Case Report

JHSMR Journal of Health Science and Medical Research

Cardiac Arrest after Adding Mirtazapine in an Older Patient with Depression Who Already Used Escitalopram: A Case Report

Kanthee Anantapong, M.D., Ph.D.[1], Pongsanae Duangpakdee, M.D.[2], Treechada Wisaratapong, M.D.[3], Ply Chichareon, M.D.[3]

[1]Department of Psychiatry, Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkhla 90110, Thailand.

[2]Division of Cardio-Thoracic Surgery, Department of Surgery, Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkhla 90110, Thailand.

[3]Division of Cardiology, Department of Internal Medicine, Faculty of Medicine, Songklanagarind Hospital, Prince of Songkla University, Hat Yai, Songkhla 90110, Thailand.

Received 6 September 2024 ● Revised 25 February 2025 ● Accepted 4 March 2025 ● Published online 10 June 2025

Abstract:

A 65-year-old woman with underlying hypertension and ischemic stroke was diagnosed with dysthymia and prescribed escitalopram 10 mg/day by a psychiatrist. Three months later, she received mirtazapine 15 mg/day from another physician to alleviate myofascial pain syndrome and sleeping problems. The following day, she developed jaw pain and later suffered cardiac arrest at the emergency unit, with her electrocardiogram revealing a prolonged QT interval. Emergency coronary artery angiography suggested myocardial infarction. Antidepressants were immediately discontinued, and she underwent coronary artery bypass grafting. After one year, her clinical symptoms had stabilised, allowing her to continue daily activities without chest pain, though she still experienced recurrent mild headaches and sleeping problems. This case underscores the importance of vigilant medication management in older adults with depression, especially in the context of a combination regimen and polypharmacy.

Keywords: depression, escitalopram, heart arrest, humans, mirtazapine

Contact: Kanthee Anantapong, M.D., Ph.D.
Department of Psychiatry, Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkhla 90110, Thailand.
E-mail: kanthee.a@psu.ac.th

J Health Sci Med Res 2026;44(2):e20251221
doi: 10.31584/jhsmr.20251221
www.jhsmr.org

Introduction

Depression is a prevalent and often underrecognised mental health disorder in older adults, significantly impacting their quality of life, physical health, and overall well-being[1]. This demographic frequently faces unique challenges, including social isolation, the loss of loved ones, chronic medical conditions, and declining physical health, all of which can contribute to the onset of depressive symptoms[2]. Moreover, the interaction between depression and chronic illnesses, such as heart disease and diabetes, can create a cycle of worsening health.

Antidepressants, especially selective serotonin reuptake inhibitors (SSRIs) and tricyclic antidepressants (TCAs), are frequently prescribed for managing depression in older adults[3]. This demographic often faces unique challenges, including polypharmacy, where patients take multiple medications to manage various health conditions. Despite ongoing debates surrounding their efficacy and safety, the use of these medications in older individuals can carry significant potential risks, particularly concerning cardiovascular health. Notably, some studies have indicated an increased incidence of cardiac arrhythmias, including atrial fibrillation and ventricular tachycardia, as well as the risk of cardiac arrest associated with the use of these antidepressants[4,5].

This case report highlights a unique and concerning instance of cardiac arrest in an older patient with depression who experienced a serious adverse event after adding mirtazapine, an atypical antidepressant, to their existing regimen of escitalopram, a widely used SSRI. The incident underscores a critical need for heightened awareness and vigilance in medication management for this vulnerable population. Older adults, due to age-related physiological changes, such as altered drug metabolism and increased sensitivity to medications, may exhibit varied responses to pharmacological treatments, leading to an increased risk of side effects. Moreover, the combination of different classes of antidepressants, while often prescribed to enhance therapeutic efficacy, can inadvertently lead to cumulative side effects that may compromise cardiac health. In this context, healthcare professionals must prioritise comprehensive assessments, close monitoring, and individualised treatment plans in order to mitigate the risks while effectively managing depression in older adults.

