IDIS Independent Drug Information Service

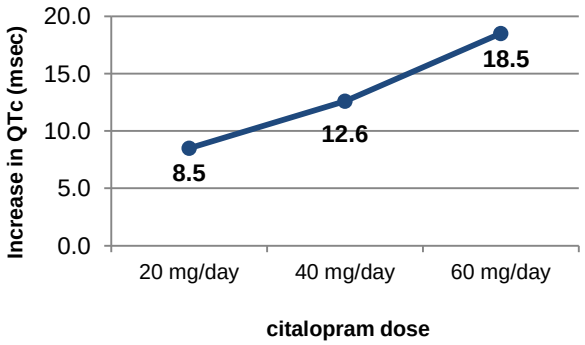
PEARL:
Prompt Evidence Assessment and Review of the Literature

Citalopram increases the QT interval and risk of sudden death

Choosing a different antidepressant or a lower dose can address the problem

The clinical issue: In spring 2012, the FDA once again warned prescribers that the SSRI antidepressant citalopram (Celexa and generics) can prolong the cardiac QT interval, especially when used at higher doses, putting patients at increased risk of arrhythmia and sudden death.[1]

The new evidence: Following reports of QT prolongation and severe ventricular arrhythmias in patients taking citalopram, clinical studies confirmed that citalopram in doses over 20 mg/day can increase the QT interval substantially, raising the risk of potentially fatal ventricular arrhythmias. (See graph; an increase in the corrected QT interval [QTc] of over 10 milliseconds is considered a clinically significant change.) While a dose-dependent increase in QTc also occurred with escitalopram (Lexapro), the changes were much smaller, exceeding 10 msec only for patients taking a 30 mg/day dose. Despite the increased risk, there is no added clinical benefit of 60 mg citalopram compared to lower doses. The new FDA warning recommends avoiding doses of citalopram over 40 mg/day in all patients, and over 20 mg/day in all patients over age 60, and certain others (see table).



Do not exceed 20 mg/day of citalopram in patients who:	Do not use citalopram at any dose in patients with:
• are over age 60; • have hepatic impairment; • are CYP 2C19 poor metabolizers; • take inhibitors of this enzyme (e.g. cimetidine, omeprazole, oral contraceptives, and others).	• congenital long QT syndrome; • bradycardia; • hypokalemia; • hypomagnesemia; • recent acute MI; • uncompensated heart failure; • concurrent use of other drugs that can prolong the QT interval.*

* These include ziprasidone, quetiapine, triptans for migraine, quinolone antibiotics, and others (see www.QTdrugs.org for a complete list).

Patients with a QTc over 500 msec should be tapered off citalopram. Given the smaller QTc changes seen with escitalopram (Lexapro and generics), no warnings were issued for this agent.

Limitations: Not enough is known about the actual rate of dangerous arrhythmias caused by use of citalopram in routine practice, or about the QT effects of other antidepressants apart from escitalopram.

Bottom line: Because of these safety concerns and the fact that citalopram's efficacy is no better than that of other SSRIs, citalopram is no longer the best first-line agent for new patients who require an antidepressant. Sertraline (Zoloft and generics) is a preferable first-line choice,[3] as is escitalopram, now available generically. Bupropion is another reasonable option.[4] For a patient currently taking citalopram:

- If over age 60, avoid use of citalopram at a dose over 20 mg/day whenever possible; If an SSRI is required at a higher dose, consider switching to another drug such as sertraline or escitalopram, especially if the patient has any other risk factors for arrhythmia;
- If clinical circumstances require continuation of citalopram in a given patient:
  - Discuss risks and benefits with the patient, using FDA materials as a guide;[1]
  - Check the EKG: a QTc interval over 450-500 msec puts the patient at increased risk of arrhythmia;
  - Make sure that levels of potassium and magnesium are normal;
  - Avoid other medications that can also prolong the QT interval.

References: [1]http://www.fda.gov/Drugs/DrugSafety/ucm297391.htm?utm_source=fdaSearch&utm_medium=website&utm_term=citalopram&utm_content=1**.** [2]Catalano G, Catalano MC, Epstein MA, Tsanbiras PE. QTc interval prolongation associated with citalopram overdose: A case report and literature review. Clin Neuropharmacol 2001;24:158-162. [3]Cipriani A et al. Lancet 2009;373:746-58. [4]Trivedi MH et al. J Clin Psychiatry 2001;62:776-81.

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These are general recommendations only; specific clinical decisions should be made by the treating physician based on an individual patient's clinical condition.

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