatoid arthritis.[15] Canalith repositioning has been found to be effective in patients with benign paroxysmal positional vertigo.

A **perilymphatic fistula** is usually suspected when episodic vertigo is precipitated by Valsalva or exertion, accompanied with a progressive sensory-neural hearing loss. The condition is usually caused by head trauma or barotrauma or occurs after middle ear surgery.

VERTIGO OF VESTIBULAR NERVE ORIGIN

Having many of the characteristics of labyrinthine vertigo, this condition involve the nerve in the petrous bone or the cerebellopontine angle The adjacent auditory division of the eighth cranial nerve is usually affected due to tumor, usually a schwannoma (acoustic neuroma) or a meningioma. These tumors grow slowly leading to such a gradual reduction of labyrinthine output that central compensatory mechanisms can prevent or minimize the vertigo. Auditory symptoms of hearing loss and tinnitus are the most common manifestations. Acute

inflammation of the vestibular nerve is a common cause of acute, prolonged vertigo. The vertigo usually lasts a few days and resolves within several weeks. Many cases of vestibular neuronitis or labyrinthitis are attributed to self-limited viral infections.[16] Treatment concentrates on symptomatic relief using vestibular suppressant medications, followed by vestibular rehabilitation exercises. Vestibular compensation occurs more rapidly and more completely if the patient begins twice-daily vestibular rehabilitation exercises as soon as tolerated after the acute vertigo has been alleviated with medications.

CENTRAL VERTIGO

Lesions of the brainstem or cerebellum can cause acute vertigo. Occasionally, an acute lesion of the vestibulocerebellum may present with monosymptomatic vertigo indistinguishable from a labyrinthopathy. Vertigo may be a manifestation of a migraine aura but some patients with migraine have episodes of vertigo unassociated with their headaches. Antimigrainous treatment should be considered in such patients with otherwise enigmatic vertiginous episodes. Vestibular epilepsy, vertigo secondary to temporal lobe epileptic activity, is rare and almost always intermixed with other epileptic manifestations.

However vertiginous migraine has been reported to respond better to migraine treatments than to other interventions. Treatments include dietary changes involving reduction or elimination of aspartame, chocolate, caffeine, or alcohol. Lifestyle changes include exercise, stress reduction, improvements in sleep patterns. Medications such as benzodiazepines, tricyclic antidepressants, beta blockers, selective serotonin reuptake inhibitors [SSRIs], calcium channel blockers and antiemetics accompanied with vestibular rehabilitation exercises forms a part of the treatment approach. [17]

PSYCHOGENIC VERTIGO

Vertigo commonly is associated with anxiety disorders (e.g., panic disorder, generalized anxiety disorder) and, less frequently, depression. Hyperventilation usually occurs and can result in hypocapnia with reversible cerebral vasoconstriction. Hyperventilation and hypocapnia, accompanied by dyspnea, chest pain, palpitations, or parasthesias often occurs. A psychogenic etiology is almost certain when nystagmus is absent during a vertiginous episode. Subclinical vestibular dysfunction has been measured in patients with anxiety disorders or depression, most commonly panic disorder with moderate to severe agoraphobia.[18] Conversely, classic vertigo resulting from more ostensible vestibular pathology usually induces severe anxiety symptoms and thus can be hard to distinguish from a primary anxiety disorder.

Vestibular suppressants and benzodiazepines most frequently are used to treat dizziness that is associated with anxiety disorder, but these medications provide only transient or inadequate relief. SSRIs such as citalopram, fluoxetine, paroxetine, and sertraline may provide better relief.[19] Other medications that are effective in patients with anxiety disorders or depression, such as norepinephrine- serotonin reuptake inhibitors (e.g., venlafaxine) and tricyclic antidepressants (e.g., nortriptyline, desipramine) have not been evaluated in patients with concomitant vertigo. Nonpharmacologic treatments for anxiety disorders, such as cognitive behavior therapy, may be helpful.