Case report

A 65-year-old retired female government officer with long-standing hypertension and a history of left-frontal ischemic stroke visited a psychiatric clinic at Songklanagarind Hospital, Thailand. She presented with chronic low-intensity depression and somatic symptoms, including poor appetite, chronic headache, dizziness, and insomnia, stemming from guilt related to a family member's death 6 years earlier. Diagnosed with dysthymia, she was prescribed escitalopram 10 mg/day and lorazepam 0.5 mg/day. While her mood and appetite improved after a month, somatic symptoms persisted. Lorazepam was discontinued, and Circadin PR 2 mg was added to address sleep issues. In fact, she had frequent visits to the emergency unit and internal medicine clinic over the past decade for recurring headaches and dizziness. See Table 1 for a summary of her prior laboratory investigations and medications.

Three months later, she was diagnosed with myofascial pain syndrome at the internal medicine clinic and prescribed mirtazapine 15 mg/day, along with etoricoxib and tolperisone for her headache. The following morning, she experienced severe jaw pain radiating to her head, prompting a visit to the emergency unit, where she received Fentanyl 30 mcg IV. Within an hour, she went into cardiac arrest, initiating cardiopulmonary resuscitation (CPR). Initial electrocardiogram (EKG) revealed ventricular fibrillation, requiring defibrillation once. Return of spontaneous circulation was achieved after 2 CPR cycles and a dose of 1 mg adrenaline. Post-arrest EKGs at 10 and 20 minutes

showed QTc intervals of 444 and 487 msec, respectively, with ST depression in multiple leads.

During hospitalisation, a comprehensive investigation into potential causes of the cardiac arrest was conducted. This included an evaluation of the patient's existing medical prescriptions and cardiac conditions. Diagnostic tests performed encompassed blood laboratory analysis, chest x-ray, echocardiogram, and emergency CT brain scan. Notably, blood tests revealed hypokalaemia, a condition that could have been a pre-existing factor contributing to QT prolongation. Additional investigation findings are summarised in Table 1. Coronary angiography was performed as part of the routine workup for the underlying cause of ventricular fibrillation. Coronary angiogram revealed significant triple-vessel disease, indicating the need for coronary revascularisation.

In accordance with Class I recommendations from the 2021 American Heart Association (AHA) guideline, coronary artery bypass grafting surgery was then initiated promptly following the diagnosis of significant triple-vessel disease. This decision was made in collaboration with the multidisciplinary cardiac team, considering the patient's clinical presentation and guideline-directed therapy. The patient underwent successful coronary artery bypass grafting surgery and exhibited a favourable recovery postoperatively. Antidepressant-induced malignant

Table 1 Clinical, laboratory and instrumental data of our patient

Prior to cardiac arrest
• EKG (2021, pre-operative evaluation for elective surgery): normal sinus rhythm (NSR), QTc 400 msec, normal PR interval, no STT changes • Medications: Clopidogrel (75mg) 1x1, Losartan (50mg) 1x1, Simvastatin (40mg) 1x1, and Manidipine (20mg) 0.5x1, Escitalopram (10mg) 1x1, Circadin PR (2mg) 1x1, Mirtazapine (15mg) 1x1 (added a day earlier)
At emergency department (the event of cardiac arrest)
• Blood tests: CBC: WBC 12,920/uL, Hb 12.3 g/dL, Hct 39.0%, Platelet 288,000/uL; BUN 15.6 mg/dL, Cr 1.04 mg/dL, Na 142 mmol/L, K 3.29 mmol/L, Cl 108.0, mmol/L, Total CO2 9.8 mmol/L; Troponin T (ng/L): 45.6 ng/L (1-hour post arrest), 393 ng/L (4-hour post arrest) • EKG 10-minute post arrest: QTc 444 msec • EKG 20-minute post arrest: sinus rhythm with ST depression in I, aVL, II, aVF, V2-6. QTc 487 msec • EKG 6-hour post arrest: NSR rate 80/min, QTc 460 msec, ST depression and T wave inversion in V5, V6, II, III, aVF, no Brugada pattern, no early repolarisation, no delta wave • Chest X-ray: increased bilateral perihilar infiltration with cephalisation, sharp bilateral costophrenic angle, mild cardiomegaly • Echocardiogram: left ventricle normal sized, left ventricular ejection fraction = 53%, basal to mid anteroseptal hypokinesia, basal inferoseptal and inferior wall hypokinesia, diastolic dysfunction Grade I • CT brain with contrast emergency: no intracranial haemorrhage or tumour
During hospital admission
• Coronary artery angiography: severe stenosis of ostial left anterior descending artery (LAD), total occlusion of mid-LAD, severe stenosis of mid-left circumflex artery, significant stenosis of right coronary artery (RCA) - right posterolateral (RPL) - right posterior descending (RPD) branch
Discharged from the hospital
• Home medications: Clopidogrel (75mg) 1x1, Aspirin (81mg) 1x1, Atorvastatin (40mg) 1x1, Bisoprolol (2.5mg) 0.5x1, Amlodipine (5mg) 1x1, Furosemide (40mg) 0.5x1, Valsartan (80mg) 1x1, Gabapentin (100mg, for myofascial pain) 1x1, Omeprazole (20mg)1x1, Lorazepam (0.5) 1x1

