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Betahistine in Vertebrobasilar Insufficiency

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Abstract: The aim of this study was to observe the usefulness of betahistine dihydrochloride—Betaserc—in therapy for vestibular disorders in patients with vertebrobasilar insufficiency. Two groups of patients, in each of which were 150 patients (mean age, 52,2 years), were tested on the basis of videonystagmography and stabilometry. Betaserc was administrated in two separate doses: 8 mg three times daily and 16 mg three times daily for 120–180 days (mean, 132 days). In every case before and after therapy, visuo-oculomotor and vestibulo-oculomotor reflexes were tested, and amplitude and velocity of the sway were measured during dynamic posturographic testing. After Betaserc treatment, pathological visuo-oculomotor reactions and pathological cervical test results disappeared in most cases: Smooth pursuit improved in 59.9% of cases and saccadic movements in 55.9% of patients, and cervical nystagmus disappeared in 62.2% of tested people. During stabilometry, mean and maximal platform amplitude and mean head velocity decreased as compared with results from tests performed before treatment. These observations were significant after the greater dose of Betaserc; nonetheless, improvement was noted after both doses. The usefulness of Betaserc in vertebrobasilar insufficiency was proved, 4–6 months' therapy was sufficient, and the effect on central compensation seemed to be most probable.

Key Words: betahistine; posturography; videonystagmography

Betahistine is well-known as an H_3-receptor antagonist, increasing the synthesis, turnover, and release of histamine [1]. Histamine has a vasodilating effect on blood vessels, plays an important role in vestibular compensation, and is able to modulate the action of histamine in histamine receptors and probably other synaptic transmission (dopamine, norepinephrine, muscarine) [1,2]. The goal of our study was to estimate, on the basis of objective vestibular findings, the usefulness of betahistine in patients suffering from vertebrobasilar insufficiency.

SUBJECTS AND METHODS

We tested two groups of participants, each group consisting of 150 patients (74 male, 76 female in each group). They ranged in age from 32 to 67 years (mean, 52.2 years) and had presented with vertebrobasilar insufficiency (Table 1). The diagnosis of vertebrobasilar insufficiency was made by a neurologist on the basis of anamnesis, typical neurological examination, radiological pictures of the cervical vertebral column, transcranial Doppler sonography of the vertebral and basilar arteries, and computed tomography or magnetic resonance imaging to exclude other organic reasons. An oculist examined the patients for the same purpose. The laryngologic findings were obtained from tonal audiometry, videonystagmography (VNG), and stabilometry. Additional laboratory tests, such as evaluation of cholesterol levels, glucose, and sex hormones, were included in our diagnostic procedures in those cases in which the indication was very important for further treatment.

Every person complained of vertigo or dizziness, imbalance, hypoacusis, headache, and fluctuating visual disturbances. Sometimes, tinnitus accompanied the pathological signs. To compare the effect of betahistine on the vestibular system before and after pharmacological treatment, VNG and stabilometric examinations

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Table 1. Criteria for Recruitment of Patients

Clinical
Paravertebral and paraspinal pain
Hypomobility of the cervicospinal tract on physiological movements
Neurovegetative symptoms: nausea, vertigo, headache
Neurological symptoms: paresthesia of the upper limbs, hypoesthesia, occipital neuralgia
Radiological
Standard x-rays in anteroposterior and laterolateral projections for assessment of cervical lordosis: reduction, elimination, inversion
Transoral x-ray to exclude damage to the odontoid process of the axis
Functional x-rays at maximum extension to assess spinal stability

were performed. During VNG (VNG-Ulmer, Synapsys, France), we evaluated the following reactions: spontaneous nystagmus, positional nystagmus, cervical nystagmus in Greiner's test, saccadic movements, eye-tracking test, optokinetic nystagmus, and gaze nystagmus. A caloric test according to Brünings was the last examination during VNG, and we observed unilateral weakness, directional preponderance, and excitability of the labyrinth. A stabilometer (Freyss, Synapsys, France) was used to estimate postural disturbances. It consisted of a movable platform and head-velocity detector fixed on the head. The platform was able to move backward and forward and to the sides, so the test consisted of four sequences: first backward-forward with eyes open, then with eyes closed, then to the sides with eyes open and with eyes closed. We calculated the mean and maximal amplitude of platform sway, mean velocity of the platform, and mean velocity of the head.

Oral betahistine was administered in two different doses: 8 mg three times daily and 16 mg three times daily, for 120–180 days (mean, 132 days). The test was not random, but the evaluation was objective because of objective findings (not voluntary vestibular reactions in VNG). The results were compared statistically among all others using the Student's *t*-test for parametrical values.

