has been described. However, to our knowledge, detailed description of movement disorders secondary to cervical disc prolapse with cord compression has not been previously highlighted.

Our patient presented with upper limb hypoesthesia and dystonia associated with tingling sensation of the fingers. However, there was no objective sensory loss. Neurophysiologic testing revealed right CTS. There was no electrophysiologic evidence of posterior column abnormality on somatosensory evoked potential examination. Her movement disorders were ascribed to disc prolapse with cord compression for the following reasons: first, the almost complete resolution of her movement disorders after surgery; second, the movements were accompanied by tingling sensation in her fingers that may be caused by underlying cervical nerve root irritation or compression. Interestingly, her hand dystonia showed some characteristic dystonia features such as relief by certain “sensory tricks” and rest, and aggravated by action and stress and anxiety.

A number of hypotheses underlying movement disorders in patients with cervical cord lesions have been proposed. These include altered sensory input (in particular proprioceptive pathways), abnormal processing of both input and output signals in the spinal inter-neurons, and increased excitability of the spinal motor neurons. Disruption of the somatosensory pathways or motor cortex to the striatum also may produce abnormal movements without sensory loss. It is not clear why movement disorders secondarily affect the thalamus to such a degree that these disorders are under-recognized and hence under-reported. Despite the lack of clinical and electrophysiologic evidence of sensory abnormalities in our patient, we cannot rule out subclinical proprioceptive or cutaneous abnormalities resulting in aberrant sensory input as a possible mechanism. Although there were no structural basal ganglia abnormalities on MRI, we speculate that subclinical basal ganglia dysfunction contributed to altered input and output signals at cortical, subcortical, or spinal levels also could be a predisposing factor. Functional brain imaging with surgical correlation may be useful to address this hypothesis.

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References


Zolpidem improves dystonia in “Lubag” or X-linked dystonia-parkinsonism syndrome

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The effects of the hypnotic agent zolpidem on Lubag or X-linked dystonia-parkinsonism syndrome are described in this article. Lubag affects adult men from the Philippine island of Panay and is often resistant to therapy. Zolpidem binds to gamma-aminobutyric acid-A (GABA_A) receptors, particularly the omega-1 (ω1) subtype receptor. Zolpidem was reported to improve parkinsonism in some patients with PD or progressive supranuclear palsy (PSP); its effects on dystonia are unknown.

Case reports. Patient 1. A 41-year-old man with Lubag, presented at age 37 with head pulling to the right, arm posturing, jaw opening, tongue protrusion, involuntary eye closure, and limb tremor. On examination he had a Burke–Fahn–Marsden (BFM) dystonia score of 66, with severe phasic dystonia of the jaw, neck, trunk, and limbs. Body and limb bradykinesia, symmetric limb rigidity, and shuffling gait were noted; motor United PD Rating Scale (UPDRS) score was 38.5, with severe retrotorticollis, and truncal and arm hyperextension. Body and limb bradykinesia, and diffuse rigidity also were observed; motor UPDRS score was 53.5. In the physician’s office he was given 10 mg zolpidem PO. Improvement was noted within 45 minutes and was optimal at the first hour; BFM score dropped to 0 (100% improvement), and motor UPDRS score dropped to 22.5 (40% improvement). The effect on dystonia lasted 8 hours per dose initially, but shortened to 2 hours with chronic use. With the slow dose escalation and caffeine intake, he adapted to the sedation to taking zolpidem 10 mg every 2 hours. On follow-up 1 year after, efficacy was still maintained.

Patient 2. A 38-year-old man with Lubag, presented at age 36 with leg and trunk posturing, pulling of the neck to the left, and slowness in movements. On examination he had a BFM score of 30, with torticollis, action flexion dystonia of the legs, and leg hyperextension at rest. Body and limb bradykinesia and diffuse rigidity were noted; motor UPDRS score was 36.5. In the physician’s office he was given 10 mg zolpidem PO. Improvement was noted within 40 minutes and was optimal at the second hour; BFM score dropped to 20.5 (32% improvement), and motor UPDRS score dropped to 24 (34% improvement). The effects on dystonia lasted 3 hours initially and on chronic use at 10 mg BID (he could not afford higher doses). Six months after, he developed diarrhea that ceased on discontinuing zolpidem.

Patient 3. A 36-year-old man with Lubag, presented at age 34 with left arm posturing, trunk and neck hyperextension, shuffling gait, and hand tremors. On examination he had a BFM score of 39.5, with severe retrotorticollis, and truncal and arm hyperextension. Body and limb bradykinesia, and diffuse rigidity also were observed; motor UPDRS score was 53.5. In the physician’s office he was given 10 mg zolpidem PO. Improvement was noted within 45 minutes and was optimal at the first hour; BFM score dropped to 26.5 (31% improvement), whereas motor UPDRS score remained unchanged. The effect on dystonia lasted 2.5 hours. Because he was unemployed, a benefactor supplied the patient with 120 free tablets of zolpidem, which he stretched out by taking only 1 tablet BID. Each dose lasted 2 hours from the first month onward. No side effects were noted. He ran out of medicine 2 months later.

