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Case Report

Third-degree atrioventricular block induced by escitalopram and quetiapine in a patient with depression: a case report

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Abstract: Third-degree atrioventricular block (AVB) associated with the use of escitalopram and quetiapine is rare, with limited cases reported. We present a case of drug-induced third-degree AVB in an elderly patient undergoing treatment for depression. A 70-year-old woman with a history of depression was initially treated with milnacipran and alprazolam, but the regimen was altered due to insufficient therapeutic response. Two weeks after initiating escitalopram and quetiapine, she developed third-degree AVB. Electrocardiogram (ECG) revealed sinus rhythm with complete AV block, atrioventricular junctional escape rhythm, QT interval prolongation, and a heart rate of 45 bpm. Emergency pacemaker implantation was performed. This case highlights the potential for escitalopram and quetiapine to induce serious cardiac conduction abnormalities, particularly in elderly patients. Regular ECG monitoring is essential when prescribing these agents to minimize the risk of malignant arrhythmia.

Keywords: Third-degree atrioventricular block, escitalopram, quetiapine, depression, case report

Introduction

In modern society, the prevalence of depression is increasing annually, particularly among the elderly, drawing growing concern from both the medical community and the broader public [1]. According to the World Health Organization, approximately 300 million people worldwide suffer from depression, with especially alarming rates observed in older populations [2]. Age-related physiologic decline, changes in social roles, and shifts in living environments often predispose elderly individuals to psychological challenges such as loneliness, loss, and helplessness.

Depressive symptoms in the elderly are frequently misinterpreted or overlooked. For instance, emotional decline in older adults is often dismissed as a natural part of aging, masking underlying clinical depression [3]. The manifestations of depression vary widely and may include fatigue, reduced appetite, sleep disturbances with vivid dreams, and a pervasive loss of interest in life. This emotional state not only imposes psychologic distress on individuals but also poses a substantial burden to families and society. Consider an elderly person who once actively engaged in community life but, due to depression, becomes withdrawn and socially isolated [4]. Such changes affect the emotional health of those around them as well as themselves.

Depression in older adults is not merely a personal issue; it presents broader implications for family dynamics and societal health. Individuals with depression often struggle to self-regulate, and their persistent low mood can strain familial relationships, sometimes leading to emotional detachment or conflict [5]. Children of affected parents may feel helpless - willing to provide support but unsure how to help. Moreover, depression may exacerbate physical health problems, as it is associated with impaired immune function and increased susceptibility to chronic illnesses such as cardiovascular disease and diabetes, creating a detrimental feedback loop [6].

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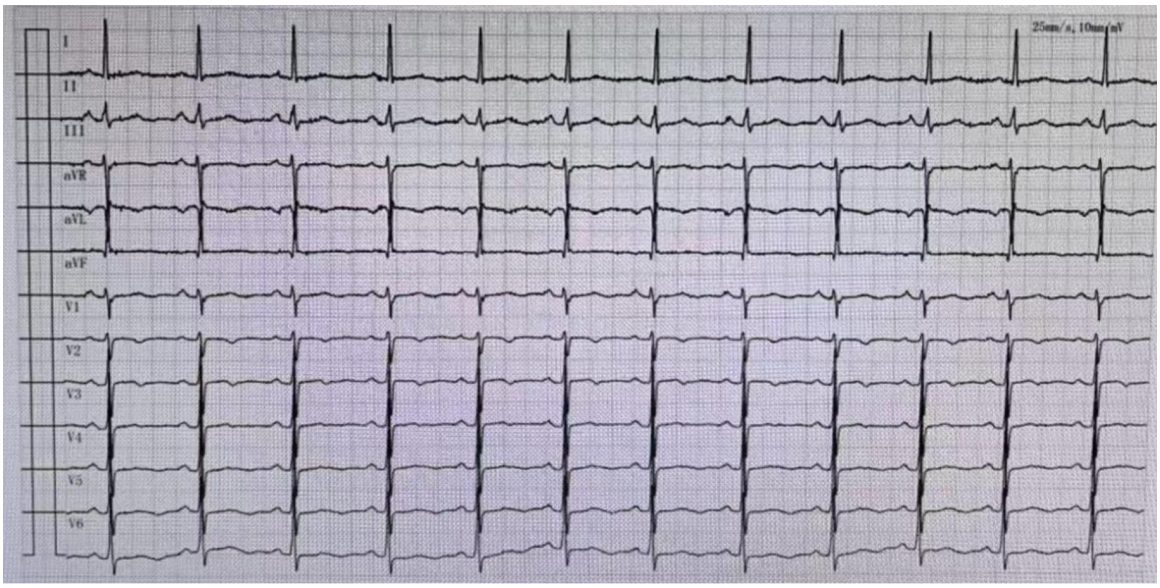

Figure 1. Initial electrocardiogram.

