PPI 치료에 대한 불응성 상태의 대처 방안

이 혁

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제 16회 소화기병 심포지움

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Putative mechanisms for PPI failure

Patients

Higher likelihood
Visceral hypersensitivity
Weakly acidic reflux
Duodeno-gastro-esophageal bile reflux
Delayed gastric emptying
Psychological co-morbidity
Concomitant functional bowel disorder

Lower likelihood
Helicobacter pylori infection

Unknown
Eosinophilic esophagitis

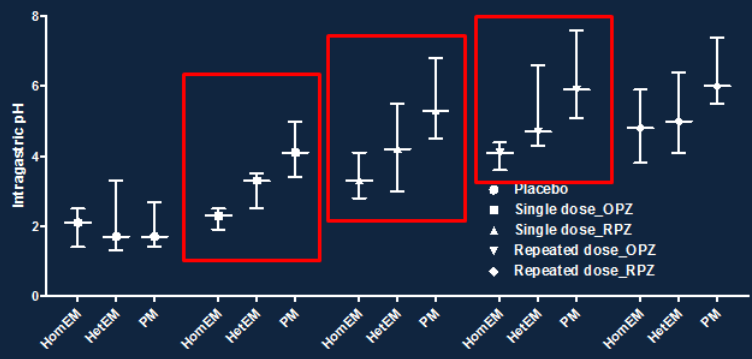
Proton pump inhibitor

Lower likelihood
Rapid metabolism
Nocturnal acid breakthrough
Reduced bioavailability
PPI resistance

Distribution of CYP2C19 Genotype in Korea

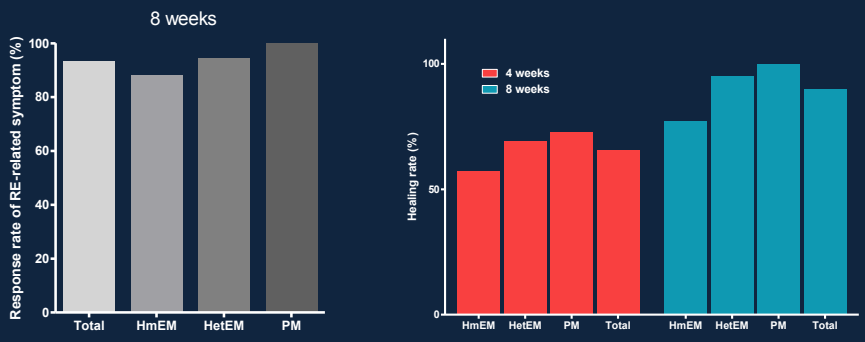
RM	IM	PM
171	219	73
36.9%	47.3%	15.8%
wt/wt 171	wt/m1 167 wt/m2 52	m1/m1 40 m2/m2 30 m1/m2 3

