

CORRESPONDENCE

QTc Prolongation by Psychotropic Drugs and the Risk of Torsade de Pointes

by Dr. med. Katharina Wenzel-Seifert, Dr. med. Markus Wittmann, Prof. Dr. med. Dr. med. habil. Dr. rer. nat. Ekkehard Haen in volume 41/2011

Risk Factors Need to Be Considered

No information is provided by merely listing the occurrence of QT prolongation for different drugs without considering known risk factors, because in this way it is not possible to distinguish between the effects of either. The authors correctly state that QT prolongation is almost always affected by risk factors such as hypokalemia (30%) or hypomagnesemia. But these electrolyte imbalances still do not receive anywhere near enough attention. Magnesium, the second most common intracellular cation after potassium, is not usually included in the electrolyte status. Potassium deficiency, however, almost always goes hand in hand with magnesium deficiency and can be balanced only by administering magnesium simultaneously.

In conclusion: if the intention is to administer drugs with repolarizing or depolarizing effects, for example in potential QT prolongation, any existing hypokalemia and hypomagnesemia needs to be treated first. In acute cases, magnesium sulfate should be administered intravenously, in all other cases, oral administration of magnesium aspartate will suffice. What remains of interest subsequently is only the occurrence of Torsade de pointes in patients with balanced electrolytes, but this has to be investigated when testing a drug.

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Conflict of interest statement

The author declares that no conflict of interest exists.

In Reply:

In almost all published cases that were included in our table, in whom treatment with psychotropic drugs triggered prolongation of the QTc interval or even

episodes of Torsade de Pointes, several additional risk factors were present. These included hypokalemia (prevalence 13–16%; 20% in women older than 65) and hypomagnesemia (prevalence 5–15%; 38% in geriatric patients), which often go together and per se may cause ventricular arrhythmias. Both risk factors can be caused not only by diuretics, proton pump inhibitors, glucocorticoids, and laxatives, but can exist independently, often in a setting of alcohol misuse, malnutrition, and heart failure (owing to secondary aldosteronism). Since the serum concentration of magnesium reflects intracellular magnesium concentrations only to an unsatisfactory extent and since magnesium deficiency may be present in normal magnesium concentrations (0.73–1.06 mmol/L), it is recommended that physicians prescribe potassium and magnesium preparations (40 mmol/day and 10 mmol/day) in order to balance out hypokalemias. Both electrolytes should be monitored in high risk patients receiving psychotropic drugs and should be kept within a high normal range.

We wish to mention that Lundbeck and the Federal Institute for Drugs and Medical Devices (*Bundesinstitut für Arzneimittel und Medizinprodukte*, BfArM) informed informed prescribers on 31 October and 5 December 2011 by means of ‘Dear Doctor Letters’ (Rote-Hand-Briefe) on cipramil (citalopram) or cipralex (escitalopram) and, respectively, about the increased risk of dose-dependent prolongation of the QTc interval in patients. The letter recommended restricting the daily maximum dose of citalopram to 40 mg. Patients older than 65 should not take more than 20 mg citalopram per day/10 mg escitalopram/d. Taking citalopram and escitalopram in addition to other drugs prolonging the QTc interval is contraindicated. It is to be expected that at least the changes for prescribing cipramil outlined in the letter will be extended to include all citalopram preparations and then become legally binding.

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