Selective serotonin reuptake inhibitors (SSRIs) are commonly used for the treatment of depression and have demonstrated reliable therapeutic efficacy [7]. Escitalopram oxalate, the S-enantiomer of citalopram and a member of the SSRI class, acts on both the primary binding site and allosteric sites of the presynaptic 5-HT transporter, thereby enhancing serotonergic neurotransmission and improving antidepressant outcomes. When combined with quetiapine, an antipsychotic agent, a synergistic effect may occur [8]. However, reports of adverse reactions from this combination are scarce, particularly regarding atrioventricular conduction disturbances, which in severe cases can result in sudden cardiac death.

Case Report

A 70-year-old Han Chinese woman was admitted to Huzhou Third Municipal Hospital with symptoms of depressed mood, anhedonia, and insomnia lasting over one month. She had a 20-year history of recurrent depression and had been hospitalized multiple times with good treatment response. However, she discontinued her medications three months prior and recently experienced a relapse. She was started on milnacipran 75 mg/day and alprazolam 0.2 mg/day. The patient had no history of surgery, chronic illness, or family history of psychiatric disorders. She did not smoke or consume alcohol.

Physical and auxiliary examinations, including complete blood count, liver and kidney function tests, blood glucose, and lipid profile, showed no significant abnormalities. Baseline Electrocardiogram (ECG) revealed sinus rhythm with mild T-wave changes (**Figure 1**). There was no prior history of atrioventricular block (AVB).

Due to poor treatment response, escitalopram (Sichuan Kelun Pharmaceutical Co., Ltd., National Drug Approval Number: H20080788) was initiated at 5 mg/day on the first day of admission and increased to 10 mg/day on day 4. Alprazolam was discontinued on day 7, and the dose of milnacipran was reduced to 50 mg/day. Quetiapine (Hunan Dongting Pharmaceutical Co., Ltd., National Drug Approval Number: H20000466) 12.5 mg/day was added on day 11. Fourteen days after starting escitalopram, ECG showed third-degree AVB with an atrioventricular junctional escape rhythm, QT interval prolongation, left ventricular high voltage, and a heart rate of 45 beats per minute (**Figure 2**).

The patient underwent emergency implantation of a permanent pacemaker in the cardiology department. Escitalopram and quetiapine were discontinued, and she continued on milnacipran monotherapy. Follow-up ECGs showed no significant abnormalities.

Discussion

Third-degree AVB is a serious arrhythmia that can result in reduced cardiac output and may

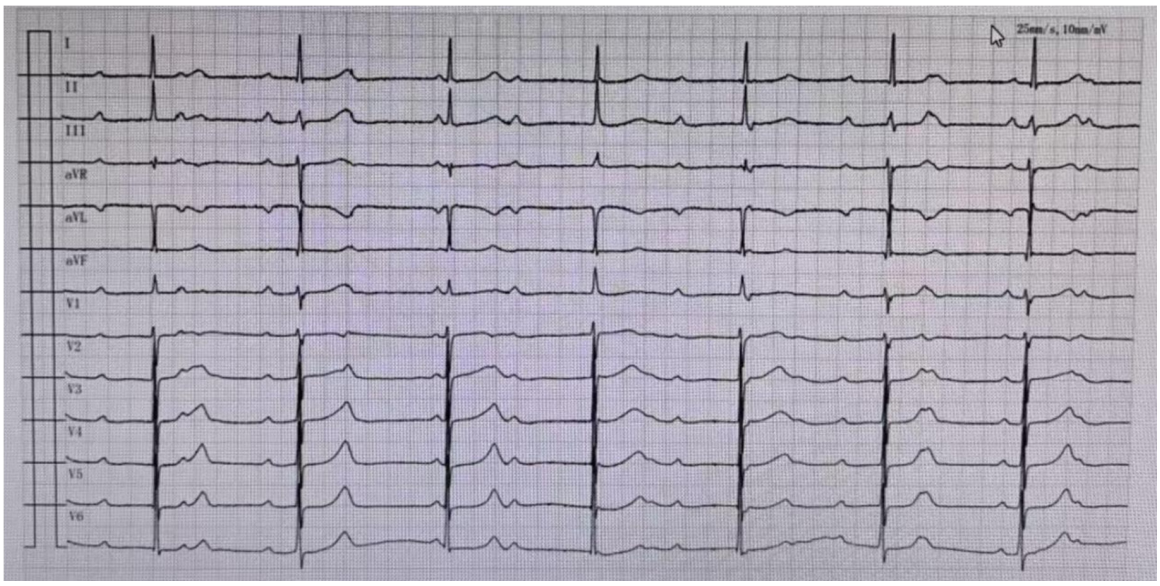

Figure 2. Electrocardiogram 14 days later.

