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THE SAFETY PROFILE OF PROTON-PUMP INHIBITORS: WHAT DO WE KNOW?

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Proton-pump inhibitors (PPIs) are a group of medications whose main action is a pronounced and long-lasting reduction of stomach acid production. PPIs are among the most widely sold medications in the world, and the first one, omeprazole, is on the WHO Model List of Essential Medicines (World Health Organization, 2019). Their favorable safety profile has led to over-prescription by physicians, resulting in the fact that 44.9% of internal and 23.3% of surgical patients are already prescribed a PPI with hospital admission (Del Giorno, R. et al, 2018).

The view on PPI as harmless co-medication has increasingly been challenged by reports of potentially related complications, e.g., increased risk of osteoporotic fractures, pneumonia, and other, especially in long-term usage. PPI users have an increased risk of developing community-acquired enteric infections compared with nonusers. The meta-analysis showed (Hafiz R A et al., 2018) that PPI users have an increased risk of developing community-acquired enteric infection (pooled odds ratio [OR]=4.28; 95% CI=3.01-6.08). There was significant heterogeneity between the studies (I2 = 85%; P < 0.001), which was partly explained by type of microorganism. The strength of the association was similar for Salmonella (pooled OR=4.84; 95% CI=2.75-8.54; I2 = 58.7%; P = 0.064) and Campylobacter (pooled OR=5.09; 95% CI=3-8.64; I2 =81%; P<0.001) but lower for studies that combined all bacteria (pooled OR=2.42; 95% CI=0.96-6.14; I2 =94.3%; P<0.001).

A growing body of research is devoted to studying the effect of PPIs on the occurrence of allergy. Alongside the mucosa-protective attributes of gastric pH elevation, pH-dependent pepsin activation for protein digestion is impaired, subsequently also affecting pancreatic digestion (Pali-Scholl, I. & Jensen-Jarolim, E., 2011). On one side, PPIs enable the persistence of ingested epitopes and lead to antigen-specific Th2 type immune responses and allergic symptoms, on the other side, these drugs may promote cellular responses towards a Th2 bias. For instance, PPIs activate mast cells via AhR thereby synergizing with IgE-FcaRI signaling and enhancing release of human mast cell mediators and CD63 expression associated with allergic symptoms (Novotna, A. et al., 2014).

In population-based analysis, covering nearly all of Austria's population (8.2 million) between 2009 and 2013 (Galateja Jordakieva et al, 2019), there was found a high prevalence of anti-ulcer drug prescription associated with a highly significant subsequent prescription of anti-allergic medications. The rate ratios for anti-allergic following gastric acid-inhibiting drug prescriptions are 1.96 (95% CI:1.95–1.97) and 3.07 (95%-CI:2.89–3.27) in an overall and regional Austrian dataset. These findings are more prominent in women and occur for all assessed gastric acid-inhibiting substances. Rate ratios increase from 1.47 (95%CI:1.45–1.49) in subjects<20 years, to 5.20 (95%-CI:5.15–5.25) in>60 year olds.

Thus, proton-pump inhibitors provide important clinical benefits for many patients. PPIs are essential in managing gastroesophageal reflux disease, in treating patients with gastroduodenal ulceration, and in reducing the probability of upper gastrointestinal bleeding from aspirin or NSAIDs in high-risk patients. They have favorable safety profile, however, observational studies have suggested an association between PPI use and some adverse events. Of course, inappropriate use of PPIs should be avoided and physicians should be aware of the side effects of the drugs.

Pavliukovych N.D. ERYTHROCYTE MEMBRANE MORPHOLOGY OF PATIENTS WITH CHRONIC HEART FAILURE AND DIABETES MELLITUS

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Blood rheological properties changes are one of the crucial points in the pathogenesis of most diseases, especially in case of comorbidity. Research aimed at investigation of possible