MISCELLANEOUS HEAD SENSATIONS

This category broadly describes conditions like dizziness that are neither faintness nor vertigo. Cephalic ischemia or vestibular dysfunction may be of such low intensity that the usual symptomatology remains unidentifiable. For example, a small decrease in blood pressure or a slight vestibular imbalance may cause sensations different from distinct faintness or vertigo but that may be identified properly during provocative testing techniques. Other causes of dizziness in this category are hyperventilation syndrome, hypoglycemia, and the somatic symptoms of a clinical depression. These patients should all have normal neurologic examinations and vestibular function tests.

CONCLUSION

With high incidence of patients presenting with vestibular complaints in the otolaryngology clinic, it becomes mandate for the clinician to use his expertise in selecting specific drugs for optimum patient benefit. Pharmacotherapy of vertigo is optimized when the prescriber has detailed knowledge of the pathophysiology of vertigo and proper understanding of etiology of the condition presented with. Various clinical studies are being conducted to search newer drugs which would address the unmet needs experienced in the treatment of vertigo.

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REFERENCES

1. Von Brevern, M; Neuhauser, H. Epidemiological evidence for a link between vertigo and migraine. Journal of vestibular research: equilibrium & orientation, 2011; 21(6): 299304.
2. Neuhauser HK, Lempert T. Vertigo: epidemiologic aspects. Semin Neurol , 2009;29 (5): 47381. [PUBMED]
3. Jonsson R, Sixt E, Landahl S, Rosenhall U. Prevalence of dizziness and vertigo in an urban elderly population. J Vestib Res. 2004;14(1):47-52.
4. Mundhenke M. Vertigo: A Common Problem in Clinical Practice. Journal of Biomedical Therapy 2010; 4(2):17-21
5. Daroff RB, Carlson MD. Syncope, Faintness, Dizziness, and Vertigo. Isselbacher KJ, Braunwald E, Wilson JD, Martin JB, Fauci AS, Kasper DL, eds. Harrison's Principles of Internal Medicine. 16th ed. McGraw-Hill 2005:131-33.
6. Singh KR, Singh M. Current perspectives in the pharmacotherapy of vertigo. Otorhinolaryngology Clinics: An International Journal 2012; 4(2):81-85
7. Baloh RW. Vertigo in older people. Curr Treat Options Neurol 2000; 2:81-9.
8. Oosterveld WJ. The effectivess of piracetam in vertigo. Pharmacopsychiatry 1999; 32(Suppl 1):52-60.
9. Claussen CF, Claussen E. Antivertiginous action of vitamin B 6 on experimental minocycline-induced vertigo in man. Arzneimittelforschung. 1988 ; 38(3):396-9.
10. Semaan M. T., Alagramam K. N., Megerian C. A. The basic science of Meniere's disease and endolymphatic hydrops. Curr. Opin. Otolaryngol. Head Neck Surg. 2005; 13: 301307
11. Takumida M., Anniko M., Ohtani M. Radical scavengers for Meniere's disease after failure of conventional therapy: a pilot study. Acta Otolaryngol. 2003;123: 697703

12. Blakley BW. Update on intratympanic gentamicin for Meniere's disease. Laryngoscope 2000;110(2 pt 1):236-40.

13. Wrisley DM, Whitney SL, Furman JM. Vestibular rehabilitation outcomes in patients with a history of migraine. Otol Neurotol 2002;23:483-7.

14. Strupp M, Arbusow V, Maag KP, Gall C, Brandt T. Vestibular exercises improve central vestibulospinal compensation after vestibular neuritis. Neurology 1998;51:838-44.

15. Epley JM. The canalith repositioning procedure: for treatment of benign paroxysmal positional vertigo. Otolaryngol Head Neck Surg 1992; 107:399-404.

16. Baloh RW. Vestibular neuritis. N Engl J Med 2003; 348:1027-32

17. Johnson GD. Medical management of migraine-related dizziness and vertigo. Laryngoscope 1998;108(1 pt 2):1-28.

18. Jacob RG, Furman JM, Durrant JD, Turner SM. Panic, agoraphobia, and vestibular dysfunction. Am J Psychiatry 1996; 153:503-12.

19. Staab JP, Ruckenstein MJ, Solomon D, Shepard NT. Serotonin reuptake inhibitors for dizziness with psychiatric symptoms. Arch Otolaryngol Head Neck Surg 2002;128:554-60.