

Perspectives in the Management of Vertigo and Dizziness: A Review

SHRINIVAS CHAVAN

ABSTRACT

Dizziness is a term which includes a wide range of medical disorders, which makes a stepwise approach towards its differential diagnosis as well as management very important. The condition is not only seen frequently in the general population, but also in a wide range of pathologies. This makes its accurate diagnosis a challenge for the physician. The different treatment approaches include drugs, physical therapy and psychotherapeutic measures based on the diagnosis. A review was conducted to study the prevalence of vertigo and dizziness, its impact on the quality-of-life of the patients, the challenges faced by a primary physician and the current management strategies for vertigo and dizziness.

Keywords: Dizziness, vertigo, management, diagnosis

Dizziness is a common and challenging condition seen in the primary care setting. Estimates show that more than one-third of Americans see a healthcare provider for dizziness during their lifetime. Dizziness is a vague term which may incorporate a wide array of medical disorders, hence, a stepwise approach to differentially diagnose the cause becomes important.¹

The etiology of vertigo and dizziness is often multifactorial. The most common causes of vertigo and dizziness are cited to be peripheral and central vestibular diseases; however, they can also be provoked by cardiovascular diseases, polyneuropathy, medication or they can have a psychosomatic origin.²

There are four common types of dizziness: (1) Presyncope, (2) disequilibrium, (3) psychogenic dizziness and (4) vertigo. While assessing the patient, the doctor should specifically ask the patient to explain their symptoms. Vertigo is a false sense of motion of either the environment or self. Patients describe vertigo as either 'the room is spinning' or 'tilting'. There are four common causes of vertigo in ambulatory settings, including benign paroxysmal peripheral vertigo (BPPV), vestibular neuritis, vestibular migraine and Meniere's disease.¹

The present article discusses the prevalence of vertigo and dizziness, challenges faced in their diagnosis and treatment, and the therapy available for the management.

METHODOLOGY

PubMed, Cochrane database and Google Scholar were the databases used for the literature search. The search strategy included a combination of 'key word search' and 'backward chronological search'. The search terms included dizziness, vertigo, epidemiology, prevalence, incidence, treatment, management, diagnosis, guidelines. Boolean operators were used for the search. Forty original research articles, systematic reviews and meta-analyses were included for the development of this review (Table 1).

PREVALENCE OF VERTIGO AND DIZZINESS

Vertigo and dizziness as symptoms are seen in a wide range of pathologies and occur frequently in the population. One of the challenges associated with them is the difficulty in making an accurate diagnosis.³

It has been reported in a study that the prevalence of dizziness in the world population is 5-10% and the prevalence rate in individuals older than 65 years is 65%.⁴ It has been reported in large population-based studies that annually, dizziness (including vertigo) affects about 15% to over 20% of adults. Vestibular vertigo accounts for about a quarter of dizziness complaints and has a 12-month prevalence of 5% and an annual incidence of 1.4%. Its prevalence

Professor and Head
Dept. of ENT
Grant Government Medical College and Sir JJ Hospital, Mumbai, Maharashtra
E-mail: shrinivasc77@hotmail.com

Table 1. Literature Search Strategy

Databases	Search terms	Result	Comments
PubMed, Cochrane, Google Scholar	Dizziness, vertigo, epidemiology, prevalence, incidence, treatment, management, diagnosis, guidelines	40 Original research articles + systematic reviews + meta-analyses	Published literature corresponding only to human subjects and in English language were selected

rises with age and is about 2-3 times higher in women than in men.⁵

Global data has shown that about 1 out of 3 elderly people suffers from dizziness.⁵ The 1-year prevalence of dizziness was reported to be 18.2% in a community of elderly population.⁶ Vertigo and dizziness occur with considerable frequency in childhood and adolescence. Most causes are benign and can be treated.⁷

There is a dearth of prevalence data from India. A study conducted in rural population in India reported an overall prevalence of 0.71%.⁸ The most commonly reported vertigo was psychogenic form in this population. However, another study conducted across many centers in India reported that BPPV accounted for a considerable percentage of the overall burden of vertigo. It was reported in this study that peripheral causes were predominant in majority (74%), with BPPV being the most frequent (68%). Other causes, like migraine, were second in occurrence which was mainly associated with lifestyle issues.⁹

Another study conducted in a teaching tertiary care hospital in Central India reported the magnitude of vertigo in geriatric patients attending outpatient clinic to be 3%, inflicting a considerable healthcare burden. In this study, it was found that BPPV was prevalent in 22% of the study population, while 78% constituted the non-BPPV group.¹⁰

