

## Trazodone- Induced Mood Switching in an Anxious Patient

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Received: 02 October 2019; Accepted: 20 October 2019

**Citation:** Mable Jing Ting Quek, Lim Eng Choon Leslie, Tan Shian Ming, et al. Trazodone- Induced Mood Switching in an Anxious Patient. Int J Psychiatr Res. 2019; 2(5): 1-3.

### ABSTRACT

**Objective:** The development of symptoms suggestive of mania or hypomania during treatment with an antidepressant, including Trazodone, has been established by previous studies. In most previous case reports, patients were receiving treatment for either major depression or bipolar mood disorder, and their symptoms of mania or hypomania remitted after cessation of the antidepressant. We present a case with features that were unique and differed from previous case reports.

**Method:** We describe Trazodone-induced mania in an anxious patient, and review the literature of the phenomenon of "mood switching" induced by antidepressants, particularly focusing on Trazodone.

**Results:** A 67-year-old man was started on Trazodone for management of generalised anxiety disorder. He developed symptoms of mania on the 8th day of taking Trazodone. Despite cessation of Trazodone, the patient remained symptomatic and required treatment with mood stabilizers. Despite achieving remission, he was noted to have 2 relapses of mania requiring inpatient management in the following 3 months.

**Conclusion:** Our case suggests that antidepressant-induced mood-switching may not be as reversible or treatable as suggested by previous case reports. It also demonstrates that switching can occur in anxious patients, even at a low dose of Trazodone.

### Keywords

Trazodone, Mood-switching, Antidepressant, Bipolar disorder, Mania.

### Introduction

Trazodone is an antidepressant which functions by means of weakly inhibiting serotonin re-uptake, and also serves as a potent antagonist of serotonin 5-HT<sub>2a</sub> and 5-HT<sub>2c</sub> receptors. It is mainly used in the treatment of major depressive disorder, anxiety and insomnia [1]. There have been several case reports in which patients receiving trazodone treatment for unipolar depression or the depressive phase of bipolar disorder developed hypomania or mania, presumably induced by trazodone [2-5].

We present a case in which a patient with no history of major mood disorders developed mania after being treated with trazodone for

generalized anxiety disorder.

### Case Report

A 67-year-old man with no past history of mood disorder received treatment for generalised anxiety disorder and restless legs syndrome. He was prescribed pregabalin 175mg nocte with improvement in his symptoms. Over the course of 12 months, he developed unpleasant gastrointestinal side effects to pregabalin and elected to stop taking this medication. Within 2 months, he experienced recurrence of anxiety. He was subsequently started on trazodone 25mg nocte, up-titrated to 75mg nocte over the next 4 days.

However, on the 8th day, the patient developed symptoms of mania. His family noticed a drastic change in his mental state and behavior. He became significantly more talkative, with pressured

speech and flight of ideas, and seemed much more energetic despite not having had much sleep. He also expressed the desire to make multiple impulse purchases of high-value items, including a new car and a new property, and demonstrated thoughts of grandiosity by recounting personal encounters with politicians and exaggerating his close connections with them. Subjectively, the patient experienced elevated mood and expressed a desire to accomplish multiple goals.

Despite the cessation of trazodone, his symptoms persisted for a week, after which he was started on Lithium which was gradually up-titrated to 800mg nocte, and Olanzapine 20mg daily. Subsequently, his mood stabilized, and he was discharged after his behavior and mental state returned to baseline. However, despite adherence to Lithium and Olanzapine, the patient had 2 further episodes of mania over the next 3 months, requiring inpatient treatment for stabilization and adjustment of medications. He eventually achieved remission on a combination of Risperidone 3mg nocte and Sodium Valproate 1g daily.

## Discussion

The development of symptoms suggestive of mania or hypomania during treatment with an antidepressant has been established by previous studies [2-5]. Of note is that compared to its previous editions, the 5th edition of the *Diagnostic and Statistical Manual (DSM-5)* now categorizes hypomania/mania induced by antidepressant medications as a manifestation of Bipolar disorder. This phenomenon of “mood switching” has been found to occur in up to 8% of patients being treated by an antidepressant for unipolar major depressive disorder [6]. Particular classes of antidepressant medications have been shown to have higher associations with this phenomenon, for example tricyclic antidepressants and specific serotonin and noradrenaline reuptake inhibitors [7-9]. The precise mechanisms for “mood switching” are still unclear, although several possible mechanisms have been proposed [9]. Involvement of the cholinergic system appears to be supported by the relatively higher rates of the phenomena being observed in patients who had been using tricyclic agents [9,12]. However, other studies have also suggested that the catecholaminergic and dopaminergic systems could be involved [7,11].

There have also been several case reports of patients who developed mania after being treated with trazodone [2-5]. Most patients were receiving trazodone as monotherapy for depression, with daily doses ranging from 100mg to 400mg [2,4]. Cases in which patients developed mania or hypomania on lower doses of trazodone were associated with the concurrent use of other antidepressants including Fluvoxamine and Venlafaxine [4,5]. In most cases, symptoms of hypomania or mania resolved after the cessation of trazodone, with some cases requiring the commencement of mood stabilisers. In 2 of the cases, recurrence of depressive symptoms was observed after the cessation of trazodone [4].

Several other factors have also been linked with an increased risk of medication-induced mood switching, including family history of bipolar disorder or psychosis, history of cyclothymic

or hyperthymic traits, and patients belonging to the juvenile age-group [6,7]. We note that our patient had reported a family history of bipolar disorder in his sister.

## Conclusion

There are several differences that stand out in our patient as compared to previous case reports. Firstly, our patient developed manic symptoms at a relatively low dose of Trazodone monotherapy in contrast to the other cases where either higher doses of Trazodone were used as monotherapy or where lower doses of Trazodone in combination with other antidepressants were used [4,6,7]. Furthermore, our patient continued to display symptoms and signs of mania despite cessation of trazodone, and which required treatment with Lithium for mood stabilization to achieve symptom resolution. Moreover, he experienced manic relapses in subsequent months, which remitted with a combination of sodium valproate and risperidone. This could suggest that antidepressant-induced switching may not be as easily reversed as suggested by previous case reports. Also, unlike our patient who had never had a previous diagnosis of a major mood disorder, most of the previous reported cases of mania or hypomania associated with trazodone use involved patients who had previously been diagnosed with a mood disorder, such as major depression or Bipolar affective disorder.

Caution needs to be exercised in persons with risk factors for mania or hypomania, especially in those with a family history of bipolar disorders, as in our patient. Our case also demonstrates that switching can occur in anxious patients, even at a low dose of Trazodone.

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