Is there a drug interaction between Kytril® and Perfalgan®?

Kytril® (granisetron) is indicated for the prevention and treatment of acute nausea and vomiting associated with chemotherapy and radiotherapy as well as post-operative nausea and vomiting. Perfalgan® is a paracetamol solution for infusion registered for the short-term treatment of mild to moderate pain. Kytril® and Perfalgan® may therefore possibly be used together in the postoperative setting.

Tropisetron and granisetron may block the analgesic effects of paracetamol. The exact mechanism of this interaction has not been fully determined.

A placebo-controlled, crossover study in 26 healthy subjects found that tropisetron and granisetron completely block the analgesic effect of paracetamol in humans. Because plasma concentrations were unchanged when tropisetron and granisetron was given concomitantly with paracetamol, this antagonism of analgesia was not a result of a pharmacokinetic interaction. As a consequence, the effect of 5-HT₃ antagonists on the reversal of paracetamol analgesia is due to a pharmacodynamic interaction.

Other preclinical studies looking into the mechanism of action of paracetamol have also suggested an interaction.

A preclinical study in rats set out to investigate which subtype of spinal serotonin (5-HT₃) receptors were involved in paracetamol-induced antinociception. Granisetron was used to determine the inhibitory effect of the 5-HT₃ receptor antagonists on the antinociceptive effect of paracetamol. Granisetron at a dose of 10 µg did not significantly affect the antinociception induced by paracetamol. However, it tended to nonsignificantly inhibit the effect of paracetamol after 10 µg.

Another preclinical study in rats reported that tropisetron but not ondansetron and granisetron (up to the dose of 10 µg) reversed the antinociceptive effect of paracetamol. However at the highest doses used (20 µg) granisetron also inhibited the action of paracetamol 40 and 60 minutes after administration.

References:

Is antihistamine use contraindicated in patients with epilepsy?

Patients with epilepsy should not only be aware of the possibility that certain medication may interact directly with the antiepileptic medication they are taking but that some medication may lower their seizure threshold and make them more liable to have seizures.

First generation antihistamines seem to be more likely to lower seizure threshold. They cross the blood brain barrier more quickly and easily than the second generation antihistamines and produce more central nervous system effects. A study in rats demonstrated that multiple first generation H1 antagonists caused behavioural and EEG seizures. In contrast, the second generation H1 antagonists did not induce detectible epileptogenic activity.

Although second generation antihistamines would therefore be a better choice for use in patients with epilepsy, seizures and convulsions have also been reported in the literature with the use of second generation antihistamines.

Medications which may alter the seizure threshold should therefore only be used if really necessary and no safer alternatives exist.

References:
1. Keith, L., McIvor, N.J. Toxicity and Antihistamine. eMedicine Emergency Medicine. 2010
Moduretic. Amiloride 5mg/ hydrochlorothiazide 50mg. Manufactured by MSD.