IMPACT ON THE QUALITY-OF-LIFE

With vertigo becoming a growing public health problem, patients with vertigo often experience intense emotional distress, with symptoms of anxiety, fear and depression. Moreover, patients with new onset of vertigo, imbalance, nausea and vomiting pose significant challenge. The various physical, emotional and functional disturbances associated with vertigo may impact the professional, social and overall day-to-day activities of these patients. Available evidence suggests that the impact of vertigo on the health-related quality-of-life (QoL) may be significantly underestimated.¹¹⁻¹³

Several studies have been conducted showing the impact of vertigo on overall QoL,¹⁴⁻¹⁷ emphasizing on the fear of new vertigo attacks, increase in distress and

phobias because of labyrinthopathies.¹⁷⁻¹⁹ There are a limited number of studies assessing the QoL of Indian patients with vertigo. A recent study has suggested that 50% of patients with vertigo present with the symptoms such as nausea and vomiting, which are known to have significantly negative impact on overall QoL.⁹

The patients presenting with vertigo often experience falls and suffer from postural instability, disturbances and risk of falling. Patients suffering with central syndromes are at risk of recurrent and injurious falls.^{20,21} In this regard, it is important to adopt an individualized approach for the management of vertigo.

CHALLENGES IN THE MANAGEMENT OF DIZZINESS AND VERTIGO IN THE PRIMARY CARE PHYSICIAN'S CLINIC

Dizziness and vertigo are some of the most common reasons for seeking medical help but are often inaccurately diagnosed. The management of acute dizziness and vertigo require interdisciplinary cooperation.²² Various balance disorders which present with symptoms of dizziness and vertigo are due to various diseases. The appropriate clinical approach provides an opportunity to timely identify emergency situations and most common causes.²³

The choice of therapy (liberatory maneuvers of misplaced otoliths, physiotherapy, prescription of medications, adjustment of medication regimes or cognitive behavioral therapy) is dependent on an accurate diagnosis of the underlying cause of the symptoms.²⁴ Despite the fact that once accurately diagnosed, the treatment follows a simple straightforward path, a cloud of uncertainty still hovers over the management of vertigo in primary physician's care.^{24,25}

Evidences suggest that there are almost 86% of cases which could have been correctly diagnosed by the primary and secondary care physicians who otherwise received a diagnosis of 'unspecific dizziness' and hence incorrect treatment.² The responsibility of deciding on the diagnostic approach for the patient lies with the primary care physician who will decide on initiating

diagnostic procedures and treatment or to refer the patient to the appropriate specialist.²⁶ If the assessment at the primary care physician level is not correct, the patient may have to bear the brunt of redundant or unnecessary procedures and medication intake.² Evidence suggests that there is an unmet need with respect to the diagnostic and therapeutic requirements of patients with vestibular disease.²⁴ This leads to chronification and the development of secondary, functional symptoms.²⁷ Data shows that almost 45% vertigo and dizziness patient's first contact with healthcare is with the primary care physician and hence the expertise of a primary care physician is of utmost importance.²⁸

MANAGEMENT APPROACH IN THE TREATMENT OF VERTIGO AND DIZZINESS

It is clear now that the difficulty associated with the treatment of vertigo is due to the fact that it is not a definite disease but a symptom. It usually occurs due to a disturbance in the vestibular system. There are various modes of treatment of the vestibular diseases, dependent on the etiology. These include drugs, physical therapy, psychotherapeutic measures and rarely, surgery. Physical therapy has also emerged as an effective modality in the management of balance disorders.²⁹

The specific regimen of drug therapy can be tailored for the treatment of vertigo based on the four broad causes of vertigo. Otological vertigo includes disorders of the inner ear including Meniere's disease, vestibular neuritis, BPPV and bilateral vestibular paresis. In both Meniere's disease and vestibular neuritis, vestibular suppressants such as anticholinergics and benzodiazepines are used. In Meniere's disease, salt restriction and diuretics are recommended to prevent flare-ups. In vestibular neuritis, only brief use of vestibular suppressants is now recommended. In the case of BPPV and bilateral vestibular paresis, drug treatment is not recommended. However, physical therapy can be very useful in both these conditions.³⁰

