

## Drug Corner

### Role of PPI and importance of anti-reflux agents in the treatment of NERD

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**Background:** Esomeprazole, an S-isomer of omeprazole, is a much more potent acid inhibitor than most other currently available PPIs and gives excellent results. Therefore, it is a first-line drug for acid-related diseases like Non-Erosive Reflux Disease (NERD). Yet, patients demand faster onset and response.

**Aim :** To establish the role of esomeprazole and the importance of anti-reflux agents like a combination of two antacids (calcium carbonate and sodium bicarbonate) and alginate in treating NERD.

**Conclusion:** Esomeprazole therapy shows potential efficacy in the continuous maintenance treatment of the NERD. However, it is suggested that to improve the efficiency of esomeprazole for the treatment of NERD; we can supplement the drug with antacids (sodium bicarbonate and calcium carbonate) and alginates.

[*J Indian Med Assoc* 2022; **120(11)**: 69-71]

**Key words :** Esomeprazole, PPI, Antacids, Non-erosive reflux disease, Alginates

**N**on-erosive Reflux Disease (NERD) is defined as a disease with gastroesophageal reflux disease (GERD)-like symptoms without any signs of endoscopic oesophageal mucosal injury. About 30-50% of NERD patients show oesophageal acid exposure within the physiological range<sup>1</sup>. GERD prevalence is anticipated to be within the range of 10 to 20% in Western countries and is about 5% in Asian countries<sup>2</sup>. On performing endoscopy, about 60% of the patients that have been observed are suffering from NERD<sup>3</sup>. In a multi-centre study conducted across Asia, on screening of a total of 690 patients in terms of racial distribution, 75.4% were Chinese, 9.8% were Malays and 14.8% were others including Indians. The majority of patients (64.8%) with the typical reflux symptoms of heartburn or acid regurgitation had NERD<sup>4</sup>.

A range of Proton Pump Inhibitors (PPIs) are available today and are considered the first line of treatment for NERD and other acid-related illnesses. However, it is suggested that to improve the efficacy for the treatment of NERD, supplementation with antacids might be helpful. Some of the commonly used

antacids are sodium bicarbonate (NaHCO<sub>3</sub>), calcium carbonate (CaCO<sub>3</sub>), magnesium oxide (MgO), and magnesium hydroxide gel (Al<sub>2</sub>O<sub>3</sub>), simethicone and alginate<sup>5,6</sup>.

#### **Role of Esomeprazole in NERD :**

Esomeprazole is the S-isomer of omeprazole; in comparison with omeprazole, esomeprazole exhibits a better pharmacokinetic profile. It has further been established that, esomeprazole is a more potent acid inhibitor over presently available PPIs. Esomeprazole daily dose of 20 or 40 mg treated chronic heartburn effectively in patients with NERD. This symptom of heartburn resolved completely after treatment for 4 weeks in 33-70% of patients with esomeprazole. Esomeprazole demonstrated good tolerance in clinical trials conducted over 4 weeks to 12 months, including more than 17 000 patients<sup>5,7</sup>.

In a comparative study for symptom relief in patients with gastroesophageal acid reflux, several PPIs were administered. Esomeprazole administration was found to be most effective for symptom relief within 2 days compared with lansoprazole, pantoprazole, and omeprazole administration. In patients with NERD, esomeprazole demonstrated clinical and pharmacological benefits higher than those seen with the other PPIs<sup>8</sup>.

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Received on : 23/08/2022

Accepted on : 09/11/2022

Response of Esomeprazole for NERD management gives excellent results. Still, there is a gap in patient satisfaction as the treatment may need incremental dosage or inapt switching to alternate medications. Moreover, the demands for immediate response and faster onset of effects against acid secretion have raised the requirement to develop treatment using a PPI combined with an antacid salt<sup>9</sup>.

### **Role of Antacids in NERD :**

Antacids help relieve NERD symptoms only temporarily. They are generally used by patients who fail to respond to standard PPI medication<sup>6</sup>.

### **Sodium Bicarbonate :**

Sodium bicarbonate is a common antacid that increases the gastric pH. It forms a chemical umbrella that guards esomeprazole and ensures its safe passage through the duodenum, enabling efficient absorption. In a study the combination of Immediate Release (IR) esomeprazole 20 mg and sodium bicarbonate 800 mg was used to alleviate the delayed action of Esomeprazole (ESO) and achieve an immediate effect. Sodium bicarbonate neutralizes gastric acid quickly, and may lead to quicker symptomatic relief independent of accelerated esomeprazole effect. In another study, a combination of sodium bicarbonate (NaHCO<sub>3</sub>) with other PPIs exhibited quicker absorption and better inception of the antisecretory effect compared to the enteric-coated PPIs and was approved by FDA in 2004<sup>2,9</sup>.

### **Calcium Carbonate :**

Calcium carbonate demonstrates good acid-neutralizing capacity in comparison to sodium bicarbonate. Therefore, it is anticipated that CaCO<sub>3</sub> might be effective even if lesser amount of the antacid salt was used. It would be able to exhibit similar pharmacokinetic and pharmacodynamic features to other fixed-dose combinations of PPIs and NaHCO<sub>3</sub>. The combination enables rapid absorption and faster onset of inhibitory action and may substitute the conventional esomeprazole for NERD patients<sup>9</sup>.

