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Midodrine Treatment of Orthostatic Hypotension in Patients with Acute Tetraplegia

Akut Tetraplejili Hastalarda Ortostatik Hipotansiyonda Midodrin Tedavisi

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Intruduction

Orthostatic hypotension (OH) is one of the complications in patients with spinal cord injury (SCI) particularly in the acute stage. Impairment in the autonomic nervous system, usually in patients with cervical and high thoracic SCI, causes OH that is defined as decrease in systolic blood pressure of at least 20 mm Hg or diastolic blood pressure of at least 10 mm Hg upon changing body position from supine to upright posture. It results from an inefficient response to postural changes in blood pressure. OH may be symptomatic or asymptomatic. Symptoms of OH include dizziness, light-headedness, fainting, blurred vision, muscle weakness, fatigue, nausea, palpitations, and headache (1-4).

Non-pharmacological interventions that have been used are salt and fluid regulation, pressure to the abdominal region, upper body exercise, functional electrical stimulation (FES) applied to the legs, compression bandages and/or pressure stockings and tilt training program (3,5). Pharmacological treatment includes agents acting on blood vessels, on blood volume or on other pressor mechanisms. The medications used are fludrocortisone, pyridostigmine, ergotamine, ephedrine, desmopressin, erythropoietin and midodrine (3,4,6).

We experienced two cases of tetraplegia having OH treated with midodrine that did not respond to conventional non-pharmacological interventions. Both of the patients were women. One of them was 33-year-old with C4 tetraplegia AIS-A and the other was 19-year-old with C5 tetraplegia AIS-A. The subjects were in acute stage of SCI that were in the first 3 months post-injury. They continued to have OH during transfer to wheelchair or tilt table exercises despite use of antiembolic compression bandage, abdominal binder, and progressive exercises with tilt table. Five mg/d midodrine in two divided doses was started. Improvement in symptoms was observed in both of the patients after 20 days, thus, the dosage was decreased to 2.5 mg/d in two divided doses. One month later, patients' tolerated tilt angle was 90 degrees, so midodrine was stopped in both of the patients. Midodrine was not continued in one of the patients. In the other patient, midodrine 2.5 mg/d was started again one week later because OH continued occasionally. Autonomic dysreflexia (AD) was not observed. No side effects were observed.

The predisposition to OH following SCI is not fully understood, but it is thought to be multifactorial (3). Following SCI, the low level of efferent sympathetic activity and the loss of reflex vasoconstriction are among the major causes of OH. OH is more common in tetraplegia than in paraplegia. OH persisting during the first month following SCI was reported to occur in 74% of cervical and in 20% of upper thoracic motor complete SCI patients (7). Both of our two patients had complete tetraplegia. We obtained supine hypotension and OH in our patients within the first three months after injury.

Non-pharmacologic measures should be the first choice of treatment in OH. In both of our two patients, we started midodrine because despite conventional non-pharmacological interventions and physical therapy, supine hypotension and HO did not resolve and progression in tilt training was slow.

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Midodrine, the prodrug of desglymidodrine, is a peripheral, selective alpha-1 adrenergic receptor agonist that increases blood pressure via arterial and venous vasoconstriction. Usual doses of midodrine ranges from 2.5 to 10 mg two or three times a day (4,8,9). We used 5 mg/d and decreased to 2.5 mg/d in our patients. With the use of midodrine, their supine blood pressures and tolerated tilt angles increased in one week and symptomatic OH resolved in one month. OH recurred in one of the patients after one week of drug cessation, thus, midodrine started again.

Since midodrine does not cross the blood-brain barrier, it is presumed to have no central nervous system effects (9). The most commonly reported side effects include piloerection, pruritus, mydriasis, palpitations, tachycardia, headaches, urinary retention and supine hypertension (4,8). None of the side effects was observed in our patients. We suggest that, in patients with higher level SCI, AD might be another adverse event with the use of midodrine since such patients are prone to develop AD. We did not observe AD in our patients.

In our opinion, among these side effects, urinary retention is especially important in patients with SCI who void voluntarily. Because of its alpha-1 adrenergic effects, midodrine causes an increase in the tone of the vesical sphincter, which may potentially lead to progressive retention of urine, particularly in patients with SCI who void urine spontaneously. Furthermore, midodrine may aggravate detrusor-sphincter dyssynergia, which can lead to hydroureteronephrosis (10). We suggest if a patient continues to require midodrine to control postural hypotension, intermittent catheterization combined with anticholinergic therapy should be recommended instead of spontaneous voiding.

OH is an important clinical problem for patients with SCI since it interferes with ability to perform exercises and activities of daily living (11). It is impossible to take steps without solving the OH problem in the rehabilitation of SCI. Thus, OH delays the rehabilitation of patients with SCI, especially in acute stage. OH prevented to get the targets and delayed rehabilitation in both of our patients which caused their longer stay at hospital.

We suggest that the use of midodrine might be considered in patients with SCI whose orthostatic symptoms are refractory to conventional non-pharmacological interventions. We obtained beneficial effects regarding symptoms and rehabilitation with no significant side effects. Urinary adverse effects, supine hypertension and AD should be followed closely in SCI patients using midodrine.

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