In cases of central vertigo, such as vertigo associated with migraine, prophylactic agents (calcium channel antagonists, tricyclic antidepressants, β -blockers) are the mainstay of treatment. In individuals with stroke or other structural lesions of the brainstem or cerebellum, an eclectic approach incorporating trials of vestibular suppressants and physical therapy is recommended. Undetermined and ill-defined causes of vertigo make up a large proportion of diagnoses and an empirical approach to these patients, incorporating trials of medications of general utility, such as benzodiazepines,

as well as trials of medication withdrawal when appropriate, physical therapy and psychiatric consultation, is recommended.³⁰

Pharmacotherapy plays a crucial role in the management of vertigo. There is no ideal drug for the treatment of vertigo, and most of the existing drugs have essentially been found during clinical use rather than developed specifically for the treatment of vertigo.³¹

PHARMACOTHERAPY IN THE MANAGEMENT OF VERTIGO AND DIZZINESS

Till date, the information available on the drug treatment of vertigo is scarce owing to the absence of multicentric, well-controlled clinical studies to show the advantage of treatment over no treatment.³²

Medications are most useful in treating acute vertigo, which lasts a few hours to several days. However, vertigo lasting more than a few days is suggestive of a permanent vestibular injury and medications should be stopped in this case to allow the brain to adapt to a new vestibular input.³¹ The various drugs used in the pharmacotherapy of vertigo and dizziness may either modify the intensity of symptoms (e.g., vestibular suppressants) or they may affect the underlying disease process (e.g., calcium channel antagonists in the case of vestibular migraine). Most of these agents, especially those that are sedating, also have a potential to modulate the rate of compensation for vestibular damage.

Vestibular Suppressants

Vestibular suppressants are the mainstay of treatment in patients suffering from vertigo today. They work by reducing the asymmetry in the vestibular tone between the ears and hence reducing the vertigo.³³ The drugs included in this category comprise of anticholinergics, antihistaminics, antidopaminergic drugs and benzodiazepines.

Acute vertigo is usually managed with vestibular suppressants and antiemetic medications. It is recommended that vestibular suppressants should be used for a few days at most because they delay the brain's natural compensatory mechanism for peripheral vertigo.³¹ It has been seen that among the various vestibular suppressants, cinnarizine and prochlorperazine are the most frequently prescribed drugs by the general physician. However, the expert opinion suggests that precaution should be exercised while prescribing prochlorperazine in patients at extremes of age.²⁰

A study was conducted to comparatively assess prochlorperazine versus cinnarizine in cases of vertigo.

An equal number of cases, selected randomly, underwent treatment with prochlorperazine ± head balance exercises and cinnarizine ± head balance exercises. At the end of 5 weeks treatment, it was seen that there was 100% subjective improvement with prochlorperazine as compared to 97.14% in cinnarizine group. Fewer side effects were seen in the case of prochlorperazine with drowsiness being the most common side effect, and was statistically more significant with cinnarizine group. The response to the treatment was significantly more in cases with vertigo of peripheral origin as compared with vertigo of central origin.³⁴

Anticholinergics

These act on muscarinic receptors and increase motion tolerance. Only centrally acting anticholinergics are useful in treating vertigo. The most effective agent in this category to prevent vertigo is scopolamine.³⁵ These are associated with prominent side effects such as dry mouth, dilated pupils, sedation, decreased alertness and impaired attention. If scopolamine transdermal patch is used for a long duration, it may lead to chemical addiction.³⁶

Antihistamines

The most commonly prescribed drugs for vertigo include H1 blockers which include diphenhydramine, cyclizine, dimenhydrinate, meclizine and promethazine.^{37,38} This is the only class of drug which has been cited to possess antivertigo properties.³⁹ They have lesser side effects as compared to anticholinergics.

Histaminergic medications

This class of drugs is represented by betahistine whose antivertigo effects are attributable to vasodilatory effect, improving blood flow in the microcirculation of the internal auditory and vestibular systems. There is low quality evidence to suggest that in patients suffering from different causes there may be a positive effect of betahistine in terms of reduction of vertigo symptoms.⁴⁰

A double-blind crossover trial was conducted to compare the therapeutic effects of prochlorperazine and betahistine on patients with confirmed Meniere's disease (range of duration 1-11 years). In spite of the superior therapeutic efficacy of betahistine, it was observed in the study that the number of vertigo attacks were reduced to an equal value by both the drugs. In addition, side effects were not seen with both betahistine and prochlorperazine.⁴¹

