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CHEST PAIN AS INITIAL CARDIOVASCULAR SIDE EFFECT OF ESCITALOPRAM: LITERATURE UPDATE ON MANAGEMENT PROTOCOL

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ABSTRACT

Background: Escitalopram is a highly selective serotonin reuptake inhibitor commonly used for the treatment of major depressive disorder and generalized anxiety disorder. In addition to the common sexual side effect. There are varying reports of its cardiovascular side effects. It is therefore imperative that a simple complaint of chest pain in a patient on escitalopram should attract a comprehensive evaluation. **Methods**: We employed a structured narrative approach to identify and review available articles on escitalopram and cardiovascular side effects. We aimed to evaluate the association between escitalopram therapy and adverse cardiovascular side effects. **Results:** We identified no direct chest pain reports during escitalopram therapy. There are documented reports of rare side effects with potential chest pain manifestation. These are QT prolongation and arrhythmias, including torsades de pointes. Others reported a safe cardiovascular profile of escitalopram. **Conclusions**: Despite its good therapeutic potential, there are nuanced reports of escitalopram's rare cardiovascular effects. Chest pain should be part of the regular evaluation of patients on escitalopram. Health education should be given to immediately call for help when the pain is sudden, severe, chest pain lasts longer than a few minutes, or is accompanied by symptoms like crushing pressure, pain radiating to the arm or jaw, shortness of breath, or nausea according to the American Heart Association guidelines.

KEYWORDS: cardiovascular, chest, escitalopram, effect, pain, side.

INTRODUCTION

Escitalopram, the (S)-enantiomer of citalopram, is a highly selective serotonin reuptake inhibitor (SSRI). It received approval from the U.S. Food and Drug Administration (FDA) for the treatment of major depressive disorder (unipolar) in both adults and adolescents (ages 12 to 17) during both acute and maintenance phases.[1] Recently, the FDA has also approved escitalopram for the treatment of generalized anxiety disorder in adults and children aged 7 and older.[1] Additionally, escitalopram is utilized off-label for various conditions, including social anxiety disorder, obsessive-compulsive disorder, panic disorder, posttraumatic stress disorder, premenstrual dysphoric disorder, and the management of vasomotor symptoms related to menopause.[2]

The pharmacokinetics of escitalopram exhibit linearity and dose proportionality within the dosage range of 10 to 30 mg/d.[3] The peak plasma concentration is generally reached in about 5 hours, while steady-state plasma concentrations are established within a period of 1 to 2 weeks. It has a high volume of distribution (12 L/kg) and a low plasma protein binding (56%).[3] Therefore, it is unlikely to provoke interactions with highly protein-bound drugs. The terminal half-life of escitalopram ranges from 27 to 33 hours. Escitalopram and its metabolites are excreted in the urine.[4]

Escitalopram exhibits a lower toxicity profile compared to older antidepressants but possesses adverse effects.[5] The most commonly reported adverse effects include insomnia, diminished libido, anorgasmia, delayed ejaculation in males, nausea, heightened sweating, fatigue, and drowsiness.[6] Other rare adverse effects include QT prolongation and serotonin syndrome, which are considered serious when they occur.[5] Escitalopram can also cause a syndrome of inappropriate antidiuretic hormone secretion (SIADH), which can lead to hyponatremia, common in older adults.[7]

The QT prolongation can cause potentially fatal cardiac arrhythmias, including torsades de pointes (TdP). Escitalopram can equally exacerbate sinus bradycardia and atrioventricular (AV) block by inhibiting sodium and calcium channels. Tdp and arrhythmias can present clinically as chest pain.

METHODS

A narrative approach was used to synthesize, interpret, and critique the findings of studies that reported the cardiovascular side effects of Escitalopram. We conducted an electronic search of PubMed, Google, and Google Scholar for peer-reviewed, English-language articles published up until August 2025. Preliminary keyword searches included combinations of "arrhythmias," "atrioventricular block," "chest pain," "QT prolongation," "torsades de pointes," and "Escitalopram."

