Hydrochlorothiazide: Risk of non-melanoma skin cancer

The EPVC (The Egyptian Pharmaceutical Vigilance Center) has announced that the Summary of Product Characteristics and Package Leaflet for hydrochlorothiazide will be updated to include the risk of non-melanoma skin cancer (basal cell carcinoma and squamous cell carcinoma) as an adverse reaction. Hydrochlorothiazide is widely used to treat hypertension, cardiac, hepatic and nephrogenic oedema or chronic heart insufficiency. Pharmacoepidemiological studies have shown an increased risk of nonmelanoma skin cancer with exposure to increasing cumulative doses of hydrochlorothiazide. Patients taking hydrochlorothiazide should be informed of the risk and advised to regularly check their skin. Also, patients should be advised to limit exposure to sunlight and UV rays, and suspicious skin lesions should be examined, potentially by performing histological examinations of biopsies.

In Nepal: Health care professionals are warned of the risk of development of nonmelanoma skin cancer with the use of hydrochlorothiazide.


Fluoroquinolone antibiotics: Strengthened warnings on the risk of hypoglycaemia and mental health adverse effects

The FDA (Food and Drug Administration) has announced that the drug labels of fluoroquinolone antibiotics should be strengthened to include coma as a potential outcome of hypoglycaemia, and to list adverse effects related to mental health such as disorientation and agitation. Fluoroquinolone antibiotics, such as moxifloxacin, delafloxacin, ciprofloxacin, are indicated to treat certain serious bacterial infections. Most fluoroquinolone antibiotic product labels include a warning on blood sugar disturbances and mental health adverse effects, but the new label changes will add that hypoglycaemia can lead to coma and will also make the mental health adverse effects more prominent and consistent by listing adverse effects such as disturbances in attention, disorientation, and agitation.

In Nepal: Health care professionals are warned of the risk of hypoglycemia and mental health adverse effects with the use of fluoroquinolone antibiotics.

Proton Pump Inhibitors: Shall we pause and rethink while prescribing?

Proton pump inhibitors (PPIs) have become the mainstay in treatment of acid-related disorders such as gastroesophageal reflux disease, Helicobacter pylori–related disorders, and gastric and duodenal ulcers. However, the overuse of PPIs has become an issue in clinical practice requiring attention. It is because of various potential adverse effects PPIs have, careful assessment of risk and benefits of PPI therapy should be evaluated. Risk associated with chronic use of PPIs:

1. *Clostridium difficile infection.* The proposed mechanism is that the vegetative form of *C. difficile*, which could have been killed by gastric acid, could contribute to disease pathogenesis in gastric contents with higher pH. Therefore, in a particular patients who are at risk of *C. difficile* infection such as immunocompromised, the elderly, hospitalized patients and those taking broad-spectrum antibiotics; an H₂-receptor blocker could be an alternative.

2. *Increased risk of bone fractures*  
An increased risk in hip, spine and wrist fractures in patients on high does and/or long-term PPIs therapy have been suggested from multiple studies and the proposed mechanism is a causal relationship between acid suppression and reduced absorption of mineral calcium in the diet.

3. *Acute interstitial nephritis (AIN)*  
Even though a small proportion of patients develop AIN from PPIs, PPIs have now become a common cause of drug-induced AIN in the developed world due to its overuse. The proposed mechanism is still not clear however some studies suggest that it is a humoral and cell-mediated hypersensitivity reaction that can occur within days of therapy initiation and as long as 18 months thereafter.

4. *Hypomagnesaemia*  
In March 2011, the FDA issued an advisory warning that patients taking PPIs may be at risk for hypomagnesemia. Although the exact mechanism is not known, in some patients, PPIs appear to interfere with active transport of magnesium across the intestinal wall or cause excessive loss into the intestinal lumen. Upon discontinuation, magnesium levels normalized within 1 to 2 weeks, but reoccurred within days after attempts to restart PPI therapy. Baseline serum magnesium levels should be obtained prior to initiating long-term therapy and monitored periodically thereafter. Precautions should be taken when coadministering with other agents that may lower magnesium levels, such as digoxin and diuretics.
5. Vitamin $B_{12}$ deficiency
Gastric acid is essential for absorption of $B_{12}$ by facilitating its release from dietary protein, such that $B_{12}$ can bind to R proteins. Theoretically, long-term PPI use may impair an individual’s absorptive ability. However, results from studies have been inconsistent and appear to not be clinically significant. Most patients who consume a normal diet probably will not experience any significant $B_{12}$ deficiency.

6. Rebound acid hypersecretion syndrome
The primary mechanism may be hypergastrinemia leading to increased gastric acid secreting capability that becomes apparent once the drug is discontinued. 40% of patients may have such symptoms and can take 2 to 3 months to resolve, depending on dose and duration of therapy. Considering tapering of PPIs may be appropriate when discontinuing in patients who are under chronic PPIs therapy.

References

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Grapefruit juice and drug interactions

Grapefruit is a citrus fruit which is a cross between an orange and a pomelo, which is an excellent source of vitamins A and C. Grapefruit juice (GFJ) possesses high interaction with almost all types of drugs that are commonly prescribed in day to day practice and causes serious adverse effects like torsades de pointes, rhabdomyolysis, myelotoxicity, respiratory depression, gastrointestinal bleeding, nephrotoxicity etc.¹

Furanocoumarins found in GFJ bind covalently to the active site of the intestinal cytochrome P450 (CYP3A4) enzyme, causing irreversible inactivation, which leads to increased bioavailability of administered medications that are substrates for intestinal CYP3A4 and causes toxic effects. Since GFJ targets intestinal CYP3A4, not liver CYP3A4, i.v. medications are usually not affected.²

A study has shown that GFJ should not be ingested concomitantly with statins group of drugs like atorvastatin, lovastatin or simvastatin as they have potential of causing rhabdomyolysis, whereas on other hand, pravastatin, fluvastatin and rosuvastatin are three statin drugs that have been shown not to interact with GFJ.³ It is believed that one whole grapefruit or as little as 200ml of GFJ is sufficient to cause clinically relevant increased systemic drug concentration and subsequent adverse events.²

Taniguchi in 2007 reported a case of purpura associated with concomitant ingestion of drugs like cilostazol, aspirin and GFJ in a 79 years old man. However his purpura disappeared after stopping the GFJ.⁴

GFJ is generally contraindicated in patients taking psychotropics as it contains active bioflavonoids that may change bioavailability of drug and raise its concentrations above the toxic levels.⁵ There are certain other drugs that show interactions with GFJ e.g. erythromycin, primaquine, clopidogrel, cisapride, ciprofloxacin, aliskiren etc.² Therefore, patients should be properly screened for and educated about potential fruit juice interactions thereby helping minimize their occurrence and reduce the likelihood of adverse events.

References


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