Suboptimal Dosing of Esomeprazole

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Letter to the Editor- Suboptimal Dosing of Esomeprazole

I read the informative research article "Night-time gastric acid suppression by tegoprazan compared to vonoprazan or esomeprazole" by Yang E et al., with great interest.

There are a few points that I would like to highlight regarding the methodology of the study. The dosing schedule used in the study for esomeprazole is likely to produce suboptimal effects. The optimal effect of esomeprazole depends on two factors i.e. timing of dosing and the cumulative effect.

* Esomeprazole which is a proton pump inhibitor (PPI) inhibits gastric acid secretion by non-competitively inhibiting the enzyme H+, K+ ATPase in parietal cells. After the meal, parietal cells are maximally stimulated which results in the activation of proton pumps, thus, it is the best time for the antisecretory effect of PPI. PPIs are recommended to be taken 30 minutes before the first meal.[1]Therefore, timing administration of PPI with meals may be critical for optimal effect.[1, 2] Plasma half-life of esomeprazole is approximately 1-1.5 hours.[3] Only the expressed acid-secreting proton pumps on the luminal membrane of parietal cells are inhibited by esomeprazole. Administering esomeprazole at night will inhibit only very few proton pumps during the brief period when the PPI is available for therapeutic action. Furthermore, bedtime PPI administration will not contribute to nocturnal acid breakthrough inhibition because the drug will have disappeared by the time night-time acid secretion is perceptible. As per the dosing schedule followed in the study, by the time patient had the maximum expression of the H+K+ ATPase, esomeprazole was already eliminated from plasma. Tegoprazan and vonoprazan, being reversible and competitive inhibitors of H+K+ ATPase are devoid of such effects. * The antisecretory action of esomeprazole increases with repeated dosing to reach a plateau phase after 3-4 days to produce 80-98 % suppression of 24-hour acid output.[4] Even when given 30-60 minutes before meals, PPIs are unable to block all proton pumps with oral formulations and single dosing because all pumps are not active during 1.5 hr half-life of PPIs. Because of this short t1/2, only 70% of pumps are inhibited.[5] Thus, approximately 20% of pumps are newly synthesized over 24 hours. As the once optimized amount of drug is reached, increasing the dose has almost no effect. An increase in the frequency of administration seems to have some effect, a morning and evening dose before food results in approximately 80% inhibition of maximal acid output.[6,7]

The drug metabolism by CYP3A4 (30.9%) is more common than CYP2C19 (6.8%).[8] As tegoprazan and vonoprazan are metabolized by CYP3A4,[9] and it makes them more susceptible to drug-drug interactions in the case of polypharmacy.

Tegoprazan and vonoprazan belong to the novel class of drugs which offers reversible and competitive inhibition of H+K+ ATPase. For their comparison with esomeprazole, the dosing schedule should be designed so that its optimal effect can be considered for comparison.

Conflict of interest: None

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