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Health Matters

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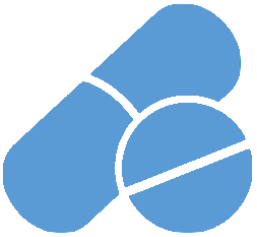
Drug Interactions Leading to QT Prolongation



Medication regimens are becoming increasingly complex, with many patients taking several medications concurrently to treat multiple conditions. Drug interactions are frequently encountered and may require modification of therapy. One of the Drug Interactions involves QT prolongation leading to ventricular tachycardia also known as Torsade de Pointes (TdP). These adverse reactions often result from the cumulative use of high-risk drugs in high-risk patients. Although TdP is rare, it may be fatal.

There are drugs such as anti-depressants (citalopram, escitalopram) or antibiotics (moxifloxacin, levofloxacin) that may prolong the QT interval causing Long QT Syndrome (LQTS). There are also drugs that slow drug metabolism (through the cytochrome P-450) which cause LQTS such as antibiotics (clarithromycin, erythromycin) *(Table 1*). A more comprehensive drug list is available at: https//crediblemeds.org/blog/crediblemeds-tdp-risk-categories

Once a patient's medication is identified as QT-prolonging, other risk factors for QT prolongation must be assessed. These risk factors are either modifiable or non-modifiable *(Table 2)*.

The initial assessment may reveal a risk of QT prolongation based on multiple risk factors. If possible consider an alternative agent that does not prolong the QT interval. However, if the use of QT prolonging drug is most appropriate or unavoidable, use the lowest effective dose and correct modifiable risk factors. A baseline electrocardiogram (ECG) is also recommended to determine the corrected QT interval (QTc) prior to initiating the therapy. A different course of action may be required depending on the QTc *(Table 3)*.

The monitoring and management of drug-related QT prolongation is multifactorial and requires pharmacist and physician collaboration. Careful monitoring and correcting modifiable risk factors can reduce the potential for LQTS and prevent TdP.

Patients being treated with QT-prolonging drugs should be instructed to report promptly any "new" symptoms including palpitations, dizziness and lightheadedness. They should also report clinical changes that could lead to hypokalemia, such as gastroenteritis or the initiation of diuretic therapy.

Table 1

Drug Class	Biggest offenders	Mechanism of Action	Alternative
Antiarrythmics	Quinidine Sotalol Amiodarone[1]	QT Prolongation	Monitor closely cardiac rhythm
Antidepressants	TCAs[2] Trazodone Citalopram Escitalopram	QT Prolongation	Sertraline Bupropion SR Desvenlafaxine
Antiemetics	Ondansetron	QT Prolongation	Prochlorperazine; metoclopramide short-term
Antipsychotics	Haloperidol Thioridazine Risperidone Ziprasidone Quetiapine Paliperidone	QT Prolongation	Aripiprazole olanzapine
Fluoroquinolones	Levofloxacin Moxifloxacin Norfloxacin	QT Prolongation	Ciprofloxacin
Macrolides	Clarithromycin Erythromycin	Macrolides can inhibit cytochrome P4503A4 enzymes and cause QT Prolongation	Azithromycin (not as a strong Cytochrome P450 inhibitor as the other macrolides)
Opioids	Methadone(high dose) Buprenorphine(BuTrans) Oxycodone	QT Prolongation	Morphine Hydromorphone Fentanyl (Duragesic patches)
Prokinetic Agents	Domperidone; Cisapride (available through Health Canada Special Access Program only)	QT Prolongation	Hold domperidone while on the antibiotic; consider safest alternative **Avoid** QT prolonging agent.

1. Amiodarone: markedly prolongs the QT interval. However, in contrast to the other class III anthiarrythmic drugs, amiodarone is rarely associated with TdP.

2. TCAs such as amithriptyline, nortriptyline, trimipramine, imipramine

Table 2

Disease States or Non-modifiable Risk Factors	Modifiable Risk Factors
Cardiovascular disease (including previous left ventricular hypertrophy, heart failure, coronary artery disease and bradyarrhythmias)	Electrolyte disturbances (hypokalemia hypomagnesemia, hypocalcemia)
Eating disorders (which may predispose a person to having electrolyte disturbances)	Use of more than one QT-prolonging medication
Female sex	Citalopram >20mg and Escitalopram > 10mg in people over 65 years old
Increasing age (>68yo)	Diuretic Use
Liver or kidney impairment (which may reduce the metabolism of a QT-prolonging medications)	Use of medication that increases the blood concentration of a QT -prolonging medication (e.g.:omeprazole reducing the metabolism of citalopram) or Long Term use PPI causing hypomagnesemia)
Baseline QTc > 450ms	

Table 3

QTc (msec)	Patient's Risk	Recommendations
<420	Very low risk for TdP	ECG monitoring may be required if patient develops additive risk factors or there is a drug interaction
420-440	Low to Moderate risk for TdP	Repeat ECGs are advised after initiation of a QT prolonging agent after 5 half-lives (steady-state) then weekly for one month and every 6 months
450-470 (males) 450-480 (females)	Moderate to High Risk for TdP	ECG monitoring is recommended as for patients with QTc of 420-440msec. Try to avoid QT prolonging agent
470-500 (males) 480-500 (females) OR When follow-up reveals an increase of greater than 60msec or >500	Very High Risk for TdP	Offending agent should be discontinued. Consider a substitute which does not cause LQTS. Monitor serum potassium and magnesium

References

- QT PROLONGATION and Torsades de Pointes.Rxfiles
- UPTODATE :Drug Induced TdP
- Ontario Pharmacist March-April 2016 : ASK OPA