Drug interactions with salbutamol or senna increasing the risk of torsade de pointes

Since early 2018, we have had a number of questions from primary care prescribers and pharmacists concerned about seemingly innocuous drug combinations flagged up on prescribing systems. Particular examples are:

- Salbutamol inhaler + clarithromycin
- Senna tablets + citalopram

These combinations have been prescribed uneventfully for many years but some computer systems now show them as high or moderate severity warnings: “drug interaction - risk of torsade de pointes”.

What is the nature of the interaction?
Hypokalaemia is a risk factor for torsade de pointes.

Salbutamol is listed in the BNF as causing hypokalaemia; clarithromycin and citalopram are listed in the BNF as causing QT prolongation.

Why are these interactions being flagged up now?
The potential interactions are not new but the BNF (from edition 74) has changed the way it presents information on interactions.

The printed BNF has tables listing examples of drugs with particular pharmacodynamic effects. Tables include:

- Table 9: Drugs that prolong the QT interval
- Table 17: Drugs that reduce serum potassium

The BNF notes: Concurrent use of two or more drugs that reduce serum potassium might increase the risk of hypokalaemia. Hypokalaemia can increase the risk of torsade de pointes, which might be additive with the effects of drugs that prolong the QT interval.

The tables are not exhaustive and do not include all examples. They are not available via the online BNF.

It appears that prescribing software has been updated to highlight the possible increased risk of torsade de pointes if a medicine that can cause hypokalaemia is co-prescribed with a medicine that can prolong the QT interval.

Are these interactions relevant?
The BNF table of drugs that reduce serum potassium includes some examples where hypokalaemia is unlikely. For example:

- Inhaled beta2 agonists are unlikely to cause hypokalaemia; it is an adverse effect more commonly associated with oral or parenteral administration.
- Similarly, hypokalaemia is a rare adverse effect of inhaled corticosteroids; it is more commonly associated with oral or parenteral administration.
- Senna is associated with hypokalaemia if there is prolonged or excessive use or overdose leading to diarrhoea. (Senna was listed as causing hypokalaemia in BNF 74 but has been removed from BNF 75.)

Most cases of hypokalaemia are due to diuretics or loss of gastrointestinal fluids through persistent vomiting, chronic diarrhoea or laxative abuse.

Combinations such as salbutamol inhaler + clarithromycin or senna tablets + citalopram need not be avoided. Such combinations have been used uneventfully for many years.

What do prescribers need to do?
Be aware of the possible greater risk of prolonged QT interval in patients taking a medicine that can cause hypokalaemia together with another medicine that prolongs QT interval.

Consider checking serum electrolytes if you think the patient may have hypokalaemia, and correct it if necessary. (Mild hypokalaemia is generally asymptomatic. In more severe cases, symptoms include generalised weakness, muscle pain and constipation.)

A UKMi Medicines Q&A What issues should be considered regarding drug-induced QT prolongation? (available via www.sps.nhs.uk) may be helpful.

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