The Use of Antiserotonin Drugs in the Nucleoreticular Vestibular Syndrome: Preliminary Observations

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Abstract: Vestibular neuronitis was described in 1949 and 1952 by Dix and Hallpike. Two groups of patients were described, those with sudden seizures and sensations of blackout (since identified as having vestibular neuritis) and a second group with symptoms of disequilibrium and feelings of top-heaviness or imbalance. The pathology was believed to be central to the inner ear. Arslan labeled these groups as having nucleoreticular vestibular syndrome. Using a suprathreshold stapedial reflex test, Bosatra localized the pathophysiology in the brainstem, an area rich in serotonergic neurons. This author has used antiserotonergic drugs, with success, in treating patients having the symptoms identified by Dix and Hallpike in their second group (which now should be labeled nucleoreticular vestibular syndrome), properly identified as a brainstem affliction. This study describes the characteristics of this disorder, the methods of diagnosis and treatment, and the outcomes in two groups of patients studied. The study concluded that antiserotonin drugs, specifically affecting 5-hydroxytryptamine2, should be considered in the management of nucleoreticular vestibular syndrome.

Key Words: antiserotonin drugs; nucleoreticular vestibular syndrome; vestibular neuritis

BACKGROUND

Vestibular neuronitis was first described by Dix and Hallpike in 1949 [1] and then in 1952 [2] as a term to indicate the uncertain location of a vestibular syndrome without cochlear symptoms. The vestibular neurons originate in the inner ear, have their cell bodies in Scarpa’s ganglion, and communicate with the brainstem through axons that make up the vestibular nerve. Dix and Hallpike therefore described symptoms that could arise anywhere in the pathway of the vestibular neurons, from its origin in the inner ear to its brainstem connections.

Those authors described two groups of patients, the first with sudden and transient seizures accompanied by sensations of blackout and the second with symptoms of disequilibrium without paroxysms, in which affected patients felt top-heavy or off-balance. The symptoms in the group with imbalance were aggravated by head movements and were more prominent on standing or walking. The proposed site of pathology was central to the inner ear.

Arslan and Sala [3] described similar groups of patients in 1956 but named the entity the nucleoreticular vestibular syndrome (NRVS). Bosatra et al. [4–6] used a suprathreshold stapedial reflex test and an auditory lateralization test to identify brainstem abnormalities in this disorder. Silvoniemi [7] defined vestibular neuritis as characterized by a sudden intensive rotating vertigo with spontaneous nystagmus directed toward the normal ear. This correlated only with Dix and Hallpike’s first group of patients. Coats [8] had already defined this entity in a similar fashion. Schuknecht and Kitamura [9], Zajtchuk et al. [10], and Lindsay and Hemenway [11], however, noted lesions in the vestibular nerve in this type of patient, who presented with an acute attack of spinning vertigo with nystagmus. Silvoniemi’s and Coats’s vestibular neuritis was correctly labeled as vestibular neuritis.
Thus, group 1 patients with spinning vertigo can be separated from group 2 patients having chronic disequilibrium. The author has seen patients present with spinning vertigo and develop chronic disequilibrium after resolution of the vertigo. This would indicate that the initial pathology was in both the nerve and brainstem and that, after the acute spinning vertigo subsided, the less dramatic brainstem affliction surfaced. The key point is that the pathology of group 1 and group 2 patients is in a different part of the vestibular system and that the site of pathology determines the symptom presentation, (to wit, spinning vertigo for the site in the nerve and chronic disequilibrium for the site in the brainstem).

Serotonin, or 5-hydroxytryptamine (5-HT), was identified in the cell bodies of brainstem neurons and as a neurotransmitter in the brainstem by multiple investigators [12–16]. Lehrer and Poole [unpublished manuscript] identified 5-HT activity in the reticular formation and raphe nuclei of the brainstem when brain 5-HT was increased by a high-carbohydrate, low-protein meal.

This report describes the use of anti-5-HT2 [17,18] drugs in patients with NRVS (group 2 patients). Periactin (cyproheptadine [CH]), Optimine (azatadine [OPT]), and Sansert (methysergide [MS]) have all been used. Pizotifen is another such drug but is not available in the United States. MS's side effects proved intolerable, and OPT is not presently available in the United States, leaving only CH for present use in my practice.

METHOD
Six criteria for efficacy for these drugs were described. First, the apparent course of the disease must have been beneficially interrupted. Second, the disease must have responded to the drug after other drug therapy had failed. Third, objective physical findings must have improved within a short time. Fourth, patient improvement in findings or symptoms (or both) often was dose-related. Fifth, worsening of findings or symptoms (or both) often was dose-related. Sixth and finally, patients on occasion required a maintenance dose of medication to remain free of findings or symptoms.

RESULTS
Twenty cases were presented [19], all patients having fulfilled these criteria for efficacy of CH. Experience with OPT was also reported [20]. Follow-up of 139 of 185 consecutively treated patients having NRVS and treated with OPT revealed improvement in all patients followed up, with failure of complete resolution in only 10%. The starting dosage of OPT was 0.5 mg. The starting dosage of CH was 2 mg.

DISCUSSION
The presenting symptoms of NRVS are basically those of Dix and Hallpike's group 2 patients. However, the range of symptoms that have been observed has included not only imbalance, top-heaviness, and disequilibrium. Symptoms that can occur include disorientation and feeling drunk, ear or head fullness, lightheadedness, swaying and falling, spatial disorientation in stores and malls, and blurred vision and feeling tilted or feeling the floor moving, in addition to short episodes of spinning that last only seconds.

What must be emphasized is the absence of a symptom or finding of hearing loss in these patients, thus distinguishing the presentations from Ménier's disease (in which hearing loss should always be present) and perilymphatic fistula (in which hearing loss may be present). A finding of mild imbalance is essential to establish the diagnosis. In this study, the Quix Test [21, 22] was used.

For the Quix test, the patient stands with feet together, chin up, with eyes closed and arms extended and the index fingers pointing straight out. A shakiness or lateral sway is observed, sometimes after only 20 seconds of holding the position. The test is repeated twice to increase its sensitivity. Shakiness or a slight sway can also be observed on the Romberg test. Falling on either test is too extreme a finding for this entity. Bosatra's suprathreshold stapedius muscle reflex test is used to confirm the diagnosis. Perilymphatic fistula, which can also present with mild disequilibrium without cochlear symptoms or findings, must be excluded. NRVS can occur with or without head trauma.

Abnormalities in Bosatra's reflex test include decreases in slope or amplitude, an increase in latency, or asymmetry of responses. Such abnormalities may improve during therapy. A suppression effect on the reflex may also be observed. The mechanism of action proposed for these drugs is that they assist in central compensation by modulating the neurotransmitter effect of 5-HT in the brainstem. Vestibular rehabilitation (physical therapy) may be used as adjunctive therapy, particularly in the elderly and post-head-trauma patients.

CONCLUSION
Vestibular neuronitis was originally used as a nonspecific term to describe two separate and distinct presentations of vestibular disease: vestibular neuritis (in which the nerve is the site of the lesion, in patients with acute spinning vertigo) and NRVS (when the brainstem is the primary site of lesion, in patients with chronic disequilibrium). NRVS is diagnosed by history, a finding of mild imbalance, and an abnormal suprathreshold
stapedial reflex test. Preliminary observations with anti-5-HT2 drugs have indicated that such a therapeutic approach may prove to be efficacious.

ACKNOWLEDGMENT
I acknowledge my long-time collaborator, Ms. Donrue Poole, now retired. Her intellect, efforts, and dedication made all our work possible.

REFERENCES