

The role of betahistine dihydrochloride in the treatment of peripheral vestibular syndrome in dogs – study of 3 cases

Rolul diclorhidratului de betahistină în tratamentul sindromului vestibular periferic la câine – studiu pe 3 cazuri

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Abstract

Vestibular syndrome is a pathology whose frequency has increased significantly among the neurological patients in veterinary medicine. A correct and complete clinical examination, followed by neurological examination, localization of the lesion within the nervous system and differential diagnosis are essential steps that ensure the success of the therapy and guide the owners on the prognosis. Head tilt, leaning or horizontal nystagmus are characteristic signs of peripheral vestibular syndrome. Depending on the etiology involved and the type of vestibular syndrome, the classes of drugs used include systemic antibiotics, anti-inflammatory drugs, anti-emetic drugs or vasodilators. Betahistine dihydrochloride is a compound that has structural and pharmacological characteristics similar to histamine. Although betahistine hydrochloride is widely used in human medicine, the literature in veterinary medicine includes few articles dealing with this topic. In consequence, the purpose of this article is to make a brief review on the literature and to present the results obtained following the administration of betahistine hydrochloride in three patients diagnosed with peripheral vestibular syndrome.

Rezumat

Sindromul vestibular reprezintă o patologie a cărei frecvență a crescut semnificativ în ultima vreme în cazul pacienților neurologi din medicina veterinară. Un examen clinic corect și complet, urmat de examenul neurologic, neurolocalizarea leziunii și diagnosticul diferențial sunt etape cheie care asigură succesul terapiei și orientează proprietarii asupra prognosticului. Capul înclinat, alunecarea pe o parte sau nistagmusul orizontal sunt semne specifice sindromului vestibular periferic. În funcție de etiologia implicată și de tipul sindromului vestibular, clasele de medicamente utilizate includ antibiotice sistemice, antiinflamatoare, antiemetice sau vasodilatatoare. Diclorhidratul de betahistină este un compus care are caracteristici structurale și farmacologice similare cu histamină. Deși este utilizat pe scară largă în medicină umană, în medicina veterinară, literatura include puține articole care tratează acest subiect. În consecință, prezentul articol are ca scop o scurtă revizuire a literaturii și prezentarea rezultatelor obținute consecutiv administrării diclorhidratului de betahistină la trei pacienți diagnosticați cu sindrom vestibular periferic.

Introduction

The vestibular system is a component of the inner ear whose main function is to maintain balance and adjust the movements of the eyes, trunk and limbs in accordance with the position of the head and the center of gravity.

Any lesion that affects the receptors or the vestibular branch of the vestibulo-cochlear nerve on the path to the spinal cord, will generate a clinical syndrome that is called peripheral vestibular syndrome. In current veterinary practice in our country, the number of patients with vestibular disorders occupy a significant percentage of the total number of

animals that are presenting for consultation with neurological deficits.

According to a study carried out in 2018 in the Clinic of the Faculty of Veterinary Medicine in Bucharest, out of a total of 209 cases, 22 cases had a lesion localised in the vestibular apparatus (13%), a higher number compared to the number of cases with cerebellar disease - 8, or brainstem lesions - 3 (10).

For this reason, the early recognition of clinical signs that are characteristic for the vestibular syndrome and also the correct differentiation between a central or a peripheral vestibular disease are key elements that must be fulfilled before initiation of the therapy.

Symptoms like head tilt, vestibular ataxia with leaning, pathological nystagmus or strabismus should guide the examiner to diagnose a lesion of the vestibular system (3, 6). The main differences between peripheral and central vestibular syndrome are shown comparatively in Table 1 (7).

Table 1.
Differentiating clinical features of peripheral and central vestibular disease (Rossmeis, 2010)

Clinical sign	Peripheral vestibular lesion	Central vestibular lesion
Head tilt	Toward lesion	To either side
Pathologic nystagmus	Direction not altered by head position Horizontal or rotatory Fast phase away from lesion	Direction may change with head position Horizontal, rotatory or vertical
Postural reactions	Normal	Deficits ipsilateral to lesion
Conscious proprioception	Normal	Deficits ipsilateral to lesion
Cranial nerve deficits	±ipsilateral cranial nerve (CN) VII	±CNN V-XII ipsilateral to lesion
Horner syndrome	±postganglionic	±preganglionic (rare)
Consciousness	Normal Disoriented if acute	Normal to comatose

An etiological diagnosis and management of central lesions generally involve expensive investigations for confirmation and an aggressive therapeutic approach. Instead, peripheral lesions are associated with a positive prognosis and they can be diagnosed by practicing physicians using less expensive and more accessible methods (2).