CBC=complete blood count, WBC=white blood cell, Hb=haemoglobin, Hct=haematocrit, BUN=blood urea nitrogen, Cr=creatinine, Na=sodium, K=potassium, Cl=chloride, CO2=carbon dioxide, L=litre, dL=decilitre, uL=microliter, g=gram, mg=milligram, ng=nanogram, mmol=millimoles

arrhythmia was identified as the precipitating factor of acute myocardial infarction and subsequent cardiac arrest, leading to the discontinuation of both antidepressants. The patient remained hospitalised for 19 days and was discharged with lorazepam 0.5 mg/day, among the other medications listed in Table 1. One year later, her overall condition was stable with no depressive symptoms but occasional difficulties in sleeping, mild headaches, and dizziness, which did not significantly impact her daily life.

Discussion

Escitalopram and mirtazapine are 2 commonly prescribed antidepressants, each belonging to different classes of medications used to manage depression and anxiety disorders[6]. Both drugs, while effective in treating these conditions, have been linked to QT interval prolongation, a significant cardiac concern that can increase the risk of fatal arrhythmias. This side effect underscores the need for careful consideration when prescribing these medications, especially to vulnerable populations such as older adults who may have multiple comorbidities and be taking various medications.

Myofascial pain syndrome and depression often coexist, creating a complex interplay between physical and psychological symptoms. The relationship between myofascial pain syndrome and depression appears to be bidirectional, with chronic pain potentially exacerbating depressive symptoms and vice versa[7]. Antidepressants have emerged as a valuable treatment option for managing both the pain and psychological aspects of myofascial pain syndrome particularly, a serotonin–norepinephrine reuptake inhibitor (SNRI) and TCAs. Mirtazapine has shown promise in treating chronic pain conditions, including fibromyalgia, which shares some similarities with myofascial pain syndrome[8]. The mechanism of action for these antidepressants in pain management is thought to involve the modulation of serotonin and norepinephrine pathways, which play crucial roles in both pain perception and mood regulation. However, a Cochrane review found no benefit of mirtazapine over a placebo for pain relief of 50% or greater, quality of life, or the reduction of fatigue or negative mood [9]. While antidepressants offer promising results, it is important to note that their efficacy may vary among individuals, and a multidisciplinary approach to treatment, including physical therapy and psychological interventions, is often recommended for the optimal management of myofascial pain syndrome and any associated depressive symptoms.