Table 1. Literature related to arrhythmia caused by escitalopram and quetiapine

Drug (yr)	Types of arrhythmia
Escitalopram (2022)	Serious arrhythmia
Escitalopram (2016)	Ventricular Arrhythmia
Escitalopram (2022)	Ventricular Arrhythmias
Quetiapine (2018)	QT/QTc prolongation
Quetiapine (2024)	QT prolongation

be life-threatening. Although SSRIs and atypical antipsychotic drugs (APDs) are commonly prescribed for psychiatric disorders, both classes are associated with QT interval prolongation and, in rare cases, torsades de pointes. However, third-degree AVB induced by these agents is extremely rare.

Escitalopram, an SSRI indicated for the treatment of depression and anxiety, functions by inhibiting the reuptake of serotonin, thereby increasing synaptic serotonin levels and improving mood. It is generally well-tolerated, with commonly reported adverse effects including insomnia, sexual dysfunction, nausea, sweating, fatigue, and somnolence [9, 10]. Though rare, serious adverse events such as QT interval prolongation and serotonin syndrome have been documented [11]. *In vitro* studies suggest that escitalopram may cause bradycardia by modulating autonomic tone - decreasing sympathetic activity and increasing parasympathetic input [12], which may contribute to bradyarrhythmia in susceptible individuals.

Quetiapine, an APD used for schizophrenia, bipolar disorder, and adjunctive treatment of depression, exerts its effects primarily through antagonism of multiple neurotransmitter receptors, including dopamine, serotonin, and histamine receptors. It modulates dopaminergic and serotonergic neurotransmission, thereby alleviating psychotic and affective symptoms. Severe QT prolongation (SQTP) has been reported in quetiapine users and is associated with an increased risk of ventricular arrhythmias and sudden cardiac death. Patients with known risk factors for QT prolongation should be closely monitored when receiving quetiapine [13].

Both escitalopram and quetiapine are known to prolong the QT interval by inhibition of cardiac potassium channels (**Table 1**). While monotherapy with either drug typically carries a low risk for high-grade AV conduction blocks, their combined use may exert an additive or synergistic electrophysiological effect. A thorough QT/QTc study demonstrated increased arrhythmic risk following the initiation of combination therapy with escitalopram and quetiapine, likely due to cumulative QTc prolongation [14]. Li et al. also reported sinus bradycardia as an adverse event associated with this drug combination [15]. According to the American Heart Association (AHA), risk factors for drug-induced serious

arrhythmias include age ≥ 65 years, female sex, acute coronary syndrome, and electrolyte imbalances (e.g., hypokalemia, hypocalcemia, hypomagnesemia) [16]. In this case, the patient's advanced age and female sex were both recognized risk factors.

Given these considerations, we speculate that the combined use of escitalopram and quetiapine played a synergistic role in the onset of third-degree AVB. The patient was otherwise healthy, with no history of cardiovascular, neurological, or systemic disease, and no substance use history. These factors reduce the likelihood of alternative etiologies.

Regarding concomitant medications, milnacipran is a serotonin-norepinephrine reuptake inhibitor (SNRI) that generally does not significantly affect the QT interval at therapeutic doses [17, 18]. Although severe QT prolongation has been reported at high doses or in the presence of predisposing factors, the patient had normal ECG findings while on milnacipran monotherapy. Moreover, the dose of milnacipran was reduced following the addition of escitalopram, and no further ECG abnormalities were observed after withdrawal of escitalopram and quetiapine [19-21]. Therefore, a causal relationship between milnacipran and the AVB appears unlikely.

Alprazolam, a benzodiazepine used to treat anxiety and sleep disorders, is associated with side effects such as sedation, dizziness, and fatigue. Cardiovascular effects are minimal, and it rarely causes significant ECG changes. The patient had discontinued alprazolam before the onset of AVB, further reducing the likelihood of its involvement.

Conclusion

This case highlights a rare but severe adverse event - third-degree AVB - following the combined administration of escitalopram and quetiapine. Clinicians should exercise caution when prescribing these drugs, especially in elderly patients or those with known risk factors for cardiac arrhythmias. Routine ECG monitoring and awareness of potential drug interactions are critical in mitigating risk. Further research is warranted to elucidate the underlying mechanisms by which escitalopram, quetiapine, and similar agents may induce high-grade AV conduction disturbances, and to develop evidence-based preventive strategies.

Disclosure of conflict of interest

None.

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