

77 - Antidepressant induced arrhythmia

Antidepressant-induced arrhythmia

Depression and anxiety disorders CHAPTER 3 Antidepressant-induced arrhythmia Depression confers an increased risk of cardiovascular disease¹ and sudden cardiac death.² Possible factors include platelet activation, decreased heart rate variability, reduced physical activity, and an association with an increased risk of diabetes.³ Tricyclic antidepressants have established arrhythmogenic activity, which arises as a result of potent blockade of cardiac sodium channels and variable activity at potassium channels.⁴ ECG changes produced include PR, QRS and QT prolongation and the Brugada syndrome.⁵ These actions are very evident in overdose but their effects in clinical doses is unclear. Normal clinical use of nortriptyline has been associated in one study with an increased risk of cardiac arrest,⁶ although a large cohort study did not confirm this finding.⁷ Lofepamine, for reasons unknown, seems to lack the overdose arrhythmogenicity of other TCAs, despite its major metabolite, desipramine, being a potent potassium channel blocker.⁸ Oddly, in one study,⁹ clinical use of lofepramine was associated with an increased risk of myocardial infarction (MI), whereas other antidepressants were not. Network meta-analysis suggests that TCAs have a very low risk of causing ventricular arrhythmia or sudden cardiac death outside overdose or high-dose usage.¹⁰ In patients taking tricyclics, ECG monitoring is a more meaningful and useful measure of toxicity than plasma level monitoring. There is limited evidence that venlafaxine is a sodium channel antagonist¹¹ and a weak antagonist at hERG (human ether-a-go-go-related gene) potassium channels. Arrhythmia is a rare occurrence, even after massive overdose,^{12–15} and ECG changes after overdose are no more common than with SSRIs.¹⁶ No ECG changes are seen in therapeutic dosing¹⁷ or even at supratherapeutic doses (450mg/day)¹⁸ and sudden cardiac death in clinical use is no more common than with fluoxetine or citalopram.^{7,19} Desvenlafaxine does not appear to prolong QT, even in overdose.²⁰ Moclobemide,²¹ citalopram,^{22,23} escitalopram,²⁴ bupropion (amfebutamone),²⁵ trazodone^{26,27} and sertraline,²⁸ among others,¹ have been reported to prolong the QTc interval in overdose but the clinical consequences of this are uncertain. Sertraline prolongs QT by 5–10ms at 400mg a day,²⁹ but QT changes are not usually seen with most SSRIs at normal clinical doses.^{30,31} Nonetheless, an association between SSRIs (as a group) and QT changes in normal dosing can be shown³² but this seems largely to be driven by the effects of citalopram and escitalopram.³³ The effect on QTc is dose related³³ but modest.³² Most studies have failed to find any association between citalopram

or escitalopram treatment and arrhythmia or cardiac mortality in routine clinical practice,^{7,34,35} although some have reported very small increases in mortality.³⁶ Genetic variation in CYP219 metabolic capacity may explain individual differences in cardiac toxicity, as it determines the serum concentration of citalopram metabolites,³⁷ but whether it is the parent compounds or their metabolites that are responsible for cardiotoxicity is unclear.³⁸ Vortioxetine seems to have no effect on QT.^{39–41} Similarly, agomelatine has no effect, even at supratherapeutic doses.⁴² Vilazodone has no effect on cardiac conduction.⁴³ Levomilnacipran⁴⁴ and milnacipran⁴⁵ probably have no effect on QT, at least at therapeutic doses.

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