

## Drug Induced QT Prolongation

The QT interval is measured from the beginning of the QRS interval to the end of the T wave. Manual measurement is preferred. Because QT interval shortens when heart rate is increased, corrected QT (QTc) using Bazett's formula is commonly used. The QT length represents the entire duration of ventricular systole and the repolarization to resting state. Efflux of potassium drives this repolarization. When it is hindered, such as by a pharmacologic agent, ventricular repolarization is slowed and the QT interval becomes prolonged. Slowing of repolarization can set the heart up for early after depolarizations. In some cases this can progress to polymorphic ventricular tachycardia (torsades de pointes, TdP).

Inhibition of potassium efflux is a property shared by an array of drugs. Some QT prolonging drugs may be more likely to precipitate TdP than others based upon pharmacologic differences that are incompletely understood. Higher serum concentrations and additive drug effects can increase the risk. Other risk factors for acquired QT prolongation include electrolyte abnormalities (hypokalemia, hypocalcemia, and hypomagnesemia), myocardial ischemia, bradycardia, and hypothermia. Prolonged QRS alone can cause apparent increase in the QT interval. Women and those with advanced age are at an increased risk. Genetic variations in the expression of potassium channels may also increase some individuals' susceptibility to drug induced QT prolongation.

Experts disagree on the length at which a QTc interval is prolonged and at which it becomes clinically concerning for TdP. Complicating this assessment is evidence that QTc interval prolongation does not appear to have a linear relationship with TdP occurrence<sup>1</sup>. In a recent international survey among medical toxicologists, most respondents considered a QTc interval prolonged when it is > 450 msec in men and > 460 msec in women. However, 15% did not consider QTc prolonged until it was >500 msec<sup>2</sup>. The Substance Abuse and Mental Health Services Administration has considered 500 msec as the threshold for long QT among methadone patients<sup>3</sup>. Some evidence has shown an association of QTc >500 msec with a 2-3 times higher incidence of TdP<sup>1,2,4,5,6,7,8</sup>. The presence of bradycardia in addition to QTc prolongation increases the risk of TdP<sup>4</sup>.

If QTc prolongation occurs, offending agents should be identified and removed where possible. Electrolytes should be corrected. Magnesium should be maintained between 1-2 mEq/L and potassium between 4.5-5 mEq/L<sup>8</sup>. While potassium shortens QTc interval, magnesium suppresses recurrent TdP without shortening QTc<sup>2,8,9,10,11</sup>. If TdP occurs, 1-2g of IV magnesium should be administered and repeated if necessary. The use of magnesium prophylactically for long QT with no TdP is debated and not well studied<sup>2,12</sup>. For recurrent episodes of TdP, cardiac overdrive pacing or isoproterenol may be considered.



### Did you know?

**Crediblemeds.org** is a helpful resource for identifying medications that carry risk for QT prolongation and TdP.

#### Common Drugs That Prolong QT

**Antiarrhythmics** (procainamide, quinidine, sotalol, amiodarone, flecainide)  
**Anti-infectives:** (clarithromycin, erythromycin, azithromycin, ciprofloxacin, fluconazole, levofloxacin, moxifloxacin)  
**Antiemetics:** (droperidol, IV ondansetron)  
**Antipsychotics:** (chlorpromazine, haloperidol, ziprasidone, thioridazine)  
**Antidepressants:** (citalopram, escitalopram)  
**Other drugs:** (donepezil, methadone, cocaine, propofol)

References on page 2

Gina L Stassinis, PharmD  
Clinical Toxicology Fellow  
Maryland Poison Center  
University of Maryland School of Pharmacy



@MPCToxTidbits

## QTc Prolonging Drugs

### References

1. Roden DM. Drug-induced prolongation of the QT interval. *N Engl J Med* 2004;350:1013-22.
2. Othong R, Devlin JJ, Kazzi ZN. Medical toxicologists' practice patterns regarding drug-induced QT prolongation in overdose patient: A survey in the United States of America, Europe, and the Asia Pacific region. *Clin Toxicol* 2015;53:204-9.
3. Martin JA, Campbell A, Killip T, Kotz M, Krantz MJ, Kreek MJ, et al. QT interval screening in methadone maintenance treatment: report of a SAMHSA expert panel. *J Addict Dis* 2011;30:283-306.
4. Drew BJ, Ackerman MJ, Funk M, et al. Prevention of torsade de pointes in hospital settings: a scientific statement from the American Heart Association and the American College of Cardiology Foundation. *J Am Coll Cardiol* 2010;55:934-47.
5. De Bruin ML, Langendijk PN, Koopmans RP, Wilde AA, Leufkens HG, Hoes AW. In-hospital cardiac arrest is associated with use of non-antiarrhythmic QTc-prolonging drugs. *Br J Clin Pharmacol* 2007;63:216-23.
6. Sauer AJ, Moss AJ, McNitt S, et al. Long QT syndrome in adults. *J Am Coll Cardiol* 2007;49:329-37.
7. Priori SG, Schwartz PJ, Napolitano C, et al. Risk stratification in the long-QT syndrome. *N Engl J Med* 2003;348:1866-74.
8. Kan AA, de Lange DW, Donker DW, Meulenbelt J. Management of prolonged QT interval and torsades de pointes in the intoxicated patient. *Neth J Med* 2014;72:119-26.
9. Choy AM, Lang CC, Chomsky DM, Rayos GH, Wilson JR, Roden DM. Normalization of acquired QT prolongation in humans by intravenous potassium. *Circulation* 1997;96:2149-54.
10. Yang T, Roden DM. Extracellular potassium modulation of drug block of IKr. Implications for torsade de pointes and reverse use-dependence. *Circulation* 1996;93:407-11.
11. Holstege CP, Eldridge DL, Rowden AK. ECG Manifestations: The Poisoned Patient. *Emerg Med Clin N Am* 2006;24:159-77.
12. Ibister GK. How do we assess whether the QT interval is abnormal: Myths, formulae and fixed opinion. *Clin Toxicol* 2015;53:189-91.



**Have you called the Maryland Poison Center for treatment recommendations or advice about a poisoning or overdose?**

**Did we meet your expectations?**

**Do you have suggestions for how we can improve our service to health care providers?**

**Your opinion is important to us!**

**Go to [www.mdpoison.com/healthcareprofessionals](http://www.mdpoison.com/healthcareprofessionals) and click on "Satisfaction Survey" to tell us how we're doing.**

