Midodrine for the Management of Orthostatic Hypotension in Patients With Spinal Cord Injury: A Case Report

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A 21-year-old man sustained anterior displacement and a burst fracture of C7 in a motor vehicle crash. He underwent anterior corpectomy, decompression, fusion of C6–T1 vertebrae, and halo placement. The American Spinal Injury Association grade of his spinal cord injury (SCI) was C6 C tetraplegia. Severe orthostatic hypotension in the upright position complicated the patient’s rehabilitation program. Midodrine was prescribed, and other medications with possible adverse effects were adjusted. Significant improvement after taking midodrine was reflected in the orthostatic vital signs and symptoms, as well as in FIM instrument scores. Staff noted improvements in therapy participation and functional status. The patient tolerated the midodrine well and had no significant side effects.

Key Words: Case report; Hypotension, orthostatic; Midodrine; Rehabilitation; Spinal cord injuries.

ORTHOSTATIC HYPOTENSION (OH) may occur in the acute or chronic phase of spinal cord injury (SCI). It is related to reductions in vascular tone, circulating catecholamines, and venous return. OH is defined as a decrease in blood pressure (BP) or a rise in pulse (15+ points for both parameters) on assuming the upright position. It is associated with lightheadedness, dizziness, blurred vision, weakness, or even syncope.1-3 Normally, the upright position causes pooling of blood in the lower extremities, reducing stroke volume and cardiac output. This upright position is associated with increases in the pulse rate and ejection fraction. The decline in BP activates autonomic reflexes through baroreceptors, causing parasympathetic inhibition and sympathetic stimulation. This reflex control by descending pathways is lost when the SCI is above the sympathetic outflow (T5–8). As spasticity develops, reflex control by descending pathways is lost when the SCI is above the sympathetic outflow (T5–8). As spasticity develops, reflex control by descending pathways is lost when the SCI is above the sympathetic outflow (T5–8). As spasticity develops, reflex control by descending pathways is lost when the SCI is above the sympathetic outflow (T5–8). As spasticity develops, reflex control by descending pathways is lost when the SCI is above the sympathetic outflow (T5–8). As spasticity develops, reflex control by descending pathways is lost when the SCI is above the sympathetic outflow (T5–8).

Before mobilization, the BP and pulse should be recorded in the supine and sitting positions. A number of measures can minimize the effects of OH in patients with SCI. Inciting stimuli, including sudden changes in posture, infection, hyperventilation, and excessive environmental heat, should be avoided and treated. Activities that cause strain (eg, lifting heavy objects, coughing, a hard bowel movement, voiding) may bring on hypotension. Thigh-high compression stockings, abdominal binders, adequate hydration, increased salt intake, and gradual changes in position also help maintain BP.1,4 More than 60 drugs have been used to treat OH, including fludrocortisone, sympathomimetic amines (phenylpropanolamine, ephedrine, somatostatin or its analog octreotide), caffeine, vasopressin agonists, dopamine antagonists, and ergot alkaloids.1 Most of these agents are marginally beneficial. The best results are often achieved by combining 2 or 3 agents, which can result in adequate BP management in almost all patients.1,5-7

In this case report, we describe an individual with C6 tetraplegia who had severe OH that was unresponsive to various devices and physical maneuvers but had excellent results with midodrine. A review of the medical literature reveals that this is the first case report of midodrine as the sole therapeutic agent for OH in SCI.

CASE REPORT

A 21-year-old man sustained anterior displacement and a burst fracture of C7 after a motor vehicle crash. He underwent an anterior C7 corpectomy, decompression, fusion of the C6–T1 vertebrae, and halo placement for 4 weeks. He also had a mediastinal hematoma and bilateral pulmonary contusions. His acute hospital course of 8 weeks was complicated by recurrent pneumonia, and he required intubation, ventilator support, and a temporary tracheostomy. He received an inferior vena cava filter for pulmonary embolism prophylaxis and a feeding tube for nutrition. For urosepsis, he was treated with intravenous antibiotics.

On admission for rehabilitation, he was a well-developed, young man who was wearing a cervical collar and had a sad affect. A stage 2 decubitus ulcer was present at the coccyx. Range of motion of his shoulders caused severe pain. (These 2 problems soon resolved and did not adversely affect his rehabilitation program.) Muscle testing revealed that the deltoïds were 4+ bilaterally, biceps were 4 (right) and 4 (left), triceps were 3+, wrist extensors were 4, and the grasp was 3 (right) and 2 (left). He had trace movement of the toes and 1+5/5 at the left quadriceps and hip abductors. Sensory function was absent in the lower extremities, but he was able to feel light touch at the left foot. The admission laboratory test results showed a hemoglobin of 9.5g/dL, blood urea nitrogen of 8mg/dL, creatinine 0.7mg/dL, concentrated urine with a specific gravity of 1.019, and slightly reduced oncotic pressure caused by total protein of 6.0g/dL and albumin 2.7g/dL.

On the day of admission, his vital signs ranged from a BP of 136/78 and a pulse of 72 to 99/69 and 109. On initiation of upright activities, the patient had OH and complaints of dizziness, lightheadedness, and blurred vision. Severe OH persisted despite thigh-high antiembolism stockings, an abdominal binder, and gradual placement in the upright position. Recur-
rent OH and associated symptoms prevented the patient’s full participation in therapies. On one occasion, he went from having a BP of 111/67 and a pulse of 81 while supine to having a BP of 69/48 and a pulse of 128 while sitting upright at the edge of the bed. On another occasion, his symptoms necessitated an electrocardiogram, but only sinus tachycardia was shown and he was treated with bedrest and a liter of intravenous fluids.

