Efficacy of Vonoprazan 10 mg and 20 mg for Patients with Proton Pump Inhibitor (PPI)-Refractory Functional Dyspepsia (FD): A Double-blinded, Randomized Study

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Abstract

Background:
Due to the pivotal role of acid in symptom manifestation, proton-pump inhibitors (PPI) stand as the initial pharmacological treatment of choice for individuals with functional dyspepsia (FD). However, certain patients may find inadequate relief from FD symptoms with PPI treatment. Vonoprazan, classified as a potassium-competitive acid blocker (P-CAB), demonstrates non-inferior efficacy in acid reduction compared to PPI. Notably, the existing efficacy data for vonoprazan in addressing PPI-refractory functional dyspepsia (FD) is currently limited.

Methods:
We conducted a double-blinded, randomized controlled trial study at a tertiary-care hospital (Rajavithi Hospital, Bangkok) that included patients with Functional dyspepsia (according to Rome IV criteria) who are unresponsive to the therapeutic dose of PPI for at least 4 weeks. Participants were randomly assigned to receive either 10 mg or 20 mg of vonoprazan for a 4-week duration, with a subsequent follow-up scheduled 4 weeks after treatment discontinuation.

Outcomes: The primary outcome aimed to compare the efficacy of 10 mg and 20 mg vonoprazan for treating patients with PPI-refractory FD (assessed by the Global Overall Symptoms Scale (GOSS)). The secondary outcomes are 1.the efficacy of vonoprazan in symptom alleviation in each group by GOSS, 2.the improvement in quality of life by Nepean dyspepsia index in each group, 3.The number of FD response rate (defined by greater than 50% improvement in GOSS score) in each group and 4.an assessment of the drug's safety profile and adverse events.

Results: Out of the 60 patients enrolled, 29 received 10 mg of vonoprazan, and 31 received 20 mg of Vonoprazan. The reduction in the GOSS in the 10 mg and 20 mg groups was -11.14±8.11 and -10.59±10.96 points at week 2, -16.03±9.34 and -15.78±11.55 points at week 4, and -15.59±8.74 and -16.33 ±9.93 points at week 8, respectively (all $p<0.001$ vs baseline; and $p>0.05$ between the 2 groups). The response rates (defined by >50% decrease in the GOSS) after treatment in the 10 mg and 20 mg groups were 31.0% and 35.7% at week 2 ($p = 0.937$), 75.8% and 78.6% at week 4 ($p = 1.00$), and 72.4% and 75.9% at week 8 ($p = 0.24$), respectively.

Dyspepsia-specific quality of life was improved in both groups, with the Napean dyspepsia index changing -4.00±5.99 (p=0.001) and -4.38±5.26 (p<0.001) at week 4 (p=0.853 between groups). The most frequently reported adverse event associated with vonoprazan was bloating, occurring in 6.7% of patients; no serious adverse events were observed.

Results: Out of the 60 patients enrolled, 29 received 10 mg of vonoprazan, and 31 received 20 mg of Vonoprazan. The means difference in the global overall symptoms scale between both groups at week 8 were -15.59 and -16.33 (p > 0.05) respectively. However, the reduction in the GOSS in the 10 mg were -11.14, -16.03, -18.11, -15.59 and at week2, 4,6 and 8 respectively. (p<0.001 vs baseline) As similar direction as 20 mg group, the reduction of GOSS were -10.59, -15.78, -18.33 and -16.33 respectively. (p<0.001 vs baseline) Also, Dyspepsia-specific quality of life were improved in each group, with the Napean dyspepsia index changing -4.00±5.99 (p=0.001) and -4.38±5.26 (p<0.001) at week 4 , but were indifferent between two groups (p=0.853). The response rates in the 10 mg and 20 mg groups were 72.4% and 75.9% at week 8 clinical significantly, but were indifferent between two arms (p = 0.24), respectively. The most frequently reported adverse event associated with vonoprazan were bloating (6.6%) Nausea (5%) and Constipation (3.3%). No serious adverse events were observed.

Conclusion:
Vonoprazan demonstrated significant effects in the alleviation of symptoms in PPI-refractory FD patients. There was no statistically significant difference in symptom alleviation between the 10 mg and 20 mg doses of vonoprazan. There were no serious adverse events occur in both groups during eight weeks of study.

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Keywords: PPI-Refractory Functional dyspepsia, P-CAB, Global Overall Symptoms Scale, Nepean dyspepsia index