Clonidine in spinal cord injury

Patricia W. Nance,* MD
Arthur H. Shears,* MD
Dwight M. Nance,† PhD

Spasticity is a frequent sequela of spinal cord injury and is characterized by velocity-dependent increased resistance to manipulation, hyperactive reflexes and clonus. Clonidine is known to restore limb and visceral control in cats with spinal cord injuries, both immediately and several weeks after injury.[1] Clonidine has also been used to diminish spasticity and prevent the hypertension associated with autonomic hyperreflexia in humans with spinal cord injuries.[2] We examined the effects of clonidine in four patients with spasticity following spinal cord injury.

Case reports

Case 1

A 38-year-old man with a cervical flexion injury and dislocation of the fifth cervical vertebra presented with urinary retention and flaccid paralysis below the C6 level. Within 14 weeks after the injury he regained voluntary control of micturition but began to experience spontaneous involuntary spasms of his trunk, hands and legs. Twelve weeks later therapy with clonidine, 0.05 mg given orally four times a day, was started. Within 48 hours after the first dose the hand and leg spasms disappeared (but recurred with skin stimulation), and trace voluntary movements of both legs were observed. The spontaneous spasms returned when we halved the clonidine dose because of postural hypotension. A feeling of depression lasting for 60 to 90 minutes after each dose was a further side effect. At the time of writing the patient was still taking the drug and continued to show improvement in the muscle strength and voluntary control of his legs.

Case 2

A 30-year-old man with paraplegia following traumatic myelopathy at the T2 level presented with problematic leg and abdominal muscle spasms 9 years after the spinal cord injury. Phenoxybenzamine (an α-adrenergic blocking agent), 10 mg twice a day for 2 years and then 7.5 mg/d, had been used to relieve external urethral sphincter spasticity and restore voluntary bladder control. Concomitant therapy with clonidine, 0.05 mg twice a day, was started. After the third dose his leg spasms diminished. By the third day of treatment the dosage was 0.05 mg four times a day and no spontaneous spasms were evident. In the weeks that followed, trace voluntary movements of his lower limb muscles appeared. His bladder drainage remained satisfactory despite complete withdrawal of phenoxybenzamine. The patient was still receiving clonidine at the time of writing.

Case 3

Myelopathy developed in a 20-year-old man following an L1 fracture–dislocation. Marked spasticity of the left tibialis anterior muscle and relative weakening of the opposing gastrocnemius–soleus muscle group caused tonic posturing of the foot in 15° of dorsiflexion. Therapy with clonidine, 0.2 mg/d, was started 1 month after the onset of spasticity. After 3 weeks of treatment and physiotherapy the ankle gained 5° of motion. However, the patient reported a feeling of negativism associated with clonidine therapy. Treatment with the drug was therefore stopped, and he was referred for tenotomy.

Case 4

One year after radiotherapy and 6 months after chemotherapy for small-cell carcinoma of the lung, a 52-year-old woman presented with spastic paraparesis below the T10 level. Although a definitive diagnosis was never reached, radiation- or vincristine-induced myelopathy was the most likely cause of her neurologic problem. Treatment with clonidine, the daily dose being increased from 0.05 to 0.2 mg over 4 days, was started 3 weeks after the onset of limb spasticity. Suppression of the spasticity and improved ability to transfer independently to and from a wheelchair were noted within 7 days. However, persistent postural hypotension prevented the patient from attaining an upright posture, and the drug was withdrawn.

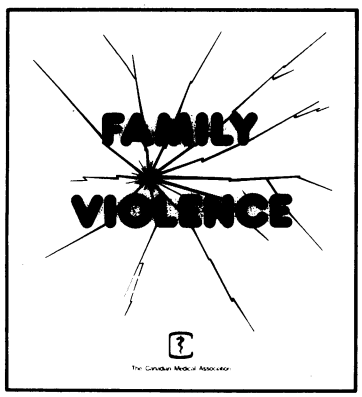
Comments

Our experience suggests that clonidine may be useful in the treatment of spasticity in some patients with spinal cord injuries. In our patients, reduction of spasticity was dose-dependent, the onset of the effect was rapid, usually occurring within the first 48 hours of treatment, and the drug was effective in both recent and long-term spinal cord injury.