A week after admission, he was placed on 2.5mg of midodrine, administered at 0800, 1200, and 1600 hours. BP, heart rate, and symptoms were monitored frequently, first with the patient supine, then after sitting at the edge of the bed for 1, 3, and 5 minutes. Although the patient continued to have OH on this low dose of midodrine, his symptoms decreased dramatically. The morning dose was increased to 7.5mg after 3 weeks and then to 10mg after 4 weeks because hypotension persisted, along with mild but rare symptoms. With resolution of his symptoms and orthostasis, the patient was able to participate fully in the rehabilitation program.

He again developed OH when a consultant started trazodone (50mg) to help with his sleep. Soon he required an increased dose of midodrine (15mg) in the morning. There were no more episodes of OH until his trazodone dose was doubled to 100mg. Because the patient was doing better with his sleep and pain management, trazodone was discontinued and he had no further OH.

He was monitored for supine hypertension while on the 15mg dose of midodrine. On occasion, the patient complained of a headache and his systolic BP was in the 150s. Therefore, the morning dose was decreased to 10mg and the 2.5mg dose was continued at 1200 and 1600 hours. This occurred about a week before the patient was discharged home. Close monitoring revealed only minimal changes in his vital signs (not OH), and there were no symptomatic episodes. Figure 1 shows the average of the range of systolic BP measurements taken in the morning (supine, sitting) at various doses of midodrine. There is an upward trend of systolic BPs from admission to discharge as the midodrine dose was increased. He made excellent progress with his therapies and his FIM™ instrument scores increased from 58 to 103 at discharge.

**DISCUSSION**

Engel and Hildebrandt studied the circulatory dynamics of orthostatic adaptation after cervical SCI in patients who were completely bedridden for several months. With orthostatic tiltable exercises over at least 2 weeks, there was no improvement in adapting to orthostatic stimuli or any significant circulatory stabilization. The ability to maintain an upright posture through effective management of OH is essential for the rehabilitation of patients with cervical or high thoracic SCI. Treatment should focus on improving the patient’s symptoms and functional capacity, rather than on a target BP.

Nonpharmacologic interventions include a carefully managed exercise program and monitoring of the environmental temperature. Devices such as elastic stockings and abdominal binders are important in the management of OH, but they are often ineffective in SCI patients. Successful treatment of OH requires an individualized approach, with a combination of exercises, devices, and pharmacologic agents such as fludrocortisone and midodrine.

The value of fludrocortisone for increasing BP in autonomic failure was first described in 1956, and it has been used successfully since then. A potent mineralocorticoid with little glucocorticoid effect, it raises BP through sodium and fluid retention. Several features of fludrocortisone complicate its use. Its full pressor action is seen in 1 to 2 weeks, a delay that is difficult for patients as well as rehabilitation staff in this era of managed care. Furthermore, fluid retention is critical to its beneficial effect, so it causes significant weight gain and edema. Therefore, it cannot be used in patients with congestive heart failure. Finally, almost half of patients will develop hypokalemia within 2 weeks and 5% will also develop hypomagnesemia. This requires constant monitoring and occasional supplementation with potassium and magnesium. Adverse reactions to the glucocorticoid component may occur with rapid withdrawal or continued use of large doses. Other side effects include osteopenia, compression fractures, impaired wound healing, fragile skin, and negative nitrogen bal-
Midodrine is an alpha-1-adrenergic agonist, a prodrug that is metabolized to desglymidodrine after absorption. An advantage of midodrine is that as a prodrug it is well absorbed (93%) with limited direct effect on the gastrointestinal vasculature, and is metabolized into an active pressor compound. The plasma concentration of desglymidodrine peaks at 1 hour, with a half-life of 3 hours. The metabolites are excreted through the urinary tract.\textsuperscript{1,6,7,11} Midodrine directly raises the BP by constricting arterioles and veins, which increases peripheral vascular resistance. It is best used in the morning and afternoon, to provide the maximum effect when patients are most active.

When compared with ephedrine and other sympathomimetic agents, midodrine causes less-frequent and less-severe alpha-adrenergic effects. Among its most common adverse effects are scalp paresthesias (18.3%), piloerection (13.4%), dysuria (13.4%), pruritus (12.2%), supine hypertension (7.3%), chills (4.9%), and pain (4.9%).\textsuperscript{1,2} These are generally mild and can be controlled by reducing the dosage of midodrine.\textsuperscript{1,6,7} Supine hypertension is the most problematic side effect of midodrine. Fortunately, patients with autonomic failure do not experience chest pain with BP elevation caused by midodrine. In some individuals, it has actually improved postprandial angina, which was probably caused by a hypertensive reduction in coronary blood flow.\textsuperscript{1,2}

Dosing should be individualized to maximize the therapeutic benefit and minimize adverse reactions. It is also essential to monitor medications that can affect the BP, such as antidepressants, narcotics, and antihypertensives. In our patient, trazodone clearly interfered with the beneficial effects of midodrine.

Our case report suggests that midodrine is effective for the treatment of OH in patients with SCI. Objective as well as subjective results were favorable within days of starting midodrine and there were no side effects. BP, heart rate, and orthostatic symptoms showed significant improvements. Functional gains occurred in the FIM score, reflecting the patient’s ability to participate in the rehabilitation program. Midodrine contributed to this progress by allowing the patient to engage in therapies without interruptions caused by OH.

**CONCLUSION**

Midodrine has been used in combination with clonidine for a patient with SCI and orthostatic hypotension,\textsuperscript{13} but ours is the first case report with midodrine as the sole agent. Midodrine is fast and effective in treating OH in patients with SCI, and has less severe side effects in comparison with other medications. For young SCI patients with OH, midodrine is an excellent option for maintaining BP, reducing orthostatic symptoms, and improving participation in rehabilitation therapies.

**References**