Dopaminergic antagonists

These drugs are commonly used to control nausea in vertiginous patients.⁴² Dopaminergic antagonists

such as prochlorperazine and chlorperazine act at the chemoreceptor trigger zone, reducing the neural impulses to the vomiting center.³¹

Various antipsychotics namely phenothiazine derivatives and butyrophenones are popularly used in this condition. They reduce the neurovegetative symptoms that commonly parallel vertigo and may improve the psychoaffective symptoms accompanying vertigo. The specific dopaminergic vestibular effects along with anticholinergic and antihistaminic (H1) properties of these drugs lead to their vestibular suppressant activity.⁴²

Prochlorperazine improves vestibular as well as associated vegetative symptoms of vertigo. In addition to its anticholinergic and antidopaminergic activity, prochlorperazine acts on serotonergic neurotransmitter system and hence could be the reason for being the drug of choice for short-term symptomatic management of vertigo associated with anxiety as a psychiatric comorbidity. Further, prochlorperazine is less sedative than cinnarizine and cinnarizine combinations and other fixed-dose combinations of vestibular suppressants. It has also been recommended that if prochlorperazine is prescribed for short-term (up to 7 days), symptomatic management of vertigo, there are no concerns regarding the extrapyramidal symptoms.²⁰

Benzodiazepines

These cause vestibular suppression through the gamma-aminobutyric acid (GABA)ergic system. Benzodiazepines enhance the role of GABA in the central nervous system and hence are effective in relieving vertigo and associated anxiety and panic disorders. The commonly prescribed benzodiazepines are diazepam, lorazepam, clonazepam, alprazolam and cause muscle relaxation, anterograde amnesia and muscle relaxation.⁴²

Calcium antagonists

Drugs such as cinnarizine and flunarizine have been used as antivertigo drugs and prevent motion sickness and are used as vestibular depressants. These drugs also possess anticholinergic, antihistaminergic and antidopaminergic action.⁴²

Sympathomimetics

These drugs are used to enhance vigilance and counterbalance the sedative effects of other antivertigo drugs such as antihistaminics. These drugs are rare in use because they have addictive potential.⁴²

Table 2. Medications Commonly used in the Treatment of Acute Vertigo and Associated Nausea and Emesis (Treatment of Vertigo)

Medication	Class	Dosage	Sedation	Antiemesis
Meclizine	Antihistamine	12.5-50 mg oral every 4-8 hours	Moderate	Mild
Dimenhydrinate	Antihistamine	25-100 mg orally, IM or IV every 4-8 hours	Mild	Moderate
Diazepam	Benzodiazepine	2-10 mg orally or IV every 4-8 hours	Moderate	Mild
Lorazepam	Benzodiazepine	0.5-2 mg orally, IM or IV every 4-8 hours	Moderate	Mild
Metoclopramide	Dopaminergic antagonist	5-10 mg orally or IM every 6 hours	Mild	Prominent
Prochlorperazine	Dopaminergic antagonist (phenothiazine)	5-10 mg orally or IM every 6-8 hours 25 mg rectally every 12 hours 5-10 mg by slow IV over 2 minutes	Mild	Prominent
Promethazine	Antihistamine	12.5-25 mg orally, IM, or rectally every 4-12 hours	Prominent	Moderate

IM = Intramuscular; IV = Intravenous.

Source: Swartz R, Longwell P. Treatment of vertigo. *Am Fam Physician*. 2005;71(6):1115-22.

A list of medications commonly used in treatment of acute vertigo and associated nausea and emesis is given in Table 2.⁴³

CONCLUSION

Vertigo is a type of dizziness, best described as the, 'illusion of motion, usually rotational motion'. Associated symptoms include nausea, emesis and diaphoresis. Vertigo can have multiple causes, especially in older patients and hence a specific diagnosis can sometimes be elusive. Medications are most useful for treating acute vertigo that lasts a few hours to several days. However, they have limited benefits in patients with BPPV, because the vertiginous episodes usually last less than 1 minute, while vertigo lasting more than a few days is suggestive of permanent vestibular injury and warrants cessation of medications. It has been seen that there is a need for alternative approaches for the management of vertigo, emphasizing timing and triggers over type, as the investigating factor. Vestibular suppressants are found to be crucial in the management of acute phase vertigo. Given the heterogeneity of treatment effect, a link between patient presentation and the type of molecule is quintessential. Prochlorperazine acts on serotonergic neurotransmitter system and this could be the reason for it being the drug of choice for short-term symptomatic management of dizziness or vertigo associated with anxiety and vomiting. Cinnarizine is more efficacious in peripheral vertigo, without nausea and vomiting. Vestibular rehabilitation therapy has also emerged as a highly effective modality for most of the disorders of the vestibular or central balance system.