Effect of CYP2C19 on gastric acid inhibition



Shirai, *et al*. Aliment Pharmacol Ther 2001

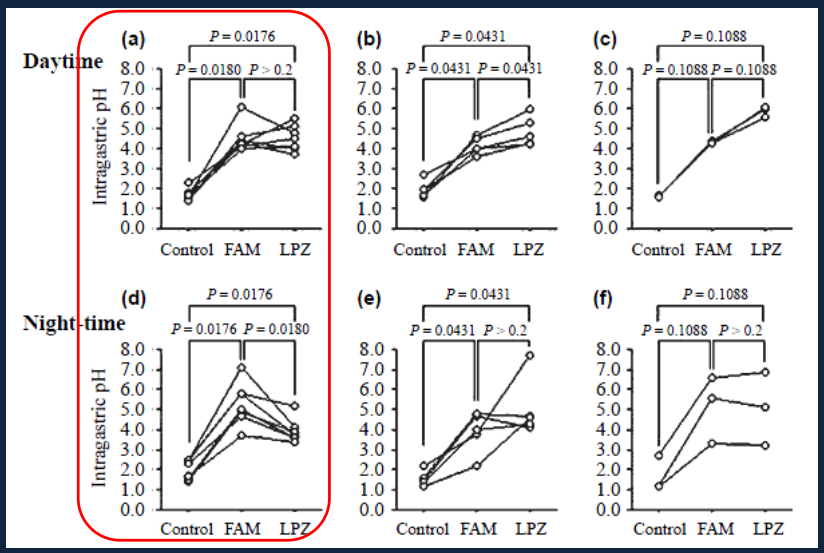
CYP2C19 in GERD



LPZ 30mg, Difference in the healing rate of erosive reflux esophagitis

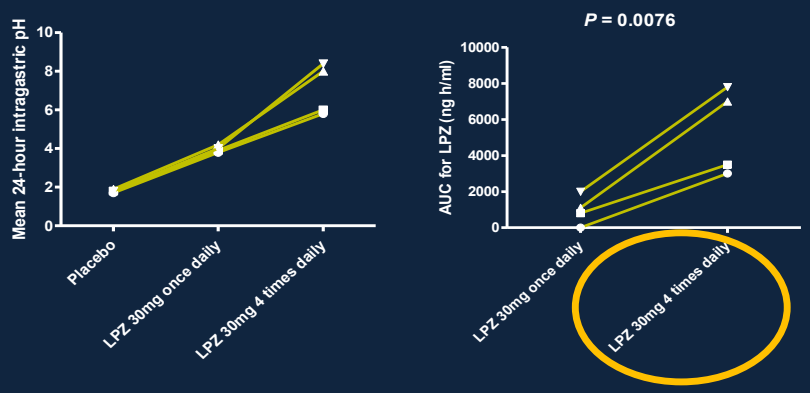
Kawamura, *et al*. Aliment Pharmacol Ther 2003

Therapeutic strategies for CYP2C19-related PPI failure



Shirai, *et al*. Aliment Pharmacol Ther 2002

Therapeutic strategies for CYP2C19-related PPI failure

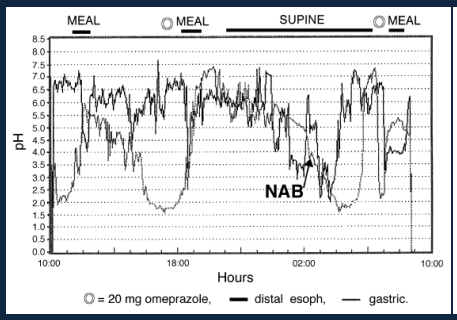


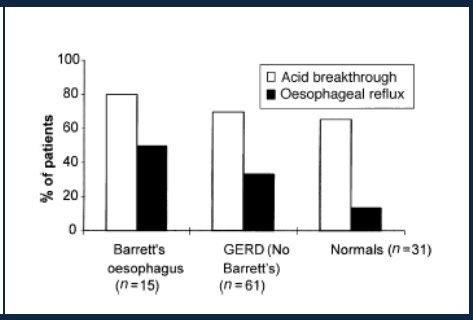
The effect of lansoprazole on intragastric pH depended significantly on CYP2C19 genotype status.

Complete acid inhibition could be achieved by the frequent administration of lansoprazole in subjects who were homozygous extensive metabolizers.

Furuta, *et al*. Clin Pharmacol Ther 2001

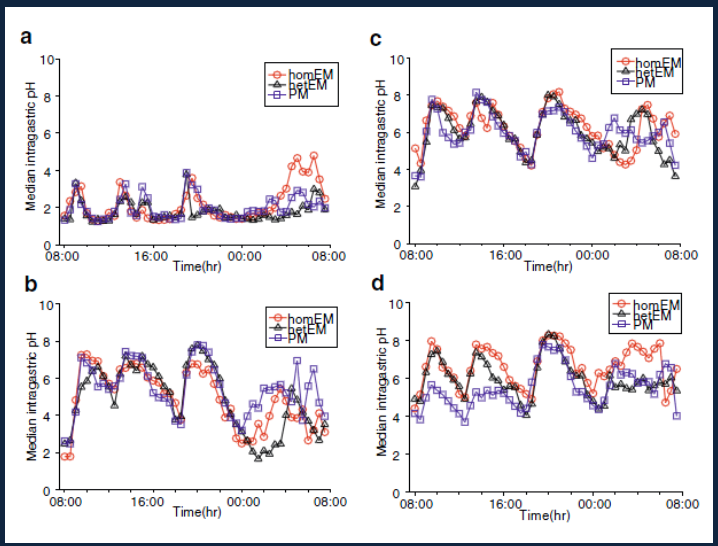
Nocturnal acid breakthrough





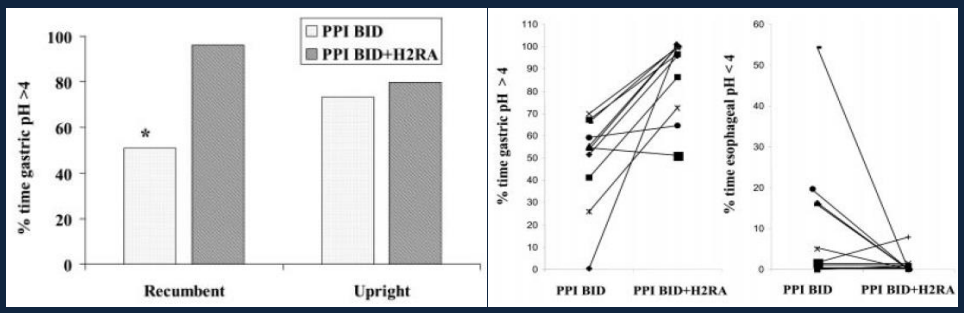
Katz, *et al.* Aliment Pharmacol Ther 1998

Timing and frequency of PPI dosing for NAB



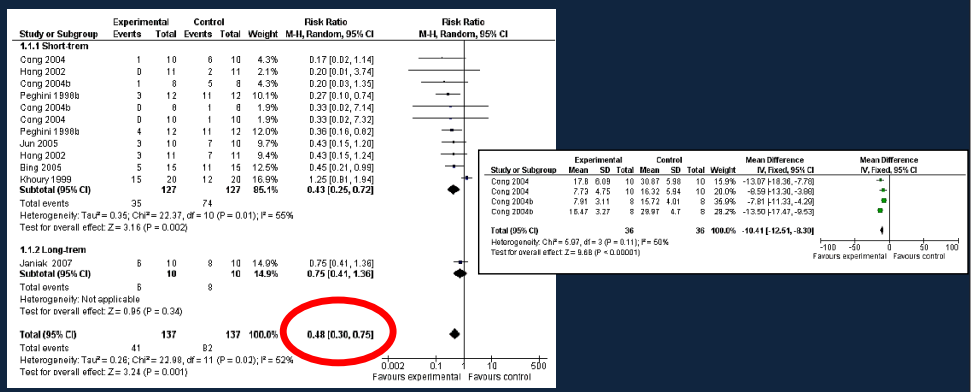
Lou, *et al.* Eur J Clin Pharmacol 2009

Additional use of nocturnal H2RA for NAB



Xue, *et al.* Aliment Pharmacol Ther 2001

H2RA for NAB: meta-analysis



Additional bedtime H2RAs can decrease the prevalence rate of nocturnal gastric acid breakthrough

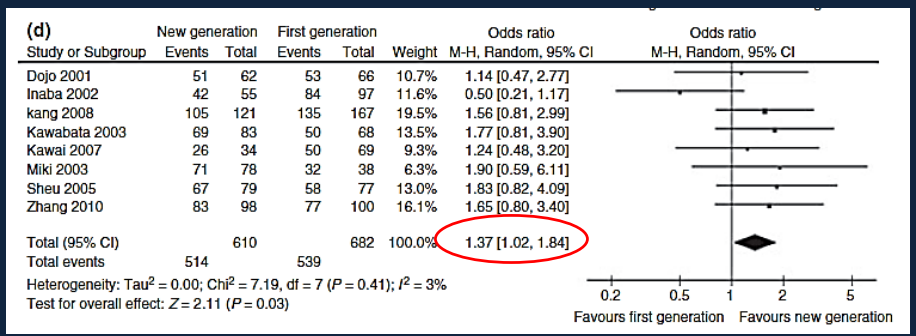
Wang, *et al.* Cochrane Database Syst Rev. 2009

CYP2C19 and *H.pylori* eradication

	Univariate Analysis OR (95% CI)	Multivariate Analysis OR (95% CI)
Sex male	1.70 (0.78–3.68)	1.13 (0.56–2.25)
CYP2C19 Hom	4.34 (1.27–14.82)	3.45 (1.11–10.70)
CYP3A4 Mutation	0.78 (0.26–2.29)	0.59 (0.22–1.62)

Sapone, *et al.* Am J Gastroenterol 2003

CYP2C19 genotype on *Hp* eradication rate: A Meta-analysis



Only extensive metaboliser patients showed higher eradication with new-generation PPIs

McNicholl, *et al.* Aliment Pharmacol Ther 2012

RAHS after H2RA

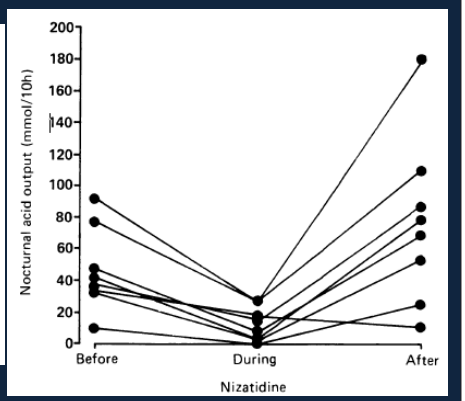
First report about H2RA

Rebound nocturnal hypersecretion after four weeks treatment with an H_2 receptor antagonist

G M FULLARTON, G McLAUCHLAN, A MACDONALD, G P CREAN, AND K E L McCOLL

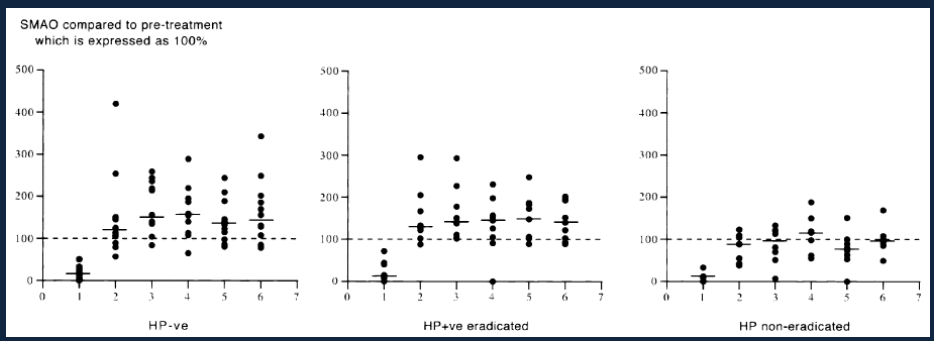
From the University Departments of Medicine and Surgery, Western Infirmary, Glasgow and Gastrointestinal Centre, Southern General Hospital, Glasgow

SUMMARY **Daytime intragastric pH, fasting and meal stimulated serum gastrin and nocturnal acid output were studied in eight male duodenal ulcer patients before, during and two days after completing nizatidine 300 mg nocte (20 00 h) for four weeks. Median nocturnal acid output (mmol/10 h) decreased during treatment to 11·6 (range 0·4–26·7) compared with pretreatment value of 39·4 (9·8–91·2); median acid inhibition 77% ($p<0·01$) which was strongest between 24 00 and 04 00 h. Two days after discontinuing treatment, nocturnal acid output increased to 74·1 (11–181). Compared with the pretreatment value this represents median rebound hypersecretion of 77% ($p<0·05$), caused by increased H^+ concentration and volume of secretion. Overall median daytime intragastric pH (09 00–21 00 h) was unchanged on the final day of treatment and two days after completing therapy, compared with the pretreatment values. Fasting serum gastrin measured between 09 30 and 10 00 h and the integrated gastrin response to an OXO breakfast taken at 10 00 h were also similar during and after treatment, compared with pretreatment values. The rebound nocturnal hypersecretion may be relevant to the high ulcer relapse rates after stopping H_2 receptor antagonists.**



Fullarton, *et al*. Gut 1989

RAHS after PPI and *H.pylori* status

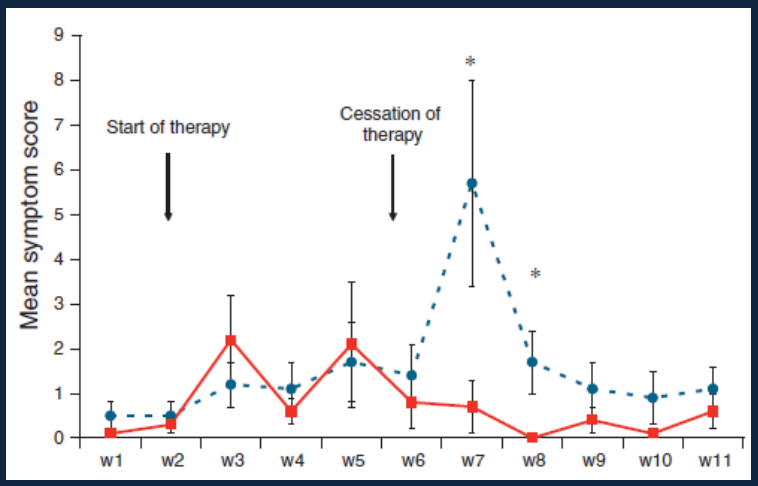


Prolonged nature of the rebound phenomenon in the *H. pylori*–negative subjects. Accentuated *H. pylori* related oxyntic gastritis induced by omeprazole.

Gillen, *et al*. Gastroenterology 2004

Clinical implication of RAHS after PPI Tx

Clinical evidences of RAHS after PPI



Niklasson, *et al.* Am J Gastroenterol 2010