RESULTS

Our search yielded a total of 9 articles. The identified studies fall under descriptive retrospective studies, including case reports, case series, cross-sectional studies, and randomized controlled trials.

In one study, conducted in 2019, 3,809 patients taking antidepressants were recruited. 1,065 were prescribed citalopram and escitalopram, and 137 met the study criteria: with 97 on citalopram and 40 on escitalopram. Complications were divided into TdP and sudden cardiac death (SCD. There were no cases of TdP, but one patient taking 15mg escitalopram followed by risperidone (antipsychotic medication) had SCD.[8] The researchers concluded that no association could be found between citalopram, escitalopram, and QT prolongation.[8]

A rare repeated sinus bradycardia event due to escitalopram was reported in an 82-year-old female patient with cardiac dysfunction on digoxin and lorazepam.[9] In treating a 25-year-old man with escitalopram for obsessive-compulsive disorder, a dose-dependent bigeminy was reported.[10] In a case presentation, escitalopram was reported to have induced TdP and cardiac arrest in a patient with surgically treated mitral valve prolapse.[11] A case of pulmonary embolism was documented in a 70-year-old woman on a 10 mg escitalopram treatment, after presenting with dyspnea, a confused mental state, decreased O2 saturation, and multifocal pulmonary embolism detected by chest CT scan.[12]

In another study, 773 participants who met the inclusion criteria were evaluated to evaluate the adverse cardiovascular reactions to escitalopram in patients with underlying cardiovascular disease. Randomized controlled trials.[13] Escitalopram was not associated with a significantly increased risk of major adverse cardiovascular events.

In evaluating the cardiovascular safety profile of escitalopram, 3298 participants were recruited to receive escitalopram at doses between 5 and 20 mg/day and placebo.[14] Patients were treated in acute (8–12 weeks) and long-term (24 weeks) studies. Cardiovascular safety assessment, including heart rate, blood pressure (BP), treatment-emergent adverse events, and electrocardiograms (ECGs), was done. In the short-term, there was a statistically significant 2 beats per minute decrease in heart rate with escitalopram compared with placebo. The disparity in systolic or diastolic blood pressure when compared to placebo was neither clinically nor statistically significant. Furthermore, the differences in mean changes in ECG values between escitalopram and placebo were not clinically relevant.[14]

In a comparative analysis of the cardiovascular safety of selective serotonin reuptake inhibitors (SSRIs) among Chinese senile depression patients, 1432 participants taking escitalopram or other SSRIs were recruited.[15] The study revealed that escitalopram was associated with a lower risk of cardiovascular reaction (CDR) than paroxetine, sertraline, citalopram, and fluoxetine.[15]

In 2016, a study was conducted to compare the cardiovascular safety of escitalopram and sertraline based on electrocardiographic alterations.[16] They recruited 209 participants in the study that evaluated ECG parameters like heart rate, RR interval, PQ/PR interval, QRS duration, and QTc interval. The researchers reported that the differences between the ECG alterations caused by either escitalopram or sertraline were statistically nonsignificant.[16]

DISCUSSION

The U.S. Food and Drug Administration (FDA) has indicated that the selective serotonin reuptake inhibitors

raise the risk of QTc prolongation and potentially fatal ventricular arrhythmias, such as Torsade de Pointes.[17] Providers were advised to exercise caution while prescribing SSRIs, and it was recommended that citalopram doses should not exceed 40 mg and escitalopram 20 mg.[18] It was further recommended that in older adults, the dose should be reduced to half in both medications. The QTc-prolongation is due to the blockade of the human ether-à-go-go-related gene (hERG) K+ channel, which is caused by escitalopram.[20] Escitalopram has been implicated in the widening of the QRS complex due to a change in the functioning of sodium channels.[19] The metabolites of escitalopram, called didesmethylcitalopram, have also been documented as the primary metabolite responsible for the cardiotoxicity effects. The effects result in varying cardiac abnormalities and ECG alterations, including atrioventricular dissociation, junctional escape cardiac rhythms with sinus arrest, and widening of the QRS complex.[20]

