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Incorporation of Pharmacist in Conducting Medication Reviews for Identification of Risk of QT Prolongation: A Neglecting Latent Approach in Cardiology

Ahmad Ullah Humza[1], Kashif Rizvi[2], Kashif Ali[3*]

[1]National Institute of Cardiovascular Diseases, Karachi, Pakistan.

[2]King Faisal Specialist Hospital and Research Centre, Riyadh, KSA.

[3]Dow University of Health Sciences, Karachi, Pakistan.

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ABSTRACT

Sudden cardiac arrest correlates with QT-interval prolongation and torsade de points (TdP). Several medicines frequently used in geriatric aged care populations can cause QT-interval prolongation. Major predisposing factors and QT-prolonging medications enhance QT-interval prolongation incidence in medical inpatients. Pharmacists can help ensure safe drug therapy and in-hospital patient safety by paying attention to QT-interval prolongation and extra risk factors for prolonged QT-interval during medication reconciliation. We recommend pharmacists improve knowledge and awareness of corrected QT-interval prolongation (QTc) when conducting drug reviews. Implementation of Pharmacist-driven QTc monitoring is required to lower the risk of QTc prolongation.

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Introduction

A prolonged QT-interval in geriatric individuals is correlated along with a higher risk of coronary heart disease fatalities. Over 6 million people die each year from sudden cardiac death (SCD) caused by ventricular tachyarrhythmias around the world (1). The QT-interval prolongation is a distinguished potential indicator of TdP, a potentially fatal ventricular arrhythmia leading to spontaneous cardiac arrest (2–5). An imbalance in the heart's ion channels, including potassium, sodium, and calcium channels, leads to a prolongation of the QT-interval. Cardiac channel irregularities may be either innate or developed, but the latter is relatively prevalent and closely linked to medicines (6,7). In 2010, the American Heart Association, and the American College of Cardiology Foundation, circulated a definitive disclosure to make people aware of the potential consequence of QT-interval medication interactions among health care providers. In inpatients, the disclosure highlighted the significance of electrocardiogram (ECG) screening and the prevention of medication induced prolongation of QTc interval and Torsade de Pointes (TdP). The American College of Cardiology (ACC) specifies a QTc of 460ms for women and 450ms for males as the maximum limit for a normal QTc (8).

The prolongation of the QT-interval is linked to various pharmacological regimens. Because the QT-interval

*Corresponding Author: Dr Kashif Ali
Address: Dow University of Health Sciences, Karachi, Pakistan.
Email: Kashif.ali@duhs.edu.pk

changes with heart rate, a corrected (QTc) value can be calculated using multiple formulae. In clinical practice, Bazett's formula is most often used. Though maybe Fridericia's or Framingham's formulas are better options (9).

There are numerous ways to account for heart rate when calculating the "corrected" QT-interval (QTc) and a patient's actual risk of arrhythmia. Even though the Bazett formula is still the most used approach for measuring QTc on automatic ECG machine interpretations, investigations continually reveal that it is incorrect at extremes of heart rate when compared to other QTc equations. Newer approaches, such as the QT nomogram and the Rautaharju formula, are simple to apply and may better predict who is at risk for ventricular dysrhythmias. More prospective studies will be required to understand the performance of these innovative approaches better (10).

QT prolongation, which might initiate lethal dysrhythmias, has an untreated interval value greater than 500ms in clinical practice. Many researchers have investigated variables linked to a higher risk of QTc prolongation in individuals. About 5% to 7% more risk of TdP is expected for every 10ms increase in QTc prolongation (11,12).

Various factors and QT-prolonging drugs are exposed to patients admitted to cardiology units, which can eventually contribute to TdP and lethal problems. Several findings addressing this concern have also been performed in cardiac tertiary care wards, but they have all been conducted in advanced nations (13–18). In undeveloped countries, specifically Pakistan, data on this subject is limited. As a result, research in this area in this demographic is recommended. Furthermore, many challenges in the relevant research, such as small participation, retrospective approach, restrictive scope by solely depending on drug-drug interactions, and the utilization of an obsolete diagnostic instrument, suggest that more thorough research should be done.

Risk Factors

The risk factor for developing a prolonged QTc interval is pharmacotherapy, encompassing potential drug-drug interactions (pDDIs)(13). Geriatric patients, female gender, electrolyte imbalances such as hypokalemia, hypocalcemia, hypomagnesemia, bradycardia, and hereditary heart abnormalities have been linked to an interaction between risk factors affecting individual tendency to QTc prolongation in the literature (1). Several drugs can cause QT prolongation, referred to as drug-induced QT prolongation. According to the Arizona Center for Education and Research on Therapeutics' CredibleMeds® QT prolonging drug lists, over 190 drugs are currently linked to QT prolongation (AZCERT). AZERT has divided QT-prolonging medications into three groups, demonstrating the level of assurance about the risk of TdP (Table 1). There are more than 50 drugs that have been identified as demonstrating a TdP risk (Table 2) (19).

