

Prescribing...

Hot Therapeutic Topics I

- This month's bulletin looks at two pieces of recent research which have hit the headlines.
- One study reported that hypnotics may be linked to increased mortality and another suggested that the long-term use of PPIs may be associated with increased fracture risk in postmenopausal women.
- Since 2010, local patients on long term hypnotics and those on long term PPIs are amongst those groups being offered MURs in participating community pharmacies.
- Despite recent price cuts prescribing of PPIs remains expensive, with significant inter-practice variability.

1. Are hypnotics linked to increased mortality?

Even when used at low levels, people on hypnotics had an increased risk of death, reports a large cohort study. Using records from a US health organisation, researchers gathered data on 10,529 patients who had had at least one prescription for a hypnotic drug over 5 years. They were matched with 23,676 controls who had not been prescribed these drugs. The mean age of the patients was 54 years.

After an average follow-up of 2.5 years, 6.1% of those prescribed hypnotics had died, compared with 1.2% of the control group. All types of hypnotics were linked to this higher risk of death, including benzodiazepines and "Z" drugs. All levels of use carried increased risk, with higher mortality rates associated with higher doses. The hazard ratio was 3.6 for patients prescribed 0.4 to 18 doses per year, 4.43 for those prescribed 18 to 132 doses and 5.32 for those prescribed more than 132 doses.

There was also an increased risk of cancer in the middle and higher tertiles of use, with hazard ratios of 1.20 and 1.35 respectively.

The researchers controlled for numerous factors including age, sex, body mass index (BMI) and self-reported alcohol use and smoking status. They also matched patients with controls diagnosed with the same combination of 12 categories of co-morbidities, including hypertension, diabetes, cardiovascular disease and asthma. However the researchers weren't able to control for depression, anxiety and other emotional factors. Multiple causal pathways may contribute to these increased risks. For example, hypnotics are often present in mixed-drug intentional overdoses and they are known to contribute to car accidents and falls.

Comment

This is not the first study to link the use of hypnotic drugs with increased mortality. But what is different about this study is that the risk was found to be present at all levels of use. One drawback of the study seems to be the lack of controlling for mental health status, as depression and anxiety are likely to be more common in people prescribed sleeping pills, and this could impact on mortality.

This study raises questions that merit further research but fully support local guidance to limit the use of these drugs to the short term use of people presenting with acute severe distress. These findings suggest even more reason for caution.

2. Long-term use of PPIs associated with increased fracture risk in post menopausal women

Proton pump inhibitors (PPIs) are one of the most commonly prescribed drugs in primary care in the Bailiwick. A suspected link with impaired calcium absorption has caused concern that they may increase the risk of fractures.

In the latest piece of work, 80,000 from the Nurses' Health Study, aged between 30 and 55 years in 1976, answered questionnaires every two years about their health, the occurrences of fractures, and whether they had regularly taken any drugs (PPIs or H2 receptor antagonists) for gastro-intestinal reflux disease in the previous two years. At each questionnaire, women also gave information about their menopausal status, lifestyle, use of HRT, thiazide diuretics, corticosteroids, bisphosphonates, calcium supplements and any diagnosis of osteoporosis. The researchers also calculated women's total intake of calcium and vitamin D from their reported consumption of foods and use of vitamin and mineral supplements. The overall rate of hip fractures was low. Amongst nearly 80,000 postmenopausal women there were 893 incident hip fractures over more than 500,000 person-years of follow-up.

Women who regularly took PPIs for at least 2 years were 35% more likely to have a hip fracture than those who didn't. This risk was higher if women were current or previous smokers, the adjusted hazard ratio for fractures was 1.51. In women who had stopped taking PPIs for more than 2 years the risk was similar to women who had never taken them. The investigators estimated that there was an associated increase of 5 hip fractures per 10,000 patient years associated with the use of PPIs.

Comment

Although the increased risk of fracture for an individual is low, the impact across a population will be significant given the widespread use of PPIs. There have been similar studies which appear to accumulate the evidence suggesting harms associated with long-term PPI use - a possible increased risk of C. Difficile infection and an increased risk of pneumonia. PPIs are effective drugs for suppressing gastric acid production but should not be prescribed long-term or in high doses without regular review and a full discussion of risks and benefits with the patient.

What about the cost?

Community pharmacists now offer MURs to all patients on long term PPIs and hypnotics, and where appropriate recommend to their GPs that they be reviewed. The cost of these treatments issued by the Guernsey practices in 2011 was as follows. Healthcare doctors prescribed more PPIs and fewer better value drugs i.e. generic omeprazole and lansoprazole, than doctors in the other practices.