Recovery of patients with vestibular syndrome requires a long time; if lesions are chronic, there is an increased risk of permanent damage. In veterinary medicine, therapeutic options are limited, but they always follow several important goals, like: treatment of the primary disease (when identified), control of the symptoms, support of the body and providing antibacterial protection by using antibiotics that penetrate the blood-brain barrier.

Betahistine dihydrochloride is a compound with pharmacological and structural properties similar to histamine, but which exerts a longer central vasodilation effect and a more reduced action in stimulating the gastric secretion.

Numerous studies have shown that betahistine is a powerful vasodilator with cerebral action. It has an increased efficiency in augmenting the blood flow from the vertebro-basilar arterial system that irrigates the posterior brain and enhances the microcirculation of the internal vestibular and auditory system.

In a recent study that included dogs injected with betahistine dihydrochloride intravenously, an average 54% increase in blood flow from the basal artery was demonstrated using electromagnetic blood flow transducers. Its action on H1 receptors in the blood vessels of the inner ear favors increased vasodilation and permeability, thus preventing volume expansion and distension of the hemolymph system. (1, 4, 5, 9).

This article shows the results obtained following the administration of betahistine dihydrochloride in three dogs diagnosed with peripheral vestibular syndrome.

1. Materials and methods

The patients included in this study were presented at the Clinic of the Faculty of Veterinary Medicine of Bucharest for specialized consultations and were randomly selected from among other 10 patients (dogs and cats) diagnosed with peripheral vestibular syndrome during the year 2018.

The proper neurological examination was preceded by a complete history and a thorough physical checking.

In order to establish the neurolocalization of the lesion, a consultation protocol has been implemented. The protocol included certain stages, whose order has been strictly followed: assessment of the mental status, posture, cranial nerves, proprioception, gait, spinal reflexes and pain sensitivity. Afterwards, a differential diagnosis was performed using the acronym VITAMIND (vascular, inflammatory / infectious, traumatic, anomalous, metabolic, idiopathic, neoplastic, degenerative) and further investigations were recommended in order to confirm the diagnosis. Therapy included betahistine dihydrochloride in all three cases and progress was monitored after 21 days from the first consultation and then monthly for another six months.

2. Results and discussions

The first case was represented by a neutered French Bulldog female, two and a half-years-old. A month ago, following ovariohysterectomy, he started to present movement difficulties, head slightly tilted on the left side, decreased appetite and multiple episodes of vomiting.

The physical examination revealed normal temperature, pink mucous membranes, mobile and painless lymph nodes. During auscultation, normal heart sounds were recorded.

After the complete neurological examination, the following deficits were observed: head tilt on the left side, a wide base stance on both thoracic and pelvic limbs, horizontal nystagmus, slight reduction of face sensitivity on the left side, vestibular ataxia characterized by imbalance, successive falls on the left side and a permanent tendency to seek wall support for maintaining the patrupodal position (Figure 1). The mental status, proprioception, spinal reflexes and deep pain sensation testing were normal. Consequently, the lesion was localised on the left peripheral vestibular apparatus. For differential diagnosis, an inflammatory and a

metabolic pathology were considered, which could have been generated by the toxicity of the previous anesthesia of the patient. The biochemical and hematological parameters were normal, and at the otoscopic examination, the ear did not show any visible modifications that may have been justifying the symptoms. Treatment with betahistine dihydrochloride (1 mg / kg, divided into two doses at 12 hours) was started and the patient was reassessed after 3 weeks, and subsequently monthly. The evolution was favorable, the clinical signs improved considerably, the nystagmus and the vomiting episodes disappeared and the inclination of the head was completely restored after about 3 months.



