MedicinesUpdateExtra

NHS Greater Glasgow and Clyde

Issue 8, July 2018 ◆ Produced by NHS Greater Glasgow and Clyde Medicines Information Service

# Drug Induced QT Prolongation – Patient Scenarios

## Scenario 1

A 65 year old male inpatient is suffering from severe nausea and vomiting. The cause of which is being investigated. He is currently prescribed citalopram 20mg daily. His U+Es, renal and liver function are normal.

### What are the issues?

A number of antiemetics are associated with QT prolongation and would therefore be contra-indicated in combination with citalopram. There is a risk of ventricular arrhythmias and sudden cardiac death associated with domperidone. The risk is higher in those over 60 years and with doses higher than 30mg daily. Ondansetron may also prolong the QT interval and should be avoided in combination with other drugs known to prolong the QT interval.

### What could be done in this case?

Cyclizine would be the anti-emetic of choice in this patient as it has not been associated with QT prolongation. Metoclopramide is a potential option although caution is required due to very rare reports of cardiac adverse events (particularly with intravenous use). Be aware that in order to minimise the risk of potentially serious neurological adverse effects metoclopramide is restricted to a maximum daily dose of 30mg (or 0.5mg/kg/day if less than 60kg), and for no longer than five days. Domperidone and ondansetron should be avoided.

## Scenario 2

A 42 year old man attends the GP surgery and is diagnosed with community acquired pneumonia (CRB65=0). The patient is penicillin allergic and is prescribed clarithromycin 500mg BD for 5 days. The patient has no cardiac history, he is an ex-intravenous drug user and his only current medication is methadone 120mg daily. There are no recent U+Es or LFTs on the system although 6 months ago these were normal.

### What are the issues?

Methadone, particularly at doses above 100mg daily, can cause prolongation of the QT interval. Clarithromycin can also cause QT prolongation and there is potential for additive QT prolonging effects. In addition clarithromycin may inhibit the metabolism of methadone and further increase the risk of QT prolongation. Caution is advised if using methadone and clarithromycin concomitantly. In this case there are no other obvious risk factors for QT prolongation, however, there are no recent U+Es.

### What could be done in this case?

To address the potential interaction, alternatives to clarithromycin should be considered. Doxycycline is an alternative therapy included in the primary care infection management guidelines for community acquired pneumonia.

## Scenario 3

A 56 year old male attends the GP surgery and is diagnosed with oral candidiasis which has not responded to a course of nystatin. Fluconazole 100mg daily for 7 days is prescribed. He has a history of hypertension and renal cell carcinoma. Current regular medications are pazopanib 800mg daily and amlodipine 10mg daily. Most recent U+Es from last month were normal.

### What are the issues?

Pazopanib is a protein kinase inhibitor which is given as a long-term daily therapy in the management of renal cell carcinoma. There is a potential interaction between fluconazole and pazopanib. Fluconazole is a moderate inhibitor of the cytochrome P450 enzyme CYP3A4 which is responsible for the metabolism of pazopanib. Strong inhibitors of CYP3A4 should be avoided in combination with pazopanib; the effect of moderate inhibitors such as fluconazole is less clear but may result in some increase in pazopanib levels and therefore increase risk of adverse effects. In addition, both pazopanib and fluconazole can prolong the QT interval which may lead to additive QT prolonging effects.

### What could be done in this case?

The patient's specialist oncology team should be contacted to determine the best course of action regarding the treatment of oral candidiasis and discuss further monitoring and investigations that may be required. This case highlights the importance of being aware of potential interactions with specialist medicines and the benefits of adding them to the primary care prescribing record (see guidance - adding medicines to VISION/ EMIS)

## Scenario 4

A 74 year old man with a history of AF attends the GP surgery reporting symptoms of light-headedness and palpitations. He is referred for an ECG which demonstrates a QTc interval of 484ms. He also has a history of major depression and congestive heart failure. His current medication regimen includes citalopram 20mg daily and amiodarone 200mg daily.

### What are the issues?

The patient has several risk factors for QT prolongation – congestive heart failure, age >65 years and concurrent use of two drugs that are known to prolong the QT interval. The patient is experiencing symptoms which are suggestive of arrhythmia and the ECG has shown QTc prolongation. The only modifiable risk factor is drug therapy.

### What could be done in this case?

Review of citalopram and amiodarone should be undertaken to address the contraindicated combination. Cardiology input may be needed.

## Scenario 5

A 72 year old female is admitted to the acute medical receiving ward with severe CAP (CURB65=3). She has a known penicillin allergy and is prescribed levofloxacin 500mg twice daily. The patient later becomes acutely confused with visual hallucinations and severe agitation. She is diagnosed with delirium due to the infection plus constipation as an additional trigger. Despite treatment for the causes of the delirium and non-pharmacological management of the distressed behaviour she is still severely agitated. Pharmacological treatment is deemed necessary to keep the patient safe.

### What are the issues?

Haloperidol is the first line pharmacological therapy for management of severe agitation and distress in delirium not responding to non-pharmacological management. However, it is contraindicated in combination with other medicines that prolong the QTc interval such as levofloxacin. This patient also has non-modifiable risk factors for QT prolongation – age and female sex.

### What could be done in this case?

Microbiology should be contacted to discuss whether levofloxacin could be changed to a non-QT prolonging antibiotic. If this is not possible, alternatives to haloperidol for the pharmacological management of delirium include risperidone or benzodiazepines. However, risperidone should be used with caution in QTc prolongation or in combination with other QT prolonging medicines. Where possible an ECG should be recorded to check the QT interval before giving treatment and if prolonged, senior advice should be sought. Also consider and correct any modifiable risk factors for QT prolongation.

Be aware that benzodiazepines can lead to a paradoxical worsening of delirium and therefore careful monitoring is needed. Senior advice should be sought prior to prescribing. Pharmacological treatment of delirium should be reviewed regularly and stopped when no longer required.

## Scenario 6

An 85 year old female is admitted to a medical ward. Medicines reconciliation reveals she is currently prescribed citalopram 40mg daily and quetiapine 50mg BD. She has a history of congestive cardiac failure and is also prescribed furosemide 40mg daily.

### What are the issues?

There are a number of issues in this patient. The maximum dose of citalopram in elderly patients over 65 years is 20mg daily; it is also contra-indicated in combination with other drugs that prolong the QT interval which includes quetiapine. The patient has a number of risk factors for QT prolongation such as congestive cardiac failure, elderly, female sex and potential electrolyte imbalance due to diuretic therapy.

### What could be done in this case?

Review of both citalopram and quetiapine should be undertaken to address the contraindication. The citalopram could be switched to an alternative such as sertraline if clinically appropriate. The decision on which medication to review may have to involve the patient's GP or specialist mental health services if they are involved in the patient's care. If the citalopram was to continue, the dose should be reduced stepwise to 20mg daily. In this case it may be prudent to do an ECG initially to determine if the patient has existing QT prolongation as this may affect the course of action and urgency of changing the medication regimen. Any modifiable risk factors such as electrolyte disturbance should be corrected.