A mechanism of action for clonidine has been postulated.[3] In the central nervous system clonidine acts as an agonist to α_2-adrenergic receptors, which are found in many areas of the cerebrum, midbrain and medulla and in the spinal cord. Autoradiography of clonidine binding in rat and human spinal cord indicates that the highest density of α_2-receptors is in the substantia gelatinosa of the dorsal horns. Given that clonidine acts in the spinal cord, the drug may suppress spasticity in patients with cord injuries by inhibiting excessive afferent sensory transmission below the level of the lesion. Conversely, the appearance of spasticity following cord transec-

From *the Division of Physical Medicine and †the Department of Anatomy, Dalhousie University, and *the Nova Scotia Rehabilitation Centre, Halifax

Reprint requests to: Dr. Patricia W. Nance, Nova Scotia Rehabilitation Centre, 1341 Summer St., Halifax, NS B3H 4K4



In response to increased public awareness of family violence and a recognized need to inform physicians of their responsibility, the Canadian Medical Association, through its Council on Health Care, has prepared guidelines on the identification and management of victims of this type of violence.

An adapted version, published in the Mar. 1, 1985 issue of *CMAJ*, provides a general overview, outlines possible sign—symptom complexes and discusses treatment of the three principal forms of family violence: wife battering, child abuse and abuse of the elderly. Concurrently, a French version was sent to all francophone members of the CMA.

A bilingual monograph that incorporates both versions of this document and is presented in booklet format is available free of charge to CMA members and at a cost of $4 to nonmembers upon request to:

Dr. N.P. Da Silva
Director, Medical Services
CMA House
PO Box 8650
Ottawa, Ont.
K1G 0G8

tion may be related to the chronic depletion of norepinephrine distal to the lesion.[4]

In case 2 spasticity was suppressed by clonidine despite the concomitant administration of a nonspecific α-blocking agent. Although this may argue against an action of clonidine via α-receptors, it is likely that the dose of phenoxybenzamine was insufficient to block all α-receptors in the spinal cord.

Although clinical experience with clonidine in hypertension has shown that the drug is safe even for long-term use,[5] in a recent study of the use of clonidine in the treatment of problematic spasticity in patients with spinal cord injuries a number of adverse reactions were reported: syncope, seizures, cerebral vascular accidents, deep vein thrombosis, autonomic hyperreflexion, lethargy, drowsiness, nausea and vomiting.[6] In our patients the major side effects were postural hypotension, emotional negativism, depression, rebound spasticity with dose reduction and transient urinary retention. Of these, postural hypotension was the most limiting.

References

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This section of CMAJ *is for brief reports of a significant clinical observation or event. Reports of a single case should not exceed two manuscript pages of text (typewritten double-spaced) — about 450 words. If several cases are being reported, an extra page may be added. An abstract is not necessary, and the introduction should be kept very brief. In addition, there may be up to six references and one or two graphs, tables or illustrations.*

In writing a brief case report it is not necessary to give the patient's history and the results of physical examination in the standard format. Negative findings and normal results of laboratory tests need only be included if they are essential for ruling out a possible diagnosis. It is sufficient to establish the reason(s) for the diagnosis and the treatment. The clinical course should be described briefly and the significant observation or event presented in enough detail to establish its credibility. Reference to the literature should be confined to supporting the principal point being made about the event or observation.

Innovations

[Of innovations] . . . when a thing was new people said "It is not true". Later, when its truth became obvious, people said, "Anyway, it is not important", and when its importance could not be denied, people said, "Anyway, it is not new".

—William James (1842–1910)