Canterbury District Health Board
Te Poari Hauora o Waitaha

Clinical Pharmacology Bulletin

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Drug-Induced QTc Interval Prolongation

The risk of developing a life threatening arrhythmia at any given QTc interval (the QT interval corrected for heart rate) varies widely between patients. In patients with a high baseline risk of QTc prolongation, QTc prolonging drugs should be either avoided or the QTc interval should be monitored closely.

QTc Prolongation

- Prolonged QTc interval can lead to Torsades de Points (TdP), ventricular tachycardia, ventricular fibrillation, and sudden death.
- QTc prolongation is a QTc interval > 440 milliseconds (ms) in men or > 460 ms in women (definition varies between sources).
- Risk of arrhythmia increases with increasing QTc interval AND predisposing risk factors.
- Some drugs prolong cardiac repolarisation. This usually occurs on starting the offending drug(s), and is apparent within days, it is often dose related and the risk is increased with intravenous administration.

Predisposing Risk Factors

- Congenital long QT syndrome or past history of long QT.
- Family history of sudden cardiac death.
- Structural heart disease (e.g. cardiomyopathy).
- Hypokalaemia, hypomagnesaemia and hypocalcaemia.
- Thyroid dysfunction.
- Bradycardia.
- Female gender.
- Age over 65 years.
- Renal or hepatic impairment can lead to high drug concentrations of drugs that prolong QTc.

Drug Interactions

- Two or more drugs that cause QTc prolongation independently will have an additive effect and increase the risk of TdP.
- One or more drugs may cause electrolyte disturbance (e.g. diuretics, β-agonists, proton pump inhibitors), bradycardia (e.g. β-blockers, donepezil) or other effects that predispose the individual to the QTc prolonging effects of another drug.

Some drugs that can prolong the QTc interval:

Antimalarial drugs	Anti-arrhythmic drugs
chloroquine*, mefloquine	amiodarone*, disopyramide*, flecainide*, sotalol*
Macrolides	**Antiemetic drugs**
azithromycin*, clarithromycin*, erythromycin*, roxithromycin*	domperidone* (doses > 30 mg daily), droperidol*, ondansetron*
Quinolones	**Antidepressant drugs**
ciprofloxacin*, levofloxacin*, moxifloxacin*	SSRIs (e.g. citalopram*, escitalopram*), tricyclic antidepressants
Triazole antifungals	**Antipsychotic drugs**
fluconazole*, itraconazole, ketoconazole, voriconazole	Most antipsychotics have a dose related risk of QTc prolongation
Others	
artemisia annua, donepezil*, lithium, methadone*, solifenacin, tacrolimus, tamoxifen, tolterodine	

*These drugs are classified by CredibleMeds® as a 'known' risk of TdP. List is not exhaustive.
Report suspected adverse effects to CARM (including those associated with complementary and alternative medicines (CAMs)).

Prevention of Drug-Induced QTc Prolongation

- Address modifiable risk factors:
  - Limit the use of QTc prolonging drugs in patients with known risk factors.
  - Use the lowest possible dose and/or administer at a slow rate.
  - Avoid drug interactions, particularly multiple drugs associated with QTc prolongation.
  - Avoid electrolyte disturbances
- Review any available ECGs prior to prescribing a QTc prolonging drug, and obtain an ECG prior to starting a second or subsequent potentially QTc prolonging drug. Dose reduction or discontinuation is recommended if the QTc is > 500 ms or if it increases > 50 ms compared with baseline. Consider cardiology review if prolonged QTc doesn't resolve with drug discontinuation.
- Advise patients to seek immediate medical attention if symptoms such as light-headedness, dizziness, palpitations, shortness of breath, or fainting occur.