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Trazodone and Omeprazole Interaction causing Frequent Second-Degree Mobitz Type 1 Atrioventricular (AV) Block (Wenckebach Phenomenon) and Syncope: A Case Report and Literature Review

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Conflict of interest: None declared

Patient: Male, 54
Final Diagnosis: Trazodone and omeprazole interaction causing second-degree Mobitz type 1 AV block and syncope
Symptoms: Syncope
Medication: —
Clinical Procedure: Trazodone and omeprazole withheld
Specialty: Cardiology

Objective: Unexpected drug reaction
Background: This case report highlights serious cardiovascular adverse effects with a conventional dose of trazodone as a result of its potential interaction with omeprazole.
Case Report: A 54-year-old man who was a former smoker, with dyslipidemia, coronary artery disease, and anxiety disorder developed lightheadedness and syncope the morning of admission. He was taking trazodone 50 mg daily, omeprazole 20 mg daily, and simvastatin 20 mg at bedtime. He doubled the dose of trazodone 50 mg on the night prior to presentation to calm his anxiety. An electrocardiogram revealed sinus rhythm at 60 beats per minute and second-degree Mobitz type 1 atrioventricular (AV) block with 5:4 AV conduction. Results of basic metabolic panel, thyroid-stimulating hormone, and chest radiograph were normal. A transthoracic echocardiogram revealed aortic valve sclerosis. We tested for Lyme disease given his history of hunting in the woods 8 months prior to presentation, but the titer was negative. Trazodone and omeprazole were discontinued. By the 3rd day of medication discontinuation, all symptoms had resolved and the frequency of second-degree AV Mobitz type 1 AV block had decreased to once per hour.
Conclusions: Due diligence and meticulous attention to detail needs to be exercised to uncover drug interactions as potential causes of lethal and nonlethal patient symptomatology, as in this case of syncope caused by concomitant use of trazodone and a widely prescribed medication, omeprazole.

MeSH Keywords: Heart Block • Omeprazole • Syncope • Trazodone

Full-text PDF: <http://www.amjcaserep.com/abstract/index/idArt/893427>

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Background

Trazodone, a triazolopyridine derivative, is a second-generation antidepressant, with a unique chemical structure and a pharmacological profile slightly different from other antidepressants [1]. It belongs to the class of serotonin receptor antagonists and reuptake inhibitors (SARIs) [2]. Trazodone can cause reversible AV block [3] and life-threatening arrhythmias that can be fatal. However, it has been reported to have less severe cardiotoxic effects compared to other antidepressants [4]. To the best of our knowledge, there are no reported cases of omeprazole potentiating the cardiotoxic effect of trazodone. We report a case of 54-year-old man with second degree AV Mobitz type 1 block and syncope after taking a double dose of trazodone while on omeprazole.

Case Report

A 54-year-old Hispanic man, former smoker, with dyslipidemia, coronary artery disease, and anxiety disorder, presented to the

emergency room following an episode of lightheadedness and syncope as he came out of the bathroom on the morning of admission. He denied palpitations, dyspnea, chest discomfort, vertigo, nausea, or vomiting. He had an episode of lightheadedness a week prior to presentation. He was taking trazodone 50 mg daily, omeprazole 20 mg daily, and simvastatin 20 mg at bedtime. He doubled the dose of trazodone 50 mg the night prior to presentation to calm his anxiety. On admission, pulse was 65/minute, irregular and blood pressure was 163/116 mm Hg with no orthostatic hypotension. An electrocardiogram revealed sinus rhythm at 60 beats per minute, second-degree Mobitz type 1 atrioventricular (AV) block with 5:4 AV conduction, ventricular rate of 52/minute, narrow QRS, and a normal QTc of 434 milliseconds (Figure 1). Telemetry revealed frequent 8:7, 7:6, 5:4, 4:3 AV conductions recurring after every few beats of normal AV conduction (Figure 2). Basic metabolic panel, thyroid-stimulating hormone, and chest radiograph were normal. A transthoracic echocardiogram revealed aortic valve sclerosis. Lyme disease titer was negative, which was tested given his history of hunting in the woods 8 months prior to presentation. In view of the probability of omeprazole

Figure 1. Electrocardiogram showing second-degree Mobitz type 1 atrioventricular block.

Figure 2. Telemetry showing second-degree Mobitz type 1 atrioventricular block recurring after every few beats of normal atrioventricular conduction.

Figure 3. Telemetry showing resolution of frequent second-degree Mobitz type 1 atrioventricular block.

potentiating trazodone accumulation, both medications were discontinued. By the 3rd day of medication discontinuation, all symptoms had resolved and the frequency of Mobitz type 1 AV block had decreased to once per hour (Figure 3).

Discussion

In 2008, trazodone was still commonly recommended as an antidepressant [5] and sleep aid [6]. The current clinical use is mainly as a sleep aid [7]. Trazodone is an antidepressant, anxiolytic, hypnotic of the SARIs class [2], predominantly blocking postsynaptic 5-hydroxytryptamine (5-HT_{2A}) receptors with mild presynaptic inhibition of 5-HT reuptake, and an alpha-1 adrenergic blocker causing postural hypotension. In spite of minimal anticholinergic muscarinic receptor blocking action, trazodone-induced 1st degree AV block and complete heart block have been reported [1,3,8], the putative mechanism being the blocking of 5-HT₄ receptors which facilitate L-type calcium²⁺ ion-mediated AV nodal conduction [9,10]. The maximum recommended dose of trazodone for depression is 400 mg/day and for insomnia it is 50–100 mg/day. The dose of 100 mg/day taken the night before presentation was well within the therapeutic dose limits, yet he developed frequent second-degree Mobitz type 1 AV blocks with syncope. Trazodone is metabolized by

liver microsome-based cytochrome P450 enzyme CYP3A4 [7] into m-chlorophenylpiperazine (m-CPP) [11]. Trazodone toxicity in our patient was attributed to long-term concomitant use of omeprazole, which is a CYP3A4 inhibitor [12], causing trazodone accumulation. From among the numerous potential mechanisms of trazodone-induced syncope, the most probable cause in this patient was documented frequent second-degree Mobitz type 1 block. Other trazodone-induced mechanisms of syncope were less likely because there was no evidence of postural hypotension, atrial fibrillation, ventricular ectopy, or torsades de pointes.

To the best of our knowledge, this is the first report of reversible second-degree Mobitz type 1 AV block with trazodone, likely potentiated by concomitant use of omeprazole.

Conclusions

Due diligence and meticulous attention to detail needs to be exercised to uncover drug interactions as potential causes of lethal and nonlethal patient symptomatology, as in this case of syncope caused by concomitant use of trazodone and a widely prescribed medication, omeprazole.

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