Case Report

Comorbid Functional Shoulder Pain and Zolpidem Dependence Treated with Pramipexole

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ABSTRACT

Pramipexole is a dopamine agonist with higher affinity for D3 receptors. Treatment with pramipexole in clinical conditions such as restless legs syndrome, fibromyalgia, and parkinsonism has been found to significantly improve measures of pain and sleep along with the other symptoms. There is no research data available that explores the usefulness of pramipexole in somatoform/functional pain syndromes. We report a case of a 65-year-old male with bilateral functional shoulder pain associated with insomnia and zolpidem dependence effectively treated with pramipexole.

Key words: *Functional pain, insomnia, pramipexole, zolpidem dependence*

INTRODUCTION

There is growing evidence supporting the role of central dopaminergic neurotransmission in modulating pain perception, although the exact mechanisms by which dopamine influences pain processing remain to be determined.[1-3] Several novel classes of medication with analgesic properties have bearing on dopaminergic activity as evident in the capacity of dopamine antagonists to attenuate their analgesic capacity.[3] Activation of mesolimbic dopamine neurons, arising from the cell bodies of the ventral tegmental area and projecting to the nucleus accumbens, plays an important role in mediating the suppression of tonic pain.[4] D3 receptors are predominantly located in the mesolimbus.[5] This plausibly explains the role of pramipexole, a dopamine agonist with 7- to 10-fold higher affinity for D3 receptor subtypes than for either D2 or D4 receptors, in reducing pain.[6] It additionally has a moderate opioid affinity and minimal alpha 2-adrenoceptor activity.[6] Treatment with pramipexole in clinical conditions such as restless legs syndrome,[7] fibromyalgia,[8] and parkinsonism[9] has been found to significantly improve measures of pain along with the other symptoms. There is no research data available that looks into the usefulness of pramipexole in somatoform/functional pain syndromes. Here, we report a single case of bilateral functional shoulder pain associated with insomnia and zolpidem dependence achieving remission with pramipexole monotherapy.

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CASE REPORT

A 65-year-old male presented with history of taking 70-80 mg zolpidem/day in 6-8 divided doses. One year back, the patient had an insidious onset of pain in both shoulders for which he had consulted an orthopedic surgeon. He also complained of difficulty in initiating and maintaining sleep, attributing it to be secondary to the shoulder pain. Investigations were done that included complete blood counts; renal, hepatic and thyroid function tests; fasting and postprandial blood sugar; vitamin B12 and D3 assay; serum uric acid,

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all of which were within the normal range. He tested negative for human immunodeficiency virus. Magnetic resonance imaging of both shoulders as well as clinical examination revealed no abnormality. Analgesics, including nonsteroidal antiinflammatory drugs and oral opioids (tramadol) reduced the pain only by 10% as reported by the patient. A psychiatric referral was sought as the pain was deemed to be functional. The patient was diagnosed as having pain disorder and was prescribed 40 mg duloxetine in two divided doses and 10 mg zolpidem HS. He discontinued duloxetine in 5 days of starting due to excessive nausea experienced each time after taking duloxetine, but continued zolpidem. Since, he also felt relieved of the shoulder pain with zolpidem apart from improved sleep; he started taking it in the daytime. He remained virtually free of pain for 1-2 h after taking zolpidem, following which the pain would gradually reappear. He increased the frequency of zolpidem intake to once every 2-3 h so that for the last 6 months, he took 7-8 tablets of 10 mg zolpidem in a day. On not taking zolpidem for 4-5 h, he felt anxious, diaphoretic, restless, and tremulous, agitated and had a resurgence of intense shoulder pain; all of these would subside after taking zolpidem. He had no past or family history of psychiatric illness or substance use. A physician evaluation affirmed the absence of any significant current medical illness.

At the time of presentation, the patient was diagnosed as having zolpidem dependence and was treated as an inpatient. Zolpidem was tapered off over a period of 10 days. He was instructed to maintain strict sleep hygiene. Along with, pregabalin was started at a dose of 75 mg HS, which was discontinued in 2 days as the patient had intolerable giddiness on it. Quetiapine 50 mg HS was then started, which also had to be discontinued as it caused physical weakness and lethargy in excess of the patient's tolerability. Thereafter, he was put on pramipexole sustained release (SR) preparation 0.26 mg HS for 5 days. As there was favorable response in the form of reduction in the intensity of pain and no adverse effects reported, the dose was increased to 1.05 mg of pramipexole SR. On follow-up for the next 6 months, the patient was maintained on the same dose of pramipexole. He no longer complained of pain or insomnia and reported of being abstinent from zolpidem.

DISCUSSION

Zolpidem, a nonbenzodiazepine hypnotic has higher abuse and dependence potiential than previously documented,[10] and our case adds to the existing literature. Based upon previous reports,[11,12] we initially tried detoxification with pregabalin and quetiapine, but were unsuccessful due to tolerability issues. Since, the patient had co morbid pain disorder and insomnia, pramipexole was started for its putative role in pain control as well as in improving sleep.

Involvement of central nervous system in the form of autonomic nervous system dysregulation has been implicated in the pathophysiology of functional pain syndromes.[13] Adrenergic arousal arising from the locus ceruleus (central sympathetic stimulation) alters nociception and fragments deep sleep. Mesolimbic dopaminergic neurotransmission has an inhibitory role, thus attenuating this central adrenergic arousal. This may enable pramipexole, a D3 receptor agonist to reduce pain and restore sleep by augmenting the mesolimbic control of excessive adrenergic arousal.[8] Pain syndromes such as migraine[14] and burning mouth syndrome[15] have been reported to improve with pramipexole. Besides, pramipexole improves sleep in patients with parkinsonism[16] and restless legs syndrome[17] as well as is effective in treating rapid eye movement sleep behavior disorder[18] and sleep related eating disorder,[19] suggesting its possible role in restoration of normal sleep.

Since this is a single case report, we do not exclude the possibility of the beneficial effect of pramipexole in our patient to be either placebo or coincidental. Placebo-controlled blinded studies are needed to establish the effectiveness of pramipexole in functional pain syndromes and associated insomnia.

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