REFERENCES

1. Wiperman J. Dizziness and vertigo. *Prim Care*. 2014;41(1):115-31.
2. Geser R, Straumann D. Referral and final diagnoses of patients assessed in an academic vertigo center. *Front Neurol*. 2012;3:169.
3. Bécares Martínez C, Arroyo Domingo MM, López Llamas A, Marco Algarra J, Morales Suárez-Varela MM. Vertigo and dizziness in hospital: Attendance, flow and characteristics of patients. *Acta Otorrinolaringol Esp*. 2017. pii: S0001-6519(17)30173-5. [Epub ahead of print]
4. Santana GG, Doná F, Ganança MM, Kasse CA. Vestibulopathy in the elderly. *Collective Health*. 2011;8(48):52-6.
5. Neuhauser HK. The epidemiology of dizziness and vertigo. *Handb Clin Neurol*. 2016;137:67-82.
6. Sloane P, Blazer D, George LK. Dizziness in a community elderly population. *J Am Geriatr Soc*. 1989;37(2):101-8.
7. Jahn K, Langhagen T, Heinen F. Vertigo and dizziness in children. *Curr Opin Neurol*. 2015;28(1):78-82.
8. Abrol R, Nehru VI, Venkatramana Y. Prevalence and etiology of vertigo in adult rural population. *Indian J Otolaryngol Head Neck Surg*. 2001;53(1):32-6.
9. Kameswaran M, Pujari S, Singh J, Basumatary LJ, Sarda K, Pore R. Clinicoetiological pattern and pharmacotherapy practices in patients with new onset vertigo: findings from a prospective multicentre registry in India. *Int J Otorhinolaryngol Head Neck Surg*. 2017;3(2):404-13.
10. Saxena A, Prabhakar MC. Performance of DHI score as a predictor of benign paroxysmal positional vertigo in geriatric patients with dizziness/vertigo: a cross-sectional study. *PLoS One*. 2013;8(3):e58106.
11. Ten Voorde M, van der Zaag-Loonen HJ, van Leeuwen RB. Dizziness impairs health-related quality of life. *Qual Life Res*. 2012;21(6):961-6.