### **Alginates :**

Alginates have been used along with antacids as over-the-counter medications. Recent studies have

found alginates better in conditions where NERD is non-responsive to inhibiting therapies. Alginic acid derivatives or alginates are extracted from seaweed. They relieve symptoms of NERD by displacing the postprandial gastric acid pocket (PGAP), preventing exposure to acid in the oesophagus<sup>6,10</sup>.

During postprandial reflux, acid secreted forms a layer on top of the meal taken. Furthermore, this acid extends close to the squamocolumnar junction (SCJ) in the postprandial period. This effect is more evident in NERD.<sup>11</sup> Alginates form an acid barrier and prevent postprandial acid reflux in the gastrointestinal tract. When they come into proximity of acid in the stomach, they form a gel and a raft that concentrates around the acid pocket<sup>10</sup>.

Alginates can be used in combination with other antacids to guard the oesophagus against effects of acid aggression. This combination is known as alginate-antacid derivative; it is entirely absorbed by the body<sup>6</sup>. The combination reduced episodes of acid reflux significantly (3.5; range, 0-6.5; P=0.03) in comparison to those patients who received only antacid (15; range, 5-20), and the time to next acid reflux episode increased significantly in patients who receive alginate-antacid combination (63 minutes; range, 23-92) compared to those receiving only antacid (14 minutes; range, 9-23; P= .01)<sup>12</sup>.

The acid reflux episodes were dependent on the acid pocket location. If the acid pocket location is above the diaphragm the occurrence of reflux episodes is 82% or if it is at the level of diaphragm the occurrence of acid reflux episode is 60%<sup>12</sup>.

Globally, PPIs that reduce the development of acid pocket, with combinations of alginate or antacid combinations that work on the acid pocket by displacing it, demonstrate the potential for selectively targeting the acid pocket in acid reflux-related diseases<sup>12</sup>. Thus, for the treatment of NERD that usually employs PPI therapy, treatment efficacy may be enhanced with antacids and alginates in NERD<sup>2</sup>.

### **Conclusion :**

Esomeprazole is the first-line drug to treat acid-related diseases like GERD, NERD, H. pylori infection,

peptic ulcers, Zollinger–Ellison syndrome, etc. While considering the rising need for a more rapid treatment response, there is a need for faster onset of the antisecretory effect.

Acid-suppressive therapy using antacids like alginates, sodium bicarbonate, and calcium carbonate combined with PPIs might be worth exploring to ensure safer and faster absorption coupled with rapid action.

#### REFERENCES

- Martinez SD, Malagon IB, Garewal HS, Cui H, Fass R— Non-erosive reflux disease (NERD) - acid reflux and symptom patterns. *Aliment Pharmacol Ther* 2003; **17**: 537-45.
- Bae S, Kwon J, Lee SB, Jang IJ, Yu KS, Lee S— Comparative Pharmacokinetics/Pharmacodynamics of Fixed-Dose Combination of Esomeprazole and Calcium Carbonate (AD-206) to the Conventional Esomeprazole. Drug design, development and therapy. 2021; 15:5099.
- Hershcovici T, Fass R. Nonerosive Reflux Disease (NERD) - An Update. *J Neurogastroenterol Motil* 2010; **16(1)**: 8-21. doi: 10.5056/jnm.2010.16.1.8
- Ang TL, Fock KM, Ng TM, Teo EK, Chua TS, Tan J — A comparison of the clinical, demographic and psychiatric profiles among patients with erosive and non-erosive reflux disease in a multi-ethnic Asian country. *World journal of gastroenterology: WJG* 2005; **11(23)**: 3558.
- Sugimoto M, Furuta T — Efficacy of esomeprazole in treating acid-related diseases in Japanese populations. *Clinical and Experimental Gastroenterology* 2012; **5**: 49.
- Ebeshi BU, Bunu SJ, Kpun HF, Ezebube CO — Analysis of gastrointestinal acid-neutralizing potency of some commercial antacid tablet formulations. *GSC Biological and Pharmaceutical Sciences* 2022; **19(2)**: 008-13.
- McKeage K, Blick SK, Croxtall JD, Lyseng-Williamson KA, Keating GM — Esomeprazole. *Drugs* 2008; **68(11)**: 1571-607.
- Zheng RN — Comparative study of omeprazole, lansoprazole, pantoprazole and esomeprazole for symptom relief in patients with reflux esophagitis. *World Journal of Gastroenterology: WJG* 2009; **15(8)**: 990.
- Kim D, Park MS, Yoo BW, Hong T, Park SJ, Kim CO — The safety, pharmacodynamics, and pharmacokinetics of immediate-release formulation containing esomeprazole 20 mg/sodium bicarbonate 800 mg in healthy adult male. *Drug Design, Development and Therapy* 2019; **13**: 3151.
- Leiman DA, Riff BP, Morgan S, Metz DC, Falk GW, French B, et al — Alginate therapy is effective treatment for GERD symptoms: a systematic review and meta-analysis. *Diseases of the Esophagus* 2017; **30(5)**: 1.
- Kwiatk MA, Roman S, Fareeduddin A, Pandolfino JE, Kahrilas PJ — An alginate antacid formulation (Gaviscon Double Action Liquid) can eliminate or displace the postprandial 'acid pocket' in symptomatic GERD patients. *Alimentary pharmacology & Therapeutics* 2011; **34(1)**: 59-66.
- Rohof WO, Bennink RJ, Smout AJ, Thomas E, Boeckxstaens GE — An alginate-antacid formulation localizes to the acid pocket to reduce acid reflux in patients with gastroesophageal reflux disease. *Clinical Gastroenterology and Hepatology* 2013; **11(12)**: 1585-91.