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Community pharmacy reports of potential QTc-prolonging drug interactions involving fluoroquinolones or macrolides: A Multi-Incident Analysis

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CMIRPS Canadian Medication Incident Reporting and Prevention System | SCDPIM Système canadien de déclaration et de prévention des incidents médicamenteux

INTRODUCTION

- **Fluoroquinolones (FQs) and macrolides have the potential to prolong the QTc** through concentration-dependent blockade of rapidly activating delayed rectifier potassium channel (IKr channel).[1] This delays ventricular repolarization and may lead to clinically significant QTc-prolongation (> 30ms from baseline or > 500ms) when used concomitantly with other QTc-prolonging agents or agents which impede with their metabolism.[2]
- **Significantly prolonged QTc may lead to torsades de pointes (TdP) in at-risk patients**, which may degenerate into ventricular fibrillation and cause sudden cardiac death.[2]
- **Although FQs and macrolides are non-potent IKr blockers (moderate QTc-prolongation potential), they are in widespread use** and 70-80% of QTc-prolongations involving these antibiotics have led to TdP and 10% have caused death.[1]

OBJECTIVE(S)

- To analyze medication incidents associated with potential QTc-prolonging drug interactions involving FQs and macrolides.
- To identify potential contributing factors and provide safety recommendations in order to fill in patient-safety gaps.

METHOD(S)

Searched ISMP Canada Community Pharmacy Incident Reporting (CPhIR)[3] Database for medication incidents involving QTc-prolonging drug interactions from April 2010 to January 2015

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Selected Incidents for final analysis

56 incidents met the inclusion criteria and were included in this multi-incident analysis

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Analyzed and categorized incidents into three mains themes and further divided into subthemes

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Identified potential contributing factors

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Provided recommendations to fill in patient-safety gaps

RESULT(S)

Theme: **Prescriber-Triggered Potential for QTc Prolongation**

Example) *Ciprofloxacin was prescribed for a urinary tract infection. However this patient has a history of tachycardia and myocardial infarction, and is currently taking sotalol and Elavil®. The pharmacist refused to dispense ciprofloxacin due to a high risk for QTc prolongation and suggested patient to see the physician for a new antibiotic prescription.*

Comments:

- According to the incidents reported, **many prescribers do not assess for drug interactions** with the potential of causing QTc-prolongation when prescribing FQs or macrolides.
- **Inadequate patient information** is likely a possible contributing factor, since antibiotics are frequently prescribed on an "urgent" basis by practitioners who may not know the patient well (e.g. emergency department or walk-in clinic prescribers).

Recommendations:

- Prescribers should attempt to regularly collect or access a complete list of medications and medical history, and make TdP risk-assessment when prescribing drugs with QTc-liability. We developed a ***QTc-Prolongation Risk Factors Checklist*** to facilitate this assessment.

Theme: **Potentially Inappropriate Pharmacist-Interventions**

Example) Doctor prescribed Biaxin® but it interacted with a patient's trazodone (decreases elimination of trazodone by up to 46%). Pharmacist called MD and had antibiotic changed.

Comments:

- **Most of our incident descriptions did not indicate or imply patient-assessment by the pharmacist.** This means that most of the reporting-pharmacists *seem* to have made their interventions without assessing the patient's risk of QTc-prolongation and TdP.
- This is a problem since susceptibility to QTc-prolongation and potential for developing TdP varies amongst patients and depends greatly on the number and type of risk factors the patient has.

Recommendations:

- **It is imperative for pharmacists to assess the patient before intervening** to insure the risk of QTc-prolongation and TdP in the patient is significant. This prevents withholding therapy that would otherwise be beneficial and most likely not harmful, which is advantageous in cases when an alternative is less effective than the originally prescribed medication.

Theme: **Patient Potentiated Risk for Harm**

Example) *A caregiver dropped off a prescription for levofloxacin, but on request, was unable to provide a list of medications that the patient was on. The pharmacist contacted another pharmacy to acquire this list, and found a significant risk for QT prolongation (mirtazapine + haloperidol + levofloxacin). The pharmacist requested the physician for a change in antibiotic therapy.*

Comments:

- **Polydoctoring and Polypharmacy -** These practices widen safety-gaps as patients often do not disclose a complete medication list and medical history to each healthcare provider.

Recommendations:

- Pharmacists should educate theirs patients about the risks of not disclosing their complete medication list and medical history to each health care provider in their circle of care.
- **Pharmacist should also provide their patients with up-to-date and comprehensive medication lists** and educate them on the importance of retaining this list.

CONCLUSION(S)

- Prescribers should seek patients' complete medication list and medical history, and make TdP risk-assessment when prescribing drugs with QTc-liability.
- Pharmacists should assess patients' risk factors for QTc-prolongation before intervening on drug-interactions.
- We developed a ***QTc-Prolongation Risk Factors Checklist*** (available upon request at cphir@ismp-canada.org) to facilitate TdP risk-assessment.
- Patients should regularly be provided with a comprehensive medication list and educated on safe medication use by pharmacists.

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3. ISMP Canada. Community Pharmacy Incident Reporting (CPhIR) Database. http://www.cphir.ca

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