Interactions can occur between grapefruit and certain drugs. Nurses must ensure patients have appropriate advice and report any suspected interactions.

Interactions between drugs and grapefruit

A pharmacokinetic interaction between grapefruit and certain drugs was first identified over 20 years ago. The British National Formulary (www.bnf.org) lists the drugs that interact with grapefruit juice and the Medicines and Healthcare products Regulatory Agency has issued specific warnings about the statins atorvastatin (MHRA, 2008) and simvastatin (MHRA, 2012). More specific advice is given in the summary of product characteristics for each drug (www.medicines.org.uk/emc).

New evidence
A review article (Bailey et al, 2012) has stated that drugs that interact with grapefruit:
- Are administered orally;
- Have very low to intermediate absolute bioavailability;
- Are metabolised by the CYP3A4 enzyme.

Grapefruit juice contains furanocoumarins, which can cause irreversible inhibition of CYP3A4, mainly in the small intestine. This results in reduced pre-systemic metabolism of the affected drug and increased systemic exposure. The clinical consequences of this interaction can vary from an asymptomatic increase in drug concentrations to potentially life-threatening events (Pirmohamed, 2013).

Case reports of serious adverse events related to grapefruit–drug interactions include torsade de pointes (a type of ventricular tachycardia) with amiodarone, and rhabdomyolysis (breakdown of skeletal muscle) with atorvastatin and simvastatin.

Older people appear to have the greatest likelihood of eating grapefruit and taking interacting medications. NT

- Anticoagulants - apixaban, rivaroxaban;
- Calcium channel blockers – amlodipine, felodipine, verapamil;
- Central nervous system drugs – quetiapine, buspirone;
- Cytotoxics – nilotinib, lapatinib;
- Immunosuppressants – ciclosporin, tacrolimus, sirolimus.

This list is not exhaustive and interactions are drug specific.

The review article suggests all sources of grapefruit (the fruit, freshly squeezed juice or juice from concentrate) and certain related citrus fruits (Seville oranges, limes and pomelos) can inhibit CYP3A4. A single usual portion of grapefruit (200–250ml of juice or a whole fruit) has sufficient potency to cause a pharmacokinetic interaction, which can persist long enough to affect interacting drugs that are administered once daily at any time during the dosing interval. However, the effect on drug pharmacokinetics seems to be greater with regular consumption, suggesting a cumulative inhibitory action.

References


Box 1. Commentary

“The true extent of grapefruit–drug interactions in clinical practice is not clear. Under-reporting of such interactions to the Medicines and Healthcare products Regulatory Agency in day-to-day clinical practice is likely and the Yellow Card Scheme (yellowcard.mhra.gov.uk) provides a straightforward mechanism for reporting any suspected events.

“The difficulty for clinical practitioners is how to translate the contents of the article into sensible practice. On the basis of the article, it seems sensible to advise patients taking any drug listed as having a high potential for a clinically significant drug interaction to avoid grapefruit. For those drugs where the risk is thought to be lower, the clinical practitioner will need to gather information from the patient on the amount and frequency of grapefruit consumption, check the summary of product characteristics closely for advice, and then aim to provide a reasoned judgement.

In practice, many clinicians may prefer to err on the side of caution and advise all patients taking lower-risk drugs to also avoid grapefruit. Practitioners will need to refrain from giving ‘avoidance advice’ to all drugs within a class, even if this is easier, and ensure that the advice is tailored to the drug concerned.”

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