RESULTS

The frequency of pathological findings on the basis of VNG before treatment with betahistine can be observed in Table 2. This table also demonstrates the frequency of pathological vestibular findings on the basis of VNG after betahistine treatment. Only the results after betahistine treatment with the higher dose were significantly different from the results obtained before therapy. Stabilometric parameters in patients before and after betahistine therapy are outlined in Table 3.

Table 2. Frequency (Number of Persons) of Pathological Vestibular Reactions During Videonystagmography Before Pharmacological Treatment and After Betahistine Treatment

Pathological Vestibular Reactions	Before Treatment	After Betahistine Treatment (dose: 3 × 8 mg)	After Betahistine Treatment (dose: 3 × 16 mg)
Eye-tracking test	124	100	50
Optokinetic nystagmus	60	54	50
Positional nystagmus	84	78	2
Cervical nystagmus	136	100	60
Gaze nystagmus	41	37	30
Unilateral weakness	40	38	35
Hypersensitivity	45	43	43
Directional preponderance	60	50	35
Spontaneous nystagmus	45	39	33
Saccades	111	99	42

DISCUSSION

The disappearance of cervical nystagmus in VNG after betahistine treatment was accompanied by decreased platform and head sway during stabilometry. It suggested the improvement of vestibulospinal reflexes [3]. Tighilet et al. [4] reported that betahistine plays an important role in compensation after unilateral neurectomy in cats with very severe balance disorders. The increase in sensorimotor alertness (in the histaminergic pathways at the cervical brain level) is supposed to be the main element of that compensation [1,4,5]. Yabe et al. [6] previously observed in guinea pigs that after H_3 antagonist infusion to the vestibular nuclei, the postural reflexes were modified. Betahistine as such an antagonist may change the asymmetry of cervical projection to the brainstem, promoting the release of histamine to the vestibular nuclei [1].

The thrice-daily dose of 16 mg of betahistine was more efficient than was the dose of 8 mg three times daily. That superiority was seen clearly in the frequency

Table 3. Comparison Between Stabilometric Parameters in Patients Before and After Betahistine Treatment with Two Differing Doses: 8 mg and 16 mg Three Times Daily

	Testing Period		
Stabilometric Parameters	Before Betahistine	After Betahistine (8-mg dose)	After Betahistine (16-mg dose)
Maximal amplitude	0.41	0.38	0.30
Mean amplitude	0.20	0.20	0.14
Sway velocity	0.21	0.19	0.18
Head velocity	0.18	0.17	0.11

of pathological eye-tracking test results, in saccadic movements, and in cervical nystagmus. Cervical nystagmus according to Greiner's test was considered to follow vascular insufficiency. Therefore, its absence may be evidence of an excitatory effect of betahistine on brain circulation [7]. The improvement in eye-tracking test results and saccadic movements as the representation of oculomotor-vestibular joining at a higher level of the central nervous system may point out the modification of neural activity in cortical and subcortical structures [1].

CONCLUSIONS

In vertebrobasilar insufficiency, visuo-oculomotor reflexes together with cervical test results are more pathological than are vestibuloocular reflexes. After betahistine treatment, the symptoms of visuo-oculomotor disorders were corrected more effectively than were vestibulooculomotor reactions. The disappearance of cervical nystagmus was accompanied by a decrease of platform and head sway during stabilometry. This finding implies improvement of vestibulospinal reflexes. The thrice-daily 16-mg dose of betahistine was more efficient than was the 8-mg dose administered three times daily.

REFERENCES

1. Lacour M. *Histamine: Vestibular Function and Vestibular Compensation*. Amsterdam: Elsevier, 1998.
2. Claussen C-F, Constantinescu L. Pharmacotherapy in Neurotology. In S Desa Souza, C-F Claussen (eds), *Modern Concepts of Neurotology*. Bombay: Prajakta Arts, 1997:426–446.
3. Uno A, Takeda N, Horri A, et al. Histamine release from hypothalamus induced by gravity changes in rats and space motion sickness. *Physiol Behav* 61:883–887, 1997.
4. Tighilet B, Lacour M. Betahistine dihydrochloride treatment facilitates vestibular compensation in the cat. *J Vestib Res* 5:53–66, 1995.
5. Prell GD, Green JP. Histamine as a neuroregulator. *Ann Rev Neurosci* 9:209–254, 1986.
6. Yabe T, De Waele C, Serafin M, et al. Medial vestibular nucleus in guinea pigs: Histaminergic receptors. *Exp Brain Res* 93:249–258, 1993.
7. Rivera VM, Meyer JS, Baer PE, et al. Vertebrobasilar arterial insufficiency with dementia. Controlled trials of treatment with betahistine hydrochloride. *J Am Geriatr Soc* 22:397–399, 1974.