Regarding the treatment of depression, the contemporary practice of psychiatry often involves a multifaceted approach to managing depression, particularly for patients who do not respond adequately to first-line treatments such as SSRIs. The addition of mirtazapine for patients demonstrating inadequate responses to SSRIs is gaining attention in clinical settings. Mirtazapine, known for its unique mechanism that enhances both serotonergic and noradrenergic transmissions, has shown potential benefits for patients who also struggle with anxiety and sleep disturbances. However, the clinical efficacy of this combination strategy remains a topic of investigation. A randomised controlled trial (RCT) conducted by Kessler et al.[10] found no significant benefit of adding mirtazapine to an SSRI or SNRI compared to a placebo in treatment-resistant patients aged 18 and older suffering from depression. Conversely, Matreja et al.[11] conducted an RCT that explored the effects of adding mirtazapine to a conventional SSRI in a more diverse group of individuals aged 18 to 75. This study reported an earlier onset of action, better overall efficacy, and a higher number of responders and remitters without significant side effects when compared to traditional SSRI monotherapy. These contrasting results highlight the complexity of psychiatric treatment and imply that the benefits of adjunctive therapies might depend on individual patient characteristics such as age, severity of illness, and specific symptom profiles.

Mirtazapine has generally been considered to have a favourable cardiovascular safety profile compared to other antidepressants[12]. However, some studies have reported a slight increase in the risk of sudden cardiac death and ventricular arrhythmia associated with mirtazapine use. A high dose of escitalopram (>10 mg) and mirtazapine (>30 mg) were also found to be associated with out-of-hospital cardiac arrest[13]. The exact mechanism is not fully understood, but it may involve multiple factors beyond QT prolongation. Effects of escitalopram and mirtazapine on cardiac ion channels, particularly potassium channels, could play a role in altering cardiac electrophysiology[14]. Additionally, their action on adrenergic and serotonergic systems may influence heart rate and rhythm[14]. While QT prolongation is associated with increased arrhythmia risk, the direct link to cardiac arrest is complex. Additionally, aging is associated with various physiological changes, including alterations in pharmacokinetics and pharmacodynamics. These changes can impact drug metabolism, increase susceptibility to side effects, and heighten the risk of adverse events, especially cardiovascular complications. Older adults, who often present with preexisting cardiovascular conditions and electrolyte abnormalities, face heightened risks when prescribed medications that can prolong the QT interval and increase the risk of cardiac arrest. The potentially life-threatening consequences of these effects necessitate a careful assessment of a patient's overall health status, medication regimen, and the specific risks associated with additional treatments[4].

As clinicians explore treatment options for depression in older adults, it is essential to recognise the delicate balance between therapeutic benefits and risks. The decision to prescribe medications such as escitalopram and mirtazapine requires a comprehensive evaluation of the individual patient's medical history, current medications, and potential drug interactions. Older patients are often prescribed multiple medications for coexisting health issues, increasing their risk for adverse drug reactions. Although mirtazapine and escitalopram have been found to be safe and effective in managing post-myocardial infarction depression[15], in the context of a combination regimen and polypharmacy, clinicians should remain vigilant for potential drug interactions and monitor patients closely, as the risk of adverse effects may be heightened in those with complex cardiovascular conditions. This complexity is compounded by the need for ongoing monitoring of heart health, particularly through baseline and regular ECG, blood pressure, and pulse evaluations to detect any potential cardiovascular conditions in people who use antidepressants, particularly those having pre-existing cardiac disorders and using TCAs[3-5].

Furthermore, the implications of antidepressant use go beyond just cardiovascular concerns. Mental health disorders not only affect the psychological well-being of patients but also have substantial effects on their overall physical health, social functioning, and quality of life[2]. The strategy for treating depression in older patients must therefore be multifaceted, encompassing not only pharmacological interventions but also psychological therapies, lifestyle modifications, and social support mechanisms[2,6]. Engaging patients in shared decision-making and discussing the potential risks and benefits of various treatment options can empower them to take an active role in managing their health[6].

In summary, the cardiovascular effects of antidepressants like escitalopram and mirtazapine are critical considerations for healthcare providers, especially when treating older patients. While the addition of mirtazapine may offer some benefits in specific contexts, the lack of consistent evidence regarding its efficacy underscores the need for a patient-centred approach to treatment planning. This case report serves as a vital reminder of the delicate balance required in treating depression in a population that is at a heightened risk for adverse cardiovascular events.

