



When proton pump inhibitors are compared, are there specific cases in which a certain proton pump inhibitors should be particularly preferred?

Altay Çelebi, Hasan Yılmaz

Department of Gastroenterology, Kocaeli University School of Medicine, Kocaeli, Turkey

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ABSTRACT

Currently, proton pump inhibitors (PPIs) are widely used either over the counter or on prescription drugs. PPIs are frequently used with other drugs when elderly and chronic disease burden population is taken to consideration. Drug interactions with PPIs are a prominent clinical problem in this direction. In this study, we reviewed potential risks of concomitant use of PPIs and other drugs and appropriate PPI choice.

Keywords: Proton pump inhibitors, drug interactions, gastroesophageal reflux disease

WHICH PPI ARE PARTICULARLY PREFERRED IN PATIENTS TAKING MEDICATION?

Proton pump inhibitors (PPI) are currently the most commonly used drugs and have risk for drug interactions in people taking multiple medications. When studies on the risk of drug interactions of PPIs are examined in the literature, it is evident that the most studied subject is the interaction of clopidogrel and PPI.

Six meta-analyses were found in the literature regarding the concomitant use of PPIs and clopidogrel. Out of these, in the meta-analysis performed by Huang et al. (1) in which the maximum number (32) of studies were evaluated, an increased risk of major cardiac event (HR 1.40, 95% CI 1.19-1.64; OR 1.27, 95% CI 1.13-1.42) and an increased risk of acute coronary syndrome (HR 1.42, 95% CI 1.14-1.77; OR 1.42, 95% CI 1.08-1.87) were reported. No risk increase has been reported for the total mortality (HR 1.30, 95% CI 0.91-1.86; OR 0.92, 95% CI 0.82-1.04) and cardiovascular death (HR 1.21, 95% CI 0.60-2.43). As a result, the concomitant use of clopidogrel and PPIs increases the risk of major cardiac events, but it has not been shown to influence total mortality (1,2). Although there is insufficient data in the literature, omeprazole and esomeprazole with high affinity of CYP2C19 should be avoided if PPI are required to be used in patients treated with clopidogrel.

Theophylline is often used in combination with PPI in advanced-age populations with respiratory diseases. In reference to the conducted studies, theophylline blood levels are not affected by the concomitant use of lansoprazole or pantoprazole with theophylline (3). Lansoprazole, pantoprazole, and omeprazole do not affect the excretion and absorption of theophylline (4). There is no change in theophylline pharmacokinetics with the use of rabeprazole (5). Treatment change is not needed in patients using theophylline together with lansoprazole, pantoprazole, omeprazole, and rabeprazole. There is no data involving esomeprazole.

In the concomitant use of warfarin and pantoprazole, it was found that pantoprazole did not change the pharmacokinetics and pharmacodynamics of warfarin. (6) Because omeprazole increases the r-warfarin blood levels and reduces thrombosis by 10%, omeprazole should be avoided in patients taking warfarin (7). There is insufficient data on other PPIs.

Limited data suggest that the serum levels of digoxin do not change in the concomitant use of this drug with pantoprazole or rabeprazole (8,9). Omeprazole increases the digoxin blood levels (10). There is no data about the other PPI.

Address for Correspondence: Hasan Yılmaz E-mail: gyurusus@yahoo.com

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In the concomitant use of lansoprazole, omeprazole, and esomeprazole with acetylsalicylic acid (ASA), the effectiveness of ASA does not change (11-13). There is no data on the other PPI.

It has been shown in studies that the concomitant use of pantoprazole or lansoprazole in patients using diazepam does not affect the metabolism of diazepam (14-16). The use of omeprazole or esomeprazole may increase the effect of diazepam (16,17).

We were able to find only one study in the literature regarding the concomitant use of PPI and oral contraceptives in which it has been reported that lansoprazole does not affect the bioavailability of low doses of oral contraceptives (18).

The concomitant use of pantoprazole, esomeprazole, omeprazole, or lansoprazole with prasugrel does not change the effect of prasugrel (19).

Only one study was found in the literature regarding the use of thyroid hormone preparations together with PPIs and it has been reported that pantoprazole does not change the absorption kinetics of levothyroxine in aforementioned study (20).

PPI may reduce the effectiveness of oral itraconazole (21).

In the concomitant use of mycophenolate mofetil and PPI, enteric-coated mycophenolate mofetil should be used (22).

WHICH PPI SHOULD BE USED WITH QUICK METABOLIZERS?

According to the current literature data, there is no significant difference among PPI in patients with higher metabolism in terms of the suppression of stomach acid on the 7th day of treatment (23,24) (level of evidence: 1b).

RECOMMENDATIONS

- The concomitant use of PPIs and clopidogrel increases the risk of major cardiac events, but its effect on total mortality could not be demonstrated (Level of evidence: 1a).
- Although there is insufficient data in the literature, omeprazole and esomeprazole with high affinity of CYP2C19 should be avoided if PPIs are required to be used in patients treated with clopidogrel (Level of evidence: 5).
- Treatment change is not required in patients using theophylline together with lansoprazole, pantoprazole, omeprazole (level of evidence: 1b) and rabeprazole (Level of evidence: 4). There is insufficient data regarding esomeprazole.
- Pantoprazole does not alter the effectiveness of warfarin in concomitant use of warfarin and pantoprazole (Level of evidence: 2b).

- Omeprazole increases the plasma levels of warfarin, but there is insufficient data in the literature regarding its clinical implications. There is insufficient data on the other PPIs (Level of evidence: 1b).
- Limited data suggest that the serum levels of digoxin do not change with pantoprazole and rabeprazole. Omeprazole increases the digoxin blood level. There is insufficient data on the other PPIs (Level of evidence: 2b).
- In the concomitant use of lansoprazole, omeprazole, and esomeprazole with acetylsalicylic acid (ASA), ASA effectiveness does not change. There is no data about other PPIs (Level of evidence: 1b).
- Pantoprazole or lansoprazole can be used if PPI use is needed in patients taking diazepam. The use of omeprazole or esomeprazole with diazepam can enhance the effect of diazepam (Level of evidence: 1b).
- There is no evidence of pharmacokinetic interactions between lansoprazole and low-dose oral contraceptives. There is no data on the other PPIs (Level of evidence: 2b).
- Pantoprazole, esomeprazole, omeprazole and lansoprazole do not change the effect of prasugrel (Level of evidence: 2b).
- Pantoprazole does not change the levothyroxine blood levels. There is no data about other PPIs (Level of evidence: 2b).
- PPIs may reduce the efficacy of oral itraconazole (Level of evidence: 2b).
- In the concomitant use of mycophenolate mofetil and PPI, enteric-coated mycophenolate mofetil should be used (Level of evidence: 3b).

Conflict of Interest: No conflict of interest was declared by the authors.

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