Escitalopram was implicated in a case of sudden cardiac death in an older adult.[9] The patient was receiving risperidone equally. However, escitalopram has an inhibitory effect on the CYP 2D6 enzyme, which is the enzyme substrate for risperidone.[21] It is possible that escitalopram augmented the toxicity of risperidone in this case. A case of bradycardia was also reported in an older adult.[10] Though discontinuation of escitalopram normalized the heart rate, the patient was also receiving digoxin and lorazepam at the same time. While lorazepam does not commonly cause bradycardia, digoxin is a well-documented cause of bradycardia.[22]

A case of pulmonary embolism was reported in a patient receiving escitalopram.[13] Escitalopram is not recognized as a direct cause of pulmonary embolism (PE) in the same manner that a virus induces a disease; rather, it serves as a potential risk factor that could elevate the likelihood of developing a deep vein thrombosis (DVT), which may subsequently result in a PE. The suggested mechanism pertains to escitalopram's influence on serotonin levels, potentially leading to heightened platelet activation and thrombosis (the formation of blood clots) during the initial treatment phase.[23] The associated risk is more intricate than it might seem, as certain theories propose that the underlying depression itself, rather than the medication, is the primary contributor to the increased risk of venous thromboembolism (VTE).

When comparing sertraline and paroxetine with escitalopram, escitalopram was found to increase the risk of mortality more in older adults.[24] Several factors contribute to the increased toxicity of escitalopram in elderly patients, mainly due to age-related alterations in drug metabolism and an elevated susceptibility to certain side effects. Significant issues encompass modified drug clearance, a heightened risk of hyponatremia, and the possibility of cardiotoxic effects.[25]

According to another study, escitalopram was not associated with a significantly increased risk of major adverse cardiovascular events.[14] Escitalopram lowers the risk of cardiac events in patients with acute coronary syndrome.[24] The administration of escitalopram for a duration of 24 weeks in individuals suffering from depression and acute coronary syndrome (ACS) has been shown to decrease the long-term risk of significant adverse cardiac events, according to findings from a placebo-controlled study. While the research did not establish a link between escitalopram treatment and mortality outcomes, it did find that reduced mortality was correlated with the remission status of depressed patients.[24]

Similarly, the differences in mean changes in ECG values between escitalopram and placebo were not clinically relevant.[15] The researchers in the study in 2013 elaborated on the cardiovascular safety profile of escitalopram.[15] A concordance study reported that escitalopram was not associated with a higher risk of ventricular arrhythmia compared with the other antidepressants.[26]

There is an under-reporting of direct chest pain associated with escitalopram therapy. Chest pain of any severity in a patient taking escitalopram is a prompt for a thorough clinical evaluation. Despite some reported safe cardiovascular profile of escitalopram, there are documented adverse effects with potential chest pain manifestation. Therefore, a patient on escitalopram with a complaint of chest pain should draw immediate clinical attention.

The current guidelines from the American Heart Association (AHA) and American College of Cardiology (ACC) recommend immediate action, including calling 911 for sudden, severe chest pain that lasts longer than a few minutes, or is accompanied by symptoms like crushing pressure, pain radiating to the arm or jaw, shortness of breath, or nausea.[27] In applying the guideline, chest pain in a patient on escitalopram must be evaluated for immediate intervention.

CONCLUSION

The literature has nuanced reports of the cardiovascular safety profile of escitalopram. Escitalopram is commonly used to treat depression. The onus lies on clinicians to explore beyond the common sexual side effects of escitalopram. Chest pain should be included as a common evaluation in patients on escitalopram, and health education should be given to immediately call for help when the pain is sudden, severe, chest pain lasts longer than a few minutes, or is accompanied by symptoms like crushing pressure, pain radiating to the arm or jaw, shortness of breath, or nausea.

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