Table 1. Medicines that can cause TdP are classified into several categories (According to Crediblemeds.org).

Known Risk	When taken according to the directions on the label, there is strong evidence that these medications enhance the risk of TdP and prolong the QT-interval.
Possible Risk	There is insufficient evidence to conclude that any of these medications can cause an increased risk of developing TdP if used as prescribed by their official labels.
Conditional Risk	Multiple studies support the claim that these medicines relate to an increased incidence of TdP, only under specified circumstances (e.g., unnecessary dose, hypokalemia, congenital LQTs, or a drug-drug interaction that outcomes in a severe QT-interval prolongation).
Medicines to prevent Inborn LQTs	There is ample proof that these medicines increase the risk of TdP in people with innate LQTs. The medication on this directory includes those in the preceding three risk classes and others that do not directly extend the QT-interval but have a theoretical risk of producing arrhythmia.

Table 2. Prescription drugs integrated to a known or possible risk of Torsades de Pointes (TdP).

Drug Class	Known Risk	Possible Risk
Anti-Arrhythmic	Amiodarone Disopyramide Procainamide Quinidine	
Anti-Hypertensive		Isradipine Nicardipine Hydrochlorothiazide
Alpha-Blocker		Alfuzosin
Anesthetic	Propofol	
Antidepressant	Citalopram Escitalopram	Clomipramine Lithium Mirtazapine Nortriptyline
Anti-Psychotics	Chlorpromazine Haloperidol	Clozapine Olanzapine Quetiapine sertindole
Anti-Biotic	Azithromycin Clarithromycin Erythromycin Ciprofloxacin Levofloxacin Moxifloxacin	Gemifloxacin Norfloxacin Ofloxacin
Anti-Viral		Atazanavir Foscarnet Rilpivirine Saquinavir
Anti-Fungal	Fluconazole	
Anti-Cancer	Arsenic trioxide Eribulin Vandetanib	Tamoxifen Dabrafenib Vemurafenib Vorinostat
Anti-Malarial	Chloroquine	Artenimol
Antiemetic	Ondansetron	Promethazine
Cholinesterase Inhibitor	Donepezil	
Histamine receptor Antagonist		Famotidine
Immunosuppressant		Tacrolimus
Muscle relaxant		Tizanidine
Opiates	Methadone	

A Missed Opportunity from the Pharmacist's site

While most pharmacists have a working knowledge of medication interactions and the consequences of QTc prolongation (i.e., torsades de pointes), only a few have a comprehensive concept of the constraints and inconsistencies associated with QTc measurement and interpretation(20). Pharmacists should be concerned about medicines that may persist the QT-interval to minimize the risk of TdP (9). It can be challenging for healthcare professionals, like pharmacists, to determine if it is harmless to treat a patient with a combination of more than two QT-prolonging medicines and whether further ECG examinations are required after therapy initiation (19).

When reviewing medications, there is an increased risk of drug induced QTc interval prolongation. Moreover, further risk-factors, for instance age and gender, increase this adverse event in many patients. When pharmacists made recommendations in medication reviews, they focused on medicines with a recognized risk of QT-interval prolongation rather than the patient's other risk factors. To better understand and recognize QT prolongation when conducting drug evaluations, pharmacists need to be better trained and knowledgeable. Studies have also demonstrated that pharmacists can assist physicians in preventing and monitoring QT-interval prolongation using appropriate decision aids. An educational module on QT-interval prolongation can be applied in pharmacy education programs. An additional in-depth cardiac safety instruction should be initiated for pharmacists working in cardiac setup. This commentary concludes that Pharmacists must recommend dose adjustments or withdrawal of QT-interval extending medications, discontinuation of drugs known to interact with QT-interval prolonging medications, electrolyte corrections, laboratory monitoring, and ECG monitoring depending on the concern to the patient (21,22).

Conclusion

QT prolongation exposes a considerable proportion of patients in cardiology wards. Three primary considerations should be addressed when prescribing QTc prolongation medicines: patient related risk factors (for example, female gender, age more than 65 years, and untreated electrolyte abnormalities). Co-prescribed drugs may raise the risk of QT prolongation and the potential risk and severity of QT prolongation connected with the recommended medication. Ongoing telematics or serial ECGs should monitor and record adverse health outcomes, such as elevated QT-prolonging medicines and definite health problems. Pharmacists are instructed to maintain a vigilant check on QT-prolonging drugs. Still, we also need to rationally analyze elements that affect QTc quality and validity, and specific factors related to patients that affect the risk of arrhythmia. Newer approaches, such as the QT-interval nomogram and the Rautaharju formula, are simple to apply and may better predict who is at risk for ventricular dysrhythmias. More prospective studies will be required to understand the performance of these innovative approaches better.

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