12. Grauvogel J, Kaminsky J, Rosahl SK. The impact of tinnitus and vertigo on patient-perceived quality of life after cerebellopontine angle surgery. *Neurosurgery*. 2010;67(3):601-9; discussion 609-10.
13. Weidt S, Bruehl AB, Straumann D, Hegemann SC, Krautstrunk G, Rufer M. Health-related quality of life and emotional distress in patients with dizziness: a cross-sectional approach to disentangle their relationship. *BMC Health Serv Res*. 2014;14:317.
14. Handa PR, Kuhn AM, Cunha F, Schaffleln R, Ganança FF. Quality of life in patients with benign paroxysmal positional vertigo and/or Ménière's disease. *Braz J Otorhinolaryngol*. 2005;71(6):776-82.
15. Grimby A, Rosenhall U. Health-related quality of life and dizziness in old age. *Gerontology*. 1995;41(5):286-98.
16. Hsu LC, Hu HH, Wong WJ, Wang SJ, Luk YO, Chern CM. Quality of life in elderly patients with dizziness: analysis of the Short-Form Health Survey in 197 patients. *Acta Otolaryngol*. 2005;125(1):55-9.
17. Santos EM, Gazzola JM, Ganança CF, Caovilla HH, GanançaFF. Impact of dizziness on the life quality of elderly with chronic vestibulopathy. *Pro Fono*. 2010;22(4):427-32.
18. Savastano M, Maron MB, Mangialaio M, Longhi P, Rizzardo R. Illness behaviour, personality traits, anxiety, and depression in patients with Ménière's disease. *J Otolaryngol*. 1996;25(5):329-33.
19. Kuhn AMB, Bocchi EA, Bulbarelli K, Casagrande MC. Vertigo and its psychological implications. In: Ganança MM, Vieira RM, Caovilla HH (Eds.). *Principles of Otoneurology*. São Paulo: Atheneu; 1998. pp. 101-5.
20. Prabhat D, Kulkarni GB, Kelkar P. Management approach to vertigo at primary care level in India: an expert opinion. *Indian J Clin Pract*. 2018;28(10):923-30.
21. Hanley K, O'Dowd T. Symptoms of vertigo in general practice: a prospective study of diagnosis. *Br J Gen Pract*. 2002;52(483):809-12.
22. Löhler J, Eßer D, Wollenberg B, Walther LE. Management of acute vertigo and dizziness: Patients in emergency departments in Germany. *HNO*. 2018 Mar 2. [Epub ahead of print]
23. Bouccara D, Rubin F, Bonfils P, Lisan Q. Management of vertigo and dizziness. *Rev Med Interne*. 2018. pii: S0248-8663(18)30040-7. [Epub ahead of print]
24. Grill E, Strupp M, Müller M, Jahn K. Health services utilization of patients with vertigo in primary care: a retrospective cohort study. *J Neurol*. 2014;261(8):1492-8.
25. Kruschinski C, Kersting M, Breull A, Kochen MM, Koschack J, Hummers-Pradier E. Frequency of dizziness-related diagnoses and prescriptions in a general practice database. *Z Evid Fortbild Qual Gesundheitswes*. 2008;102(5):313-9.
26. Rieger A, Mansmann U, Maier W, Seitz L, Brandt T, Strupp M, et al. Management of patients with the cardinal symptom dizziness or vertigo. *Gesundheitswesen*. 2014;76(6):e32-8.
27. Dieterich M, Staab JP. Functional dizziness: from phobic postural vertigo and chronic subjective dizziness to persistent postural-perceptual dizziness. *Curr Opin Neurol*. 2017;30(1):107-13.
28. Grill E, Penger M, Kentala E. Health care utilization, prognosis and outcomes of vestibular disease in primary care settings: systematic review. *J Neurol*. 2016;263 Suppl 1:S36-44.
29. Biswas A, Barui B. Specific organ targeted vestibular physiotherapy: the pivot in the contemporary management of vertigo and imbalance. *Indian J Otolaryngol Head Neck Surg*. 2017;69(4):431-42.
30. Hain TC, Uddin M. Pharmacological treatment of vertigo. *CNS Drugs*. 2003;17(2):85-100.
31. Trkanjec Z, Aleksic-Shibabi A, Demarin V. Pharmacotherapy of vertigo. *Rad Za Medicinska Znanosti, Zagreb*. 2007:69-76.
32. Ruckenstein MJ, Rutka JA, Hawke M. The treatment of Ménière's disease: Torok revisited. *Laryngoscope*. 1991;101(2):211-8.
33. Daroff, R. Dizziness, vertigo. In: Fauci, AS, et al (Eds.). *Principles of Internal Medicine*. Vol. 298, New York: McGraw-Hill, n.d. 144.
34. Singh AK, Chaturvedi VN. Prochlorperazine versus cinnarizine in cases of vertigo. *Indian J Otolaryngol Head Neck Surg*. 1998;50(4):392-7.
35. Takeda N, Morita M, Hasegawa S, Kubo T, Matsunaga T. Neurochemical mechanisms of motion sickness. *Am J Otolaryngol*. 1989;10(5):351-9.
36. Luetje CM, Wooten J. Clinical manifestations of transdermal scopolamine addiction. *Ear Nose Throat J*. 1996;75(4):210-4.
37. Cohen B, DeJong JM. Meclizine and placebo in treating vertigo of vestibular origin. Relative efficacy in a double-blind study. *Arch Neurol*. 1972;27(2):129-35.
38. Bickerman, H. Drugs for disturbances in equilibrium. In: Modell W (Ed.). *Drugs of Choice 1978-79*. St Louis (MO): CV Mosby Co; 1978. pp. 502-11.
39. Gilman, A, Rall T, Nies A, et al (Eds.). *Goodman and Gilman's Pharmacological Basis of Therapeutics*. New York: Pergamon Press; 1990. p. 585.
40. Murdin L, Hussain K, Schilder AG. Betahistine for symptoms of vertigo. *Cochrane Database Syst Rev*. 2016;(6):CD010696.
41. Aantaa E, Skinhoj A. Controlled clinical trial comparing the effect of betahistine hydrochloride and prochlorperazine maleate on patients with Ménière's disease. *Ann Clin Res*. 1976;8(4):284-7.
42. Singh KR, Singh M. Current perspectives in the pharmacotherapy of vertigo. *Otorhinolaryngology Clinics: An International Journal*. 2012;4(2):81-5.
43. Swartz R, Longwell P. Treatment of vertigo. *Am Fam Physician*. 2005;71(6):1115-22.