Extent of use of QT interval prolonging medication in Psychiatry In-Patient in a tertiary care hospital- Chayna Sarkar- NEIGRIHMS

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Abstract

Psychiatric patients constitute a population at notable risk of drug-induced QT-prolongation. Quite a number of antipsychotic and antidepressant drugs are known to cause significant QT-prolongation. The aims were to explore extent of use of QTc-interval prolonging agents in Psychiatry In-Patient in a tertiary care hospital in India. The study was carried out in the psychiatry In-Patient at NEIGRIHMS, Shillong, India. For each patient, the entire medication list was analyzed for the possibility of interactions, with particular attention on the high-risk QT prolonging ones. Arizona Center for Education and Research on Therapeutics (AZCERT) QT drug lists were used to classify TdP risks of psychotropic and other medications. 246 patients attending the psychiatry department during the 3 months study period were scrutinized. 149 patients (61%) were males whereas 97 (39%) were females in our study. Of the 246 patients, 207 patients (84%) were identified as receiving interacting medications with the ability to induce torsades de pointe (TdP). 349 (51.8%) interacting medications with torsadogenic risk were encountered out of total 674 medication prescribed to 246 patients. The most frequently interacting medications were from antidepressant (190), antipsychotic (132), antideementia (14), proton pump inhibitor (7) therapeutic categories. As per AZCERT classification (CredibleMeds TdP risk-stratification lists), 110 (31.5%), 46 (13.2%) and 193 (55.3%) of the interacting medications were associated with known, possible, and conditional risk of TdP, respectively. Concurrent prescriptions of QT-prolonging drugs is frequent in psychiatry setting. Appropriate precautions should be instituted to provide caregivers with clear guidelines on how to use these drugs in a responsible and safe way.

QT interval prolongation (QTIP) may be a well-known surrogate marker for torsades de pointes (TdP), a life-threatening ventricular arrhythmia, which will end in sudden cardiac death. QTIP may be a consequence of abnormality within the ion channels of the guts like potassium, sodium, and calcium channels. Cardiac channel abnormalities could also be congenital or acquired, the latter is more common and is usually related to drugs. Psychiatric patients are at higher risk of drug-induced TdP because majority of the psychotropic agents (antipsychotics and antidepressants) are notorious for prolonging the QT interval. The danger is further enhanced in patients with other QT prolonging risk factors like bradycardia, DM, hypertension, advance age, female sex, underlying heart diseases and illicit drugs use. Psychiatric patients are often exposed to psychotropic Polypharmacy, high dose therapy and illicit drug use, which considerably increase the probability of exposure to QT prolonging drugs and QT drug-drug interactions (QT-DDIs). In psychiatry settings, polypharmacy is a traditional and old practice that is increasingly becoming a norm rather than exception. In a review on polypharmacy in psychiatry, Kukreja et al. reported the prevalence of psychotic polypharmacy (≥2 drugs) between 13 and 90%. Another study reported, 19% prevalence of multi-class psychotropic polypharmacy among children and adolescents. According to a study, since 1974 prescriptions containing ≥3 drugs increased from 5% to 40% in 1995.

In addition, among psychiatric patients, the upper risk of QTIP is additionally thanks to frequent QT prolonging antidepressant and antipsychotic combinations. In most clinical conditions, >1 psychotropic drug is indicated. In some clinical situations, compared to one antidepressant or major tranquilizer, patients with psychiatric illnesses significantly improved after adding a second psychotropic drug within the prescription [20,21,22,23]. However, another study also reported significant increase in psychotropic polypharmacy during a psychiatry setting with many combinations of unproven efficacy that aren't supported by controlled clinical trials. Recently, a study reported higher prevalence of contraindicated combinations with two antidepressants (escitalopram or citalopram) among hospitalized patients. Using >1 QT prolonging medications simultaneously increase the risk of life-threatening ventricular arrhythmias.

Psychiatric polypharmacy, psychotropic QT prolonging drug combinations and high dose therapies are inevitable in such a population thanks to multiple illnesses and tolerance to the recommended dose of therapy. The increased prevalence of polypharmacy, contraindicated combinations and high dose therapy including poor access to health care facilities increase the danger of QTIP associated morbidity and mortality. Despite considerable safety concern for QTIP related to psychotropic drugs, studies are scarce regarding the prevalence of QTIP and its associated risk factors among psychiatric patients, particularly within the developing countries. Moreover, electrocardiographic monitoring for QTIP isn't performed in routine clinical practice despite the known risk of QTIP and TdP with psychotropic agents. Therefore, this study aimed to spot the prevalence of QTIP, its associated risk factors and prescribing patterns of QT prolonging drugs in psychiatric patients.

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A prospective observational study was conducted at the psychiatry ward of a tertiary care hospital and a psychiatry clinic of a capital. The convenience sampling technique was wont to include patients diagnosed with psychiatric diseases, who used psychotropic medications for ≥7 days, aged 18 years or more (adult), and of either gender, male or female from January 31, 2018 till July 30, 2018. The Institutional Review Board (IRB) of the hospital granted the moral approval for this study. Prior to participation, a written consent was obtained from all patients.

Patient’s relevant data required for this study was obtained from the medical profile of individual patient. After recording ECG the subsequent data were collected from the patient’s medical record; gender, age, main diagnosis, comorbidities aside from psychiatric disorders (if any), and prescribed medications.

The corrected QT interval (QTc) was manually calculated from the patient’s ECG using the Fredericia (QTcF), and Bazett’s (QTcB) correction formula (QTcB results only presented in supplementary Table S1). QT interval was measured from the start of QRS complex till the end of T wave from lead-II on the surface of ECG. The QTIP was defined as, QTc values above 450 ms and 470 ms for male and feminine patients, respectively. Whereas, values above 500 ms were considered highly abnormal regardless of gender. CredibleMeds database was used for the identification of QT prolonging drugs and their TdP risk categories. Whereas, Micromedex DrugReax® database was used for the identification of QT-DDIs.

**Biography**
Chayna Sarkar has completed her MD(Pharmacology) from PGIMER, Chandigarh, India. Now she is working as Professor of Pharmacology NEIGRIHMS, Shillong, India. She has published more than 30 research papers in reputed journals and has been serving as an ethics committee member in her institute.