



## PIC QUESTION OF THE WEEK: 1/05/09

Q: Are there any cardiac arrhythmias associated with the use of methadone?

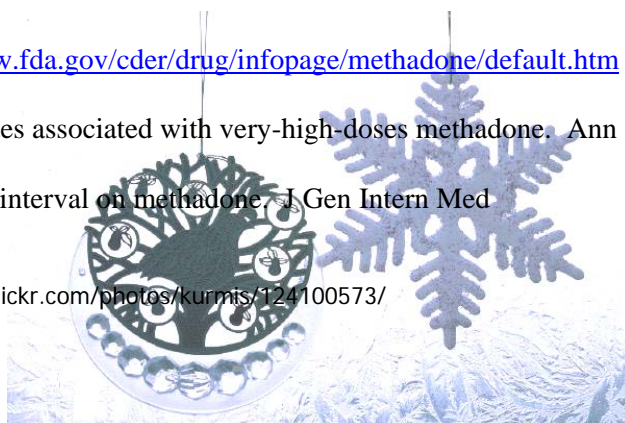
A: Methadone is a synthetic  $\mu$ -opiate receptor agonist indicated for drug detoxification, maintenance therapy in patients addicted to heroin, and the management of chronic pain. Clinically, the stimulation of  $\mu$ -receptors produces analgesia and euphoria. Methadone has a blunted euphoric effect that makes it unattractive as a drug of abuse, but an appropriate agent for the management of opiate dependence. Methadone can prolong the cardiac action potential by delaying repolarization. This is documented in the echocardiogram (ECG) by prolongation of the QT or QTc (value that corrects for the patient's heart rate) interval and indicates abnormal repolarization following depolarization (excitation). The normal QTc interval is <460 milliseconds (msec) whereas a prolonged value is considered at least 500 msec. Torsades de pointes is an arrhythmia that can develop in association with a prolonged QT interval and is characterized by *twisting* of the QRS complex. It can result in ventricular tachycardia, fibrillation, and death. The first report associating methadone with this arrhythmia was published in 2002. It described the development of a prolonged QT interval and torsades de pointes in 17 participants of a methadone maintenance program. All patients survived; however, in 14 of the cases, a cardiac defibrillator or pacemaker was implanted to correct the arrhythmia. The patient's average daily dose of methadone in this report was approximately 400 mg. In November 2006, the FDA's MedWatch program posted an alert regarding the potential for methadone to produce serious cardiac arrhythmias including QT prolongation and possible torsades de pointes. It suggested that methadone dosage be carefully titrated and patients monitored for possible cardiac toxicity. A guideline for monitoring QT interval in patients enrolled in methadone maintenance programs is expected to be published in *Annals of Internal Medicine* early in 2009. Methadone is one of many compounds known to prolong the QT interval. Others include a variety of antidepressants, antipsychotics, macrolide antimicrobials, and antiarrhythmics. Drug interaction screening programs used by pharmacists now routinely evaluate drug combinations for their potential to prolong the QT interval and produce torsades de pointes.

### References:

- FDA. Information for healthcare professionals. <http://www.fda.gov/cder/drug/infopage/methadone/default.htm> (accessed December 15, 2008).
- Krantz MJ, Lewkowicz L, Hays H, et al. Torsade de pointes associated with very-high-doses methadone. *Ann Intern Med.* 2002;137:501-4.
- Lamont P, Hunt SC. A twist on torsades: a prolonged QT interval on methadone. *J Gen Intern Med* 2006;21:C9-C12.

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