Conclusion

Clinicians must remain vigilant in monitoring for potential adverse outcomes while also considering the therapeutic benefits of these medications. As research continues to evolve, it will be paramount for healthcare professionals to stay informed and adaptable, ensuring that treatment strategies are tailored to meet the unique needs of each patient while minimising risks. By fostering a comprehensive understanding of the complexities involved in antidepressant therapy, clinicians can better navigate the challenges of treating depression in older adults and enhance the quality of care provided to this vulnerable population.

Conflict of interest

The authors declare they have no conflicts of interest.

References

1. Anantapong K, Pitanupong J, Werachattawan N, Aunjitsakul W. Depression and associated factors among elderly outpatients in Songklanagarind Hospital, Thailand: A cross-sectional study. Songklanagarind Med J 2017;35:139-48.
2. Anantapong K, Wiwattanaworaset P, Sriplung H. Association between Social Support and Frailty among Older People with Depressive Disorders. Clin Gerontol 2020;43:400-10.
3. Coupland C, Dhiman P, Morriss R, Arthur A, Barton G, Hippisley-Cox J. Antidepressant use and risk of adverse outcomes in older people: population based cohort study. BMJ 2011;343:d4551.
4. Behlke LM, Lenze EJ, Carney RM. The Cardiovascular Effects of Newer Antidepressants in Older Adults and Those With or At High Risk for Cardiovascular Diseases. CNS Drugs. 2020;34:1133-47.
5. Prasitlumkum N, Cheungpasitporn W, Tokavanich N, Ding KR, Kewcharoen J, Thongprayoon C, et al. Antidepressants and risk of sudden cardiac death: a network meta-analysis and systematic review. Med Sci (Basel) 2021;9.
6. Srifuengfung M, Pennington BRT, Lenze EJ. Optimizing treatment for older adults with depression. Ther Adv Psychopharmacol. 2023;13:20451253231212327.
7. Overmann L, Schleip R, Michalak J. Exploring fascial properties in patients with depression and chronic neck pain: An observational study. Acta Psychol (Amst). 2024;244:104214.
8. Miki K, Murakami M, Oka H, Onozawa K, Yoshida S, Osada K. Efficacy of mirtazapine for the treatment of fibromyalgia without concomitant depression: a randomized, double-blind, placebo-controlled phase IIa study in Japan. Pain 2016;157:2089-96.
9. Welsch P, Bernardy K, Derry S, Moore RA, Hauser W. Mirtazapine for fibromyalgia in adults. Cochrane Database Syst Rev 2018;8:CD012708.
10. Kessler DS, MacNeill SJ, Tallon D, Lewis G, Peters TJ, Hollingworth W, et al. Mirtazapine added to SSRIs or SNRIs for treatment resistant depression in primary care: phase III randomised placebo controlled trial (MIR). BMJ 2018;363:k4218.
11. Matreja PS, Badyal DK, Deswal RS, Sharma A. Efficacy and safety of add on low-dose mirtazapine in depression. Indian J Pharmacol 2012;44:173-7.
12. Allen ND, Leung JG, Palmer BA. Mirtazapine's effect on the QT interval in medically hospitalized patients. Ment Health Clin 2020;10:30-3.
13. Eroglu TE, Barcella CA, Gerds TA, Kessing LV, Zylyftari N, Mohr GH, et al. Risk of out-of-hospital cardiac arrest in antidepressant drug users. Br J Clin Pharmacol 2022;88:3162-71.
14. Sala M, Lazzaretti M, De Vidovich G, Caverzasi E, Barale F, d'Allio G, et al. Electrophysiological changes of cardiac function during antidepressant treatment. Ther Adv Cardiovasc Dis 2009;3:29-43.
15. Hanash JA, Hansen BH, Hansen JF, Nielsen OW, Rasmussen A, Birket-Smith M. Cardiovascular safety of one-year escitalopram therapy in clinically nondepressed patients with acute coronary syndrome: results from the DEpression in patients with Coronary ARtery Disease (DECARD) trial. J Cardiovasc Pharmacol 2012;60:397-405.