Discussion. The three patients described exhibited 31–100% improvement in dystonia (mean 54%) and 0–40% improvement in parkinsonism (mean 25%) after 10 mg zolpidem PO. The onset of effect on dystonia ranged from 15 to 45 minutes, with optimal benefits observed in 1 to 2 hours. The mean duration of action was 4.5 hours initially (range 2.5–8 hours), becoming 2 to 3 hours with chronic use. This is similar to that reported in patients with PSP, and corresponds to the drug’s 2.5-hour elimination half-life. Sleepiness was noted at doses greater than 10 mg BID.

Zolpidem may benefit parkinsonism in patients with PD or PSP. In Lubag, zolpidem benefits dystonia more perceptibly than parkinsonism. Dystonia is associated with hypoactivity of the globus pallidus interna, and widespread brain alterations in GABA_A/benzodiazepine receptors. Zolpidem-binding sites are abundant in the basal ganglia output structures—the globus pallidus interna and substantia nigra pars reticulata. By binding to these sites, zolpidem may help restore the ganglionic output influence on the thalamus and motor cortex. It is unclear why zolpidem, and not benzodiazepines, improves dystonia in Lubag patients. Whereas benzodiazepines bind nonspecifically to GABA_A receptors with α_1, α_2, α_3, or α_6 subunits, zolpidem selectively binds with the omega-1 (ω1) subtype receptor. Zolpidem was reported to improve parkinsonism in some patients with PD or progressive supranuclear palsy (PSP); its effects on dystonia are unknown.

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Neuropathies are well-known complications of therapy with amiodarone, but other antiarrhythmic drugs are rarely associated with peripheral nervous system side effects.  

References


Disopyramide-induced neuropathy

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Neuropathies are well-known complications of therapy with amiodarone, but other antiarrhythmic drugs are rarely associated with peripheral nervous system side effects. We describe a patient who developed a severe sensory-motor neuropathy during treatment with disopyramide. The neuropathy was unresponsive to corticosteroids, but improved after withdrawing disopyramide. This is, to our knowledge, the second case of disopyramide-induced neuropathy. A 71-year-old woman was admitted to our neurologic department because of a 6-month history of fatigue, paresthesias, pain, and cramps in her lower limbs. Morning stiffness, arthralgias, and aching in the thighs also were present. Her medical history was significant for cardiac arrhythmias, which had been treated with disopyramide 500 mg/d for 4 years when she came to our attention. On neurologic evaluation, she was able to walk unassisted, but her gait was unsteady and difficult on toes and heels. A predominant proximal weakness was present in all four limbs; tendon reflexes were reduced in the upper limbs and absent in the lower limbs. There was no sensory loss to light touch, pain perception, vibration, and joint position sense. C-reactive protein was increased (30.2; normal range up to 6). Normal values were found for complete blood cell count, serum protein electrophoresis, chemistry and thyroid profile, complement, immune complexes, creatin kinase, cryoglobulins, tumor markers, folate and vitamin B12, autoantibodies, venereal disease research laboratory, and serology for hepatitis. A diagnosis of polymyalgia rheumatica was made. No signs of temporal arthritis were present. Electrophysiologic studies revealed a sensory-motor polyneuropathy, with reduced motor conduction velocity (MCV) in peroneal nerves (38 m/s) with normal compound muscle action potential amplitude (10 mV). There was some evidence of muscle denervation, with fibrillation at rest and reduced patterns on maximal contraction; no sensitive potential was recorded from sural nerves. Antibodies to peripheral nerve antigens (gangliosides, sulfatides, myelin-associated glycoprotein, glycosaminoglycans) were negative. 

Started on a treatment of prednisone, the patient showed a prompt recovery from arthralgias and stiffness. Weakness and dysesthesias in the legs, however, worsened and further electrophysiologic study, 3 months later, evidenced a more severe peripheral neuropathy, with a slower MCV (31 m/s) and more evident signs of denervation; sural nerves were still inexcitable. The possible, although uncommon, association of neuropathy with polymyalgia rheumatica seemed unlikely, because the neuropathy worsened despite the dramatic improvement of the rheumatologic condition. In the absence of other known causes of neuropathy, disopyramide was considered. After a stabilized control of arrhythmias was documented by a cardiologic check-up, the drug was withdrawn. At a follow-up evaluation 4 months later, the patient showed a considerable improvement of her neuropathic symptoms, confirmed by electrophysiologic studies, which showed an improvement of peroneal nerve MCV (40 m/s) and the reappearance of the excitability of the sural nerves (43 m/s); sensory nerve action potential was 5 μV. In the following months (last follow-up evaluation 7 months after discontinuation of disopyramide), the patient presented further improvement of her neuropathic symptoms, with decreased fatigability (she could walk for longer distances than before) and reduced sensory symptoms. The lack of response to corticosteroids together with the uncommon occurrence of polyneuropathy in polymyalgia rheumatica strongly point to a lack of correlation between the two conditions. Instead, the regression of the symptoms after discontinuation of disopyramide strongly supports an iatrogenic pathogenesis of the neuropathy. The lag time between the beginning of antiarrhythmic therapy and the onset of the neuropathic symptoms (4 years) may cast doubt about a cause-effect relationship. It is known, however, that the most common disopyramide side effects may occur after years of treatment, as seen in other iatrogenic neuropathies. In this case, as in a previous case, symptoms were predominately sensory and reversible a few months after withdrawal of disopyramide. The mechanism of disopyramide neuropathy is unknown. Disopyramide-induced polyneuropathy should be considered when polyneuropathy occurs and no other causes are found. The discontinuation of the therapy may clarify diagnosis.

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