
Intolerance to Tramadol may Herald Bipolar Disease

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Citation

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Abstract

Background

The association between Tramadol and mania has been reported in a few anecdotal reports.

Case Presentations

Three cases of mania coinciding with Tramadol administration are presented. The patients all reported excellent analgesic response to Tramadol after it was restarted in combination with a mood stabilizer.

Conclusions

These cases suggest a possible association between Tramadol and mania. Intolerance to Tramadol may even signal an underlying untreated manic depression. In this case, consideration should be given to restarting the Tramadol in combination with a mood stabilizer.

INTRODUCTION

There have been only a few case reports associating Tramadol and mania. Tramadol is a centrally acting analgesic that preferentially binds the mu opiate receptor and inhibits the neuronal uptake of serotonin and noradrenalin₂.

The serotonergic and noradrenergic modulating properties of Tramadol suggest an antidepressant effect which could result in the induction of mania itself in a manner similar to that of antidepressants₃. The main reported side effects of Tramadol are nausea, abdominal pain and headaches₁. We are reporting three patients whose manic behavior may be associated with Tramadol therapy.

Case 1: Ms. S was a 26 year old woman who presented to our clinic with for coccygodynia and was prescribed Ultram ER 200mg/day. She had previously been prescribed Norco 10/325mg which she stated had helped her pain. Several years earlier she had seen a psychiatrist who diagnosed her with bipolar disease and prescribed Lithium but she never filled the prescription. She had no cognitive deficits, had never been hospitalized, but complained of several major depressive episodes interspersed with periods of elevated mood characterized by insomnia, racing thoughts, pressured speech, grandiosity and a history of self-destructive behaviors. She was euthymic. After 2 days of taking

tramadol, 200mg/day Ms. S was agitated, euphoric, and hyperactive, slept less than 3 hours a day, complained of increased sacrococcygeal pain and demonstrated rapid speech and paranoid ideation. She was conscious and oriented at all times. She stopped taking Tramadol, and her psychiatric symptoms abated within 24 hours. The patient was then started on Lithium and Tramadol was reintroduced. The patient remained calm and controlled and stated that the Tramadol was relieving her pain adequately.

Case 2: Mr. T was a 45 year old shrimp boat worker complaining of constant low back pain 8/10 and stiffness which was only moderately relieved by Methadone and Percocet. Patient was tearful, admitting to feeling depressed and was prone to paroxysms of grandiose and irritable behavior. Tramadol was started but the patient's complaints of increased anxiety, headache, nausea, and worsened pain levels prompted its discontinuation. After starting Lamictal for mood stabilization, the patient stated that while his psychiatric symptoms had resolved his pain levels were still elevated. Tramadol was reintroduced and the patient reported his pain levels decreased to 3/10.

Case 3: Ms. H was a 45 year old female with a history of bipolar disease and subtalar arthritis asking for a breakthrough pain medicine in addition to the methadone she

was already receiving. After starting Ultram ER 200mg/day, she complained of nausea, diffuse abdominal pains and increased pain levels. The Ultram was discontinued and Lithium was started. Two weeks later she was restarted on Ultram and stated that her pain levels were well controlled without any of the prior side effects.

We have presented three patients with initially untreated bipolar disease that came to our clinic for treatment of chronic or persistent pain. Tramadol may have had an adverse effect in these patients by triggering or exacerbating their manic symptoms. Tramadol-induced mania, likely due to the drugs inhibitory effects on noradrenalin and serotonin neuronal reuptake, has already been reported in the literature⁴. However, when used with the moderating effects of a mood stabilizer, these patients reported improved analgesic control. Based on these examples, we recommend that all patients should be rigorously screened for symptoms

of bipolar disease before starting treatment with Tramadol. Furthermore, we suggest that intolerance to Tramadol may herald a previously undiagnosed bipolar disorder and should prompt the physician to consider the diagnosis. In light of the clinical analgesic benefits of Tramadol and history of minimal abuse potential, a retrial of the drug may be warranted in patients with bipolar disease perhaps in combination with a mood stabilizer.

References

1. Goldsmith, T B, Shapira, N A, Keck, P E Jr. Rapid Remission of OCD with Tramadol Hydrochloride (letter). *American Journal of Psychiatry* 1999, Vol. 156, 660-661.
2. Gonzalez-Pinto, A, Imaz, H, De Heredia, J L P, Gutierrez, M, Mico, J A. Mania and Tramadol-Fluoxetine Combination. *American Journal of Psychiatry* 2001, Vol. 158(6), 964 - 965.
3. Rojas-Corrales, M O, Gibert-Rahola, J, Mico J A. Tramadol Induces Antidepressant-type Effects in Mice. *Life Science* 1998, Vol. 63, 175-180.
4. Watts, B V, Grady, T A. Tramadol-induced Mania (letter). *American Journal of Psychiatry* 1997, Vol. 154, 1624.

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