Proton pump inhibitors: indications and acid rebound

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Avhandlingen baseras på följande arbeten:

I. **Overuse of acid suppressive therapy in hospitalised patients with pulmonary diseases.**
Niklasson A, Bajor A, Bergendal L, Simrén M. Strid H, Björnsson E
Respiratory Medicine 2003; 97: 1143-50.

II. **Prevalence of gastrointestinal symptoms in patients with chronic obstructive pulmonary disease.**
Niklasson A, Strid H, Simrén M, Engström CP, Björnsson E
European Journal of Gastroenterology and Hepatology 2008; 20:335-41.

III. **Quality assessment of patients with Gastroesophageal reflux disease treated with proton pump inhibitors: impact of high dose therapy.**
Niklasson A, Sager-Lund C, Tillander L, Kilander A, Björnsson E
In manuscript

IV. **Dyspeptic symptoms development after discontinuation of a proton pump inhibitor: A double-blind placebo-controlled trial.**
Niklasson A, Lindström L, Simrén M, Lindberg G, Björnsson E.
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Proton pump inhibitors: indications and acid rebound

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Abstract

Proton pump inhibitors (PPIs) are nowadays the therapy of choice in the management of a variety of upper gastrointestinal (GI) conditions particularly gastroesophageal reflux disease (GERD). Previous studies indicate that patients commonly receive PPIs without clear indications. The proportion of GERD patients refractory to PPI treatment is unclear. The clinical importance of acid rebound is controversial.

The aims of the present study were to evaluate the use and indications for PPIs in hospitalised patients and to assess the prevalence of GI symptoms in patients with chronic obstructive pulmonary disease (COPD). Furthermore, to assess the proportion of GERD patients with persistent symptoms despite high dose PPI therapy and to evaluate if cessation of PPI therapy in healthy subjects is associated with the development of GI symptoms.

The use of PPIs was evaluated by reviewing medical records, and by interviewing patients. Gastrointestinal symptoms and psychological well-being in COPD patients were assessed by using three questionnaires: the Gastrointestinal Rating Scale, the Psychological General Well-Being and the Hospital Anxiety and Depression scale. GI symptoms and quality of life in GERD patients were measured using four questionnaires: the Reflux Disease Questionnaire, the GERD Impact Scale and the SF-36. To assess upper GI symptoms in healthy volunteers after cessation of therapy the Glasgow Dyspepsia Questionnaire was used. Gastrin and chromogranin-A (CgA) were used as indirect measures of gastric acid inhibition.

A large proportion of hospitalised patients used PPIs. Among hospitalised pulmonary patients 49% used PPIs and the majority of the indications for the use were inappropriate, with peptic ulcer prophylaxis during corticosteroid therapy being the dominating inappropriate indication. The dominating appropriate indication was treatment for GERD. Gastroscopy had only been performed in 32% of patients.

Gastrointestinal symptoms were common in patients with COPD but similar to another chronic patient group (chronic renal failure). The GI symptoms were associated with impaired psychological general well-being. COPD patients treated with PPIs had higher GI symptom severity and lower general well-being than patients not using PPIs.

GERD patients with at least moderate reflux symptoms despite PPI treatment were common. However, persistent symptoms are rare after increased dosage of PPI therapy.

Discontinuation of a four week course of PPIs in previously healthy subjects was associated with significantly higher frequencies of upper GI symptoms during the first and second week after cessation of therapy compared with subjects receiving placebo, 44% vs 9% respectively ($p<0.001$). Significant higher levels of fasting as well as meal stimulated gastrin and CgA levels were found on the last day of treatment compared with levels prior to treatment. The GI symptoms during the first week after treatment correlated with basal and stimulated gastrin levels at the end of treatment.

Conclusion: PPIs were commonly used by hospitalised patients, and were especially common among pulmonary patients. A high proportion of patients lacked an adequate indication for PPI use. Few patients with GERD are refractory to treatment with PPI after increased PPI dosage. Cessation of PPI therapy in healthy asymptomatic subjects seems to induce GI symptoms. These symptoms are related to the degree of acid inhibition and are probably due to acid rebound hypersecretion.

Key words: Proton pump inhibitors; indications; gastrointestinal symptