Personalized QT risk assessment – to inform medication prescribing?

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Background & aim

QTc interval prolongation can lead to Torsades de Pointes (TdP), a ventricular tachycardia, which can result in sudden cardiac death. Several risk factors can produce exaggerated QT prolongation, such as certain drugs and patient related factors (electrolyte disturbances, age, gender…). AzCERT (Arizona Center for Education and Research on Therapeutics) categorizes drugs based on their risk of causing QT prolongation and/or TdP (CredibleMeds lists). In AZ Sint-Jan Brugge-Oostende AV (Belgium) hospital, the clinical pharmacist provides 'QT advice' for each prescription of a QTdrug with known risk of TdP (credible meds list KR). In 2019, the pharmaceutical guideline for giving QT advice was adjusted in collaboration with the cardiologists. The threshold for checking the ECG was adapted and the definition of a recent ECG has been adjusted. The objective of this study was to compare the feasibility and clinical relevance when QT advice was provided, guided by the original and adapted QT-guideline.

Methods

In this retrospective analysis, QT advices provided by the pharmacist and documented in the clinical patient record were analyzed. The analysis includes: number of QT advices (n) given according to the original guideline (flowchart 1) (April 2018 - January 2019) and the adapted guideline (flowchart 2) (May 2019 - October 2019), number of QTdrugs (defined as drugs categorized on credible meds list KR) per prescription and QTc-interval >500ms (if known). During 1 month (15 May - 14 June 2019) the acceptance rate of all the provided pharmaceutical advices, including the QT advices (since the introduction of the adapted guideline), were registered.

Results

FLOWCHARTS

Flowchart 1

≥2 QTdrugs or **1 QTdrug** in **combination** with a **drug that inhibits the metabolism** → check ECG

Recent ECG= **ECG max. 1 year old**:

Unavailable → advice: take an ECG

Available and QTc<500ms → no advice

Available and QTc>500ms → advice: follow-up ECG, switch or stop QT drug

Flowchart 2

≥1 QTdrug → check ECG

Recent ECG= **ECG during hospitalization**:

Unavailable → advice: take an ECG

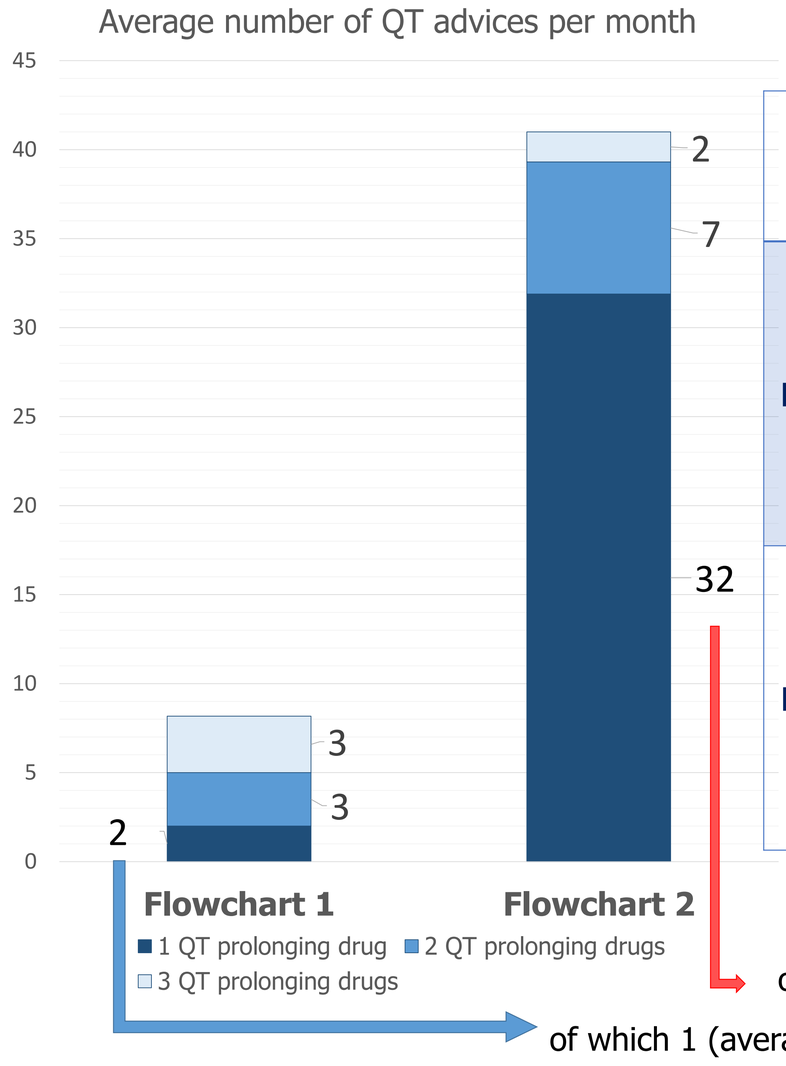
Available and QTc<500ms → no advice

Available and QTc>500ms → advice: follow-up ECG, switch or stop QT drug

*ECG only checked when:

- Prescription with daily administrations
- Duration prescription > 2 days

NUMBER OF QT ADVICES



of which 1 (average per month), QTc-interval > 500ms

of which **5** (average per month), QTc-interval > 500ms

ACCEPTANCE RATE FLOWCHART 2

QT advices = 40%

Pharmaceutical advices **without QT advices**= 79%

	Top 5 prescribed drugs (# advices)	Number of advices
Flowchart 1	1. Ciprofloxacin (31) 2. Amiodarone (25) 3. Fluconazol (24) 4. Ondansetron (16) 5. Haloperidol (15)	78 in 10 months Average of 8 per month
Flowchart 2	1. Ciprofloxacin (74) 2. Escitalopram (53) 3. Amiodarone (26) 4. Fluconazol (26) 5. Ondansetron (23)	243 in 6 months Average of 41 per month

Discussion

Adapting the QT flow that guides the pharmacist in formulating a clinical relevant QT advice resulted in a fivefold increase in number of QT advices. The rather low acceptance rate may be explained by the fact that the pharmacist only selects patients upon QTdrug prescriptions and not upon the combination of a prescription with patient related risk factors for QT prolongation. To enhance the number of clinically relevant advices, patient related risk factors such as hypokalemia, age, gender, cardiovascular co-medications (diuretics and antiarrhythmics) should be included to further optimize the QT guideline. It is necessary that personalized risk assessment systems identify patients at greatest risk for QT prolongation. In that case, the pharmacy will have to screen fewer patients, but with more clinically relevant risk factors.

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Literature:
(1) VANDAEL, Eline, et al. Risk factors for QTc-prolongation: systematic review of the evidence. International journal of clinical pharmacy, 2017, 39.1: 16-25