Figure 1. French Bulldog patient with peripheral vestibular syndrome: horizontal nystagmus and head tilted on the left side

The second case was represented by a neutered German Shepherd male, 15-years-old. The owners reported that a week ago the animal started to keep its head tilted on the right side and it was not able to move due to a severe loss of balance; also, during 48 hours, a horizontal nystagmus was observed.

From the moment of onset, slight improvements of the general condition were noticed, although the patient did not receive any treatment. Appetite was low and there were no episodes of vomiting. The physical examination revealed no significant changes: the mucous membranes were pink, the temperature was 38.7 °C and the palpable lymph nodes were mobile and normal in size.

Femoral pulse was synchronous, bilateral and cardiac sounds presented physiological

characteristics during auscultation.

Neurological examination showed a normal mental status, a posture characterized by a head tilted on the right side, a broad base on the anterior limbs and cranial nerves with no deficits at the moment of examination (Figure 2).



Figure 2. German Shepherd, 15 years old, head tilted on the right side

Proprioception was slightly delayed on the hind limbs, but the patient had a history of degenerative changes in coxofemoral joint which have been previously diagnosed radiologically. The gait was characterized by instability, loss of balance and the tendency to fall on the right side. Spinal reflexes and deep pain sensitivity were normal.

The lesion was localised within the right peripheral vestibular system, and for the differential diagnosis, idiopathic vestibular syndrome was considered - frequently in geriatric dogs, a vascular pathology generated by possible age-specific heart changes or a neoplastic pathology. Further, a specialized cardiological consultation and magnetic resonance examination were recommended in order to obtain an etiological diagnosis, but these investigations could not be carried due to financial reasons.

Treatment with betahistine dihydrochloride (1 mg/kgbw, divided into two doses at 12 hours) was initiated. Additionally, dietary supplements were recommended in order to

support the main drug and to obtain slowing of the degenerative changes within the nervous system. At the following controls, the inclination of the head was significantly reduced, the appetite returned to normal and the patient was able to walk without leaning.

The third case was represented by a 4-year-old French Bulldog female, unsterilized, vaccinated and dewormed according to the specific age protocols. For about a month, she was undergoing treatment for a chronic bilateral otitis that has been diagnosed by his attending veterinarian. For several days, the owner noticed that the animal was shaking very frequently its head, had the tendency to walk on small circles on the right side and kept his head slightly tilted on the same side. Appetite was normal, but there was an episode of vomiting with undigested food content.

At the time of examination, the patient was normothermic, the mucous membranes were pink, the capillary replenishment time was 1.5 seconds and the explorable lymph nodes had normal size and consistency. In auscultation, no heart murmurs were detected.

The neurological examination revealed a normal mental status, but a modified posture - head slightly tilted on the right side. The cranial nerves showed no significant deficiencies, except the strabismus (Figure 3).



Figure 3. French Bulldog, 4 years old, head tilted on the right side and strabismus.

Proprioception was normal on all four limb and walking was characterized by a tendency to make small circles on the right side and a slight loss of balance. Spinal reflexes and deep pain sensitivity were normal.

The localization of the lesion was established within right peripheral vestibular system, and the differential diagnosis included inflammatory lesions following chronic otitis or a metabolic pathology that could have appeared after prolonged administration of antibiotics.

A cytological examination of the auricular secretion was performed.

The result confirmed the diagnosis of otitis and the presence of *Malassezia pachydermatis*.

The therapy included betahistine dihydrochloride (1 mg / kg.bw., divided into two doses at 12 hours), to which were added topical solutions and local hygiene recommendations in order to treat the otitis.

The patient's evolution was favorable, and the inclination of the head was reduced after the first 3 weeks of treatment.

After stopping treatment, there were no recurrences.

3. Conclusions

1. For the localization of lesions within the central or peripheral vestibular apparatus, complete neurological examination is always mandatory.
2. Prior to initiating therapy, a differential diagnosis must be made between pathologies that lead to peripheral vestibular syndrome.
3. All the three cases presented in the article had a favorable evolution following the administration of betahistine dihydrochloride. The symptomatology was reduced and no adverse effects were reported.
4. Betahistine dihydrochloride can be successfully used as a monotherapy or complementary therapy in peripheral vestibular syndrome.

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