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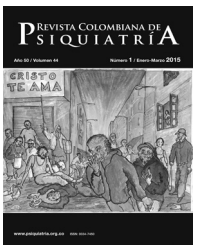

Case Report

Trazodone-induced delirium: case report

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ABSTRACT

Trazodone is used as an antidepressant in doses between 150 and 600 mg. At lower doses, it is commonly used to treat insomnia. There are few case reports about confusional symptoms as an undesirable side effect of this drug. We report a case of a patient who presented with delirium after prescription of trazodone 100 mg. She required hospitalisation but, shortly after discontinuation of trazodone, the symptoms disappeared without antipsychotic medication. Seven months after the episode, the patient remains asymptomatic.

Delirio inducido por trazodona: reporte de caso

Palabras clave:
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RESUMEN

La trazodona se usa como antidepresivo en dosis de 150-600 mg. En dosis más bajas, se usa comúnmente para tratar el insomnio. Hay pocos reportes de caso sobre síntomas confusionales como un efecto secundario indeseable de este medicamento. Se presenta el caso de una paciente que acudió con delirio después de la prescripción de trazodona 100 mg. La paciente requirió hospitalización pero, poco después de la interrupción de la trazodona, los síntomas desaparecieron sin medicación antipsicótica. A los 7 meses del episodio, la paciente permanecía asintomática.

Introduction

Trazodone is a triazolepyridine derivate with antidepressant, anxiolytic and hypnotic effects, but chemically and pharmacologic distinct from other serotonin reuptake inhibitors.[1] It has little activity on histaminergic, cholinergic, or dopaminergic transmission, and has a unique dual pharmacological profile which inhibits the synaptic serotonin

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reuptake and blocks postsynaptic serotonin receptors.[1] At low doses, trazodone acts as a serotonin antagonist, whereas at high doses acts as a serotonin agonist.

Delirium induced by tricyclic antidepressants and anticholinergic agents has been described in the psychiatric literature, but trazodone is chemically unrelated to these substances. There are few reports on cognitive adverse effects of trazodone: delirium in 3 depressed patients prescribed with low doses of trazodone, trazodone-induced mania, trazodone-associated serotonin syndrome, 3 cases of trazodone-induced delirium in bulimic patients, 2 psychotic episodes with low dose trazodone and exacerbation of psychotic symptoms in a schizophrenic patient.[1-7] We present a clinical case of trazodone-induced delirium.

Case report

Mrs. S is a 44-year-old divorced woman who works as a teaching assistant and lives with her 2 children, aged 23 and 17 years-old. She has a surgical history of cholecystectomy and cardiac ablation for arrhythmia several years ago, and a lifetime tobacco exposure of 15 pack/years. She has no chronic diseases neither previous contact with mental health services but has been taking alprazolam 1 mg, triazolam 0,25 mg, and buspirone 10 mg for several years due to insomnia. In May 2016, her family doctor proposed a cross-taper of alprazolam 1 mg to trazodone 100 mg. It was proposed that the dose of alprazolam was reduced to 0,5 mg during 2 weeks while trazodone was initiated at 100 mg. The first time she took trazodone she was awake all night and in the morning she didn't feel well, so decided to restart this medication only in August, when she was in holidays. In this period (May to July 2016) she was only medicated with buspirone and triazolam. In August she re-started trazodone 100 mg and 5 days later she attended the Psychiatric Emergency Services with worsening sleep and inappropriate behavior involving incoherent speech, purposeless aggressiveness towards children, and visual and auditory hallucinations. A diagnosis of adjustment disorder was proposed and symptoms were assumed[3] to be a dissociative feature of neurotic defense mechanisms. It was decided to maintain all drugs, namely buspirone 10 mg, triazolam 0.25 mg, and trazodone 100 mg, and to start olanzapine 5 mg. The next day she returned to the Psychiatric Emergency Service with the same clinical complains. It was then decided to discontinue buspirone and triazolam, maintaining olanzapine 5 mg and trazodone 100 mg, and to add trazodone extended release 50 mg. After 2 days, the patient returned once again[3] to the Psychiatric Emergency Service. Due to full insomnia, strange behaviors and auditory and visual hallucinations she spent the previous days in her mother's house. In this period, her mother reported she was not well for about a week, exhibiting[4] aggressive behavior towards her mother and her own children, and her speech was strange, "she said she saw fires and smoke, that there were many people at home (. . .); she's under the bed as if taking care of the children at the nursery, calling by their name and tell them to have a snack, speaking to them as if they were there, looking at the trees and calling the children by their name". In the hospital, she was agitated to the point of requiring physical and chemical restraint. Did not respond to questions and sang in high tone and enumerating names of children she worked with. There were no signs of intoxication or withdrawal. This time a full physical examination and complementary diagnostic exams were taken which reveled normal blood chemistry, normal cranial computed tomography scan, negative substance abuse drugs screening and negative viral markers. She was admitted to a psychiatric ward, and during the hospital stay a medication washout was made. Episodes of agitation and confusional symptoms ceased after discontinuation of trazodone and without antipsychotic medication. After 4 days, alprazolam 0,5 mg and mirtazapine 15 mg started to regulate sleep. The patient showed good adaptation to hospitalization. She remained calm and cooperative. Seven months after discharge from inpatient psychiatric ward, the patient remains asymptomatic.

Conclusions

The appearance of the symptoms after the introduction of the drug and their cessation after the interruption of it suggest that delirium was induced by trazodone. However, the mechanisms by which trazodone produces delirium remains unclear in the literature.[4] One hypothesis that has been pointed is an oversensitivity to the effect of meta-chlorphenylpiperazine (m-CPP). This compound is the major metabolite of trazodone, which demonstrates specific 5-HT agonistic properties on several subtypes of the 5-HT1 and the 5-HT2 receptor.[8,9] It binds with highest affinity to 5-HT 2C receptors, but also binds to 5HT2 and moderately to alpha 2-noradrenergic receptors. Hyperresponsivity to the effects of m-CPP has been described in demented patients.[10] The rare phenomenon of sleeplessness following the administration of trazodone (1.6%) is most likely caused by m-CPP.[8] In most of the cases we found, symptoms stopped promptly after discontinuation of the drug, as in our patient. In the revised literature only one patient required additional treatment with haloperidol.[1] Delirium in our patient cannot be understood as consequence of the action of the drug in a comorbid brain because no changes were evidenced in the CT-head. The patient did not suffer from thyroid changes nor from any disturbance of eating behavior.

In conclusion, trazodone induced delirium is rare, but several cases have now been reported and monitoring the patient's mental state after the introduction of this drug is mandatory. It is possible that some personal susceptibility to trazodone causes some individuals to develop this rare side effect. Further research is needed to understand which receptor is affected and how to identify the patients more likely to present with these paradoxical effects.

Conflict of interests

The authors have no conflicts of interest to disclose.

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