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Escitalopram Induced QTc Prolongation: A Case Report

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ABSTRACT

Adverse drug reaction (ADR) can be defined as any noxious change which is suspected to be due to a drug, occurs at doses normally used in man, requires treatment or decrease in dose or indicates caution in the future use of the same drug. ESCITALOPRAM is a drug which comes under the category of selective serotonin reuptake inhibitors (SSRIs) (antidepressants). It is the S-enantiomer of the racemic derivative of citalopram, which selectively inhibits the reuptake of serotonin with little to no effect on norepinephrine or dopamine reuptake. Almost all the antidepressants and antipsychotics have been linked to QT prolongation.



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INTRODUCTION

Adverse drug reaction (ADR) can be defined as any noxious change which is suspected to be due to a drug, occurs at doses normally used in man, requires treatment or decrease in dose or indicates caution in the future use of the same drug.

A QT interval or QTc is an electrocardiographic measure of ventricular repolarization and depolarization. ^(1,1)

The normal value of QT interval is less than 450ms in men and 460ms in women. ^(1,2)

Antiarrhythmics, antibiotics, antipsychotics, antidepressants are some of the medications /drugs can lead to prolonged QT interval. ^(1,3)

There are some risk factors for QT prolongation are female sex, age greater than 65year, electrolyte disturbances (hypokalemia, hypomagnesemia) concomitant QT-prolonging medications. ^(1,4)

The United States Food and Drug Administration (FDA) ICH E14 guidance for clinical evaluation of QT/QTc interval prolongation and pro-arrhythmic potential for non-arrhythmic drugs established the threshold is in Table 1:

Table No. 1: US FDA E14 guidance for drug-induced QTc prolongation

Change from baseline QTc placebo correct	Interpretation
<10 ms	Low concern
10-20ms, QTc outliers +- clinical AES	Increasing concern
>20ms, +QTc outliers +- clinical AEs	Definite concern

- QTc outliers: individual-level QTc > 500ms or change in QTc >60ms
- Clinical AEs(Adverse Events): TdP, sudden death, ventricular tachycardia, ventricular fibrillation or flutter, syncope, seizure
- AE: TdP, torsades de pointes; US FDA; US Food and Drug Administration ^(1,5)

The study conducted in Unites States from 2011 – 2014 reported that the prevalence of QTc prolongation in adults on antidepressant therapy is 1% above in 60years or more of age.

ESCITALOPRAM is a drug which comes under the category of selective serotonin reuptake inhibitors(SSRIs) (antidepressants). It is the S-enantiomer of the racemic derivative of citalopram, which selectively inhibits the reuptake of serotonin with little to no effect on norepinephrine or dopamine reuptake. Escitalopram is metabolized by hepatic metabolism via CYP2C19 and CYP3A4 to S-desmethyl citalopram (S-DCT). S-DCT is metabolized to S-di-desmethyl citalopram (S-DDCT) via CYP2D6.

There are some monitoring parameters to check if a patient is on escitalopram including QTc changes, electrolyte, liver and renal function tests. Prolonged QT interval on ECG is reported in several studies as an adverse drug reaction. ⁽⁶⁾

CASE REPORT

A 68 year old female patient was admitted for the diagnosis of osteoporotic fracture with cord compression. She was a known case of hypertension and on medication T.Amlong 10mg for the past 3 years. She was admitted under the department of neurosurgery in a quaternary care hospital. She was treated with calcium and phosphorus with vitamin D chewable tablets once daily, Teriparatide 20mg once daily, Inj.paracetamol 1gm thrice daily after the fixation surgery. The patient showed signs of depression and was advised to take Tab. Escitalopram 10mg from the second day of admission. Electrolyte disturbances were seen, a mainly hypokalemic pattern was shown in the ECG. The ECG report shows a QTc interval of 454ms on the first day. After the escitalopram treatment was initiated, the patient showed a QTc interval of 505ms. The potassium level was found to be 2.8mg/dl on the first day(hypokalemia), along with QTc prolongation, which was treated with syrup potassium chloride 15ml thrice daily and serum potassium level increased to 3.4mg/dl.

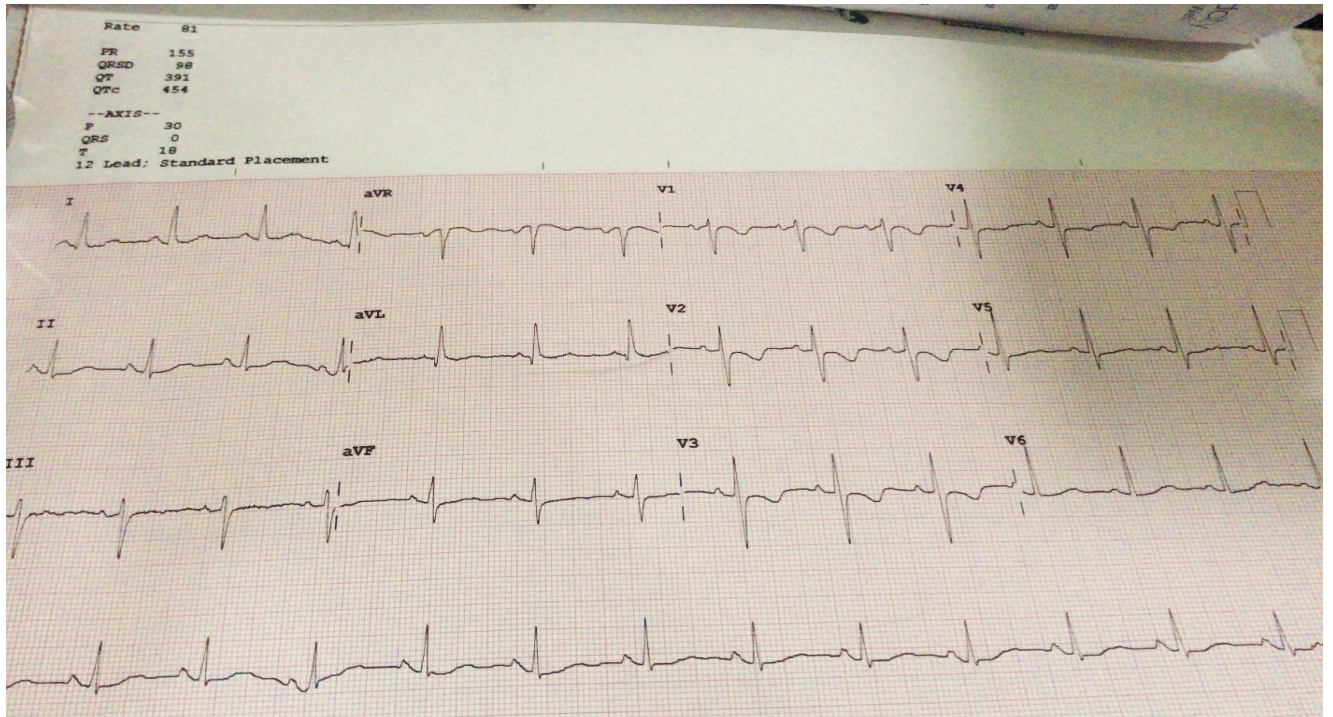


FIGURE NO. 1: ECG report before escitalopram treatment

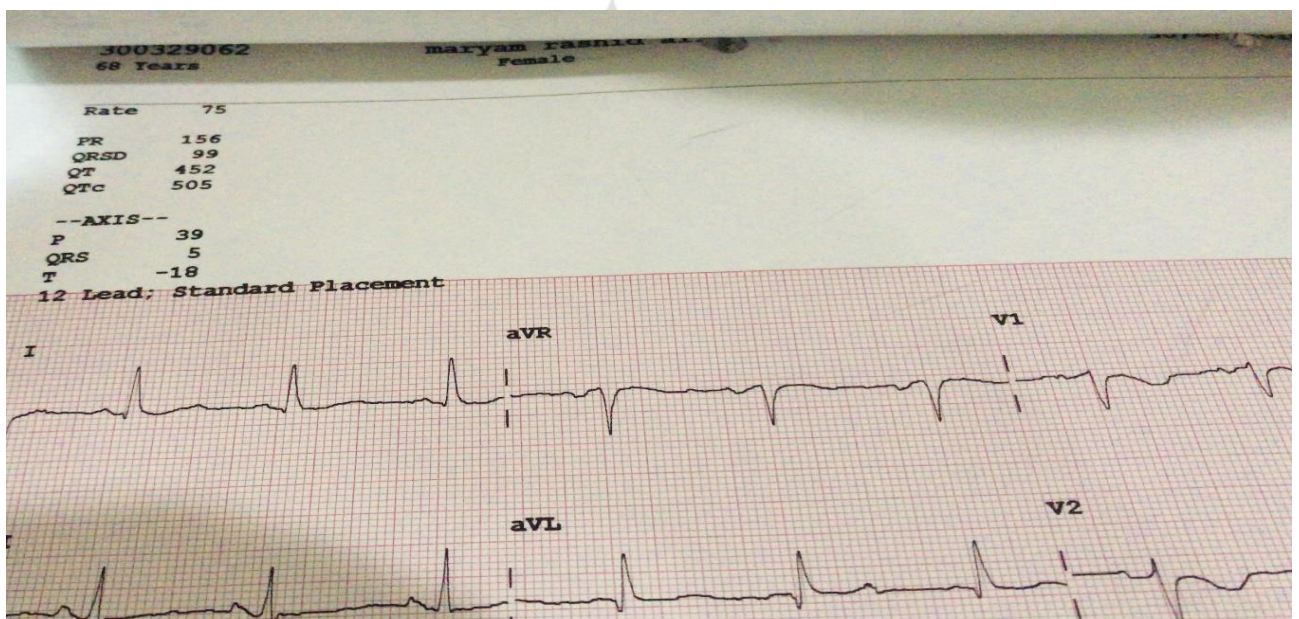


FIGURE NO. 2: ECG report after escitalopram treatment.

DISCUSSION

Depression is currently one of the fastest rising diagnosis made by the physicians during the past 5 years and hence there has been an increasing trend in the utilization of escitalopram. Three cases of QTc prolongation with escitalopram was reported. ^(7,8,9) The drug-induced QT

prolongation is thought to be caused by the inhibition of delayed potassium rectifier current IKr (rapid) by specific drugs. IKr is an outward current controlled by the potassium channel that is responsible in part for the repolarization of ventricular myocytes. When a drug interferes with this current, it thereby disrupts repolarization and hence the QT interval is prolonged. (7,10)

PSYCHIATRIC DRUGS WITH A HIGHER RISK OF QTc PROLONGATION AT THERAPEUTIC LEVELS	
DRUG CLASS	DRUG NAME
Typical antipsychotics	Thioridazine, Haloperidol Chlorpromazine
Atypical antipsychotics	Ziprasidone Iloperidone Quetiapine
SSRIs	Citalopram Escitalopram
TCA's and TeCA's	Amitriptyline Imipramine Maprotiline Nortriptyline Clomipramine
SNRIs	Venlafaxine Duloxetine
QTc corrected QT: SNRI: selective norepinephrine reuptake inhibitor, SSRI; selective serotonin reuptake inhibitor, TCA; tetracyclic antidepressants	
Source: Reference;11-16	

CONCLUSION

Almost all the antidepressants and antipsychotics have been linked to QT prolongation. The common medications that are considered to have high risk are Selective serotonin reuptake inhibitors mainly escitalopram. New studies on this topic are expected to emerge owing to the FDA's requirement to investigate the cardiac profiles of the medication.

ABBREVIATIONS

SNRI-Selective norepinephrine reuptake inhibitor, SSRI- selective serotonin reuptake inhibitor, ECG-Electrocardiogram

CONFLICT OF INTEREST

Declared none.

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