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"Non-cardiac" drugs and the QTc interval – the importance of a holistic and interdisciplinary approach in daily clinical practice

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Prolongation of the QTc interval is of great clinical significance because it drastically increases the risk of occurrence „torsades de pointes" (TdP). Most medications that prolong the QTc interval do so by blocking cardiac potassium channels (hERG), thereby delaying ventricular repolarization. Although there are minor discrepancies in the literature, the QTc interval is generally considered prolonged if it is ≥ 470 ms in men and ≥ 480 ms in women.[1,2]

The precise incidence of acquired long QT syndrome (LQTS) is unknown. In the general population, the annual incidence of drug-induced TdP is estimated at approximately 2.5 - 4.0 cases per million. Most patients with a acquired LQTS are asymptomatic. The clinical presentation of symptomatic LQTS includes palpitations, (pre)syncope, cardiac arrest, and sudden cardiac death.

Several cardiac medications prolong the QTc interval, such as amiodarone, sotalol, quinidine, ranolazine, etc. In addition, there is a wide range of non-cardiac drugs that prolong the QTc interval; typical and atypical antipsychotics such as haloperidol (especially when administered parenterally), quetiapine, thioridazine, olanzapine, and risperidone; tricyclic antidepressants (amitriptyline, imipramine, and clomipramine). Selective serotonin reuptake inhibitors (paroxetine, fluvoxamine, escitalopram, sertraline, fluoxetine) are generally safe regarding adverse cardiac effects and are recommended for the treatment of patients with cardiovascular diseases. Other drugs that significantly affect the QTc interval and are relatively frequently used in clinical practice include macrolide antibiotics, fluconazole, ribociclib (used in the treatment of breast cancer) etc.

It is important to note that the risk of fatal arrhythmia rarely depends solely on a single drug. Various conditions and agents drastically potentiate the effects of the aforementioned drugs: diuretics (which do not directly prolong the QTc interval but can cause hypokalemia and hypomagnesemia), the combination of two or more drugs capable of prolonging the QTc interval, electrolyte imbalances, structural heart disease (heart failure with reduced ejection fraction), advanced age, chronic renal failure, etc. In clinical practice, it is not uncommon to encounter a patient with significant cardiovascular comorbidities and most of the described risk factors for QTc prolongation who, due to comorbidities, requires treatment by specialists such as psychiatrists, oncologists, infectious disease specialists etc.

In conclusion, because of the potential for adverse interactions and the induction of malignant arrhythmias (TdP), a holistic and interdisciplinary approach to treating such complex patients is essential (careful selection and avoidance of therapeutic options that carry a risk of further QTc prolongation). Only with such an approach can a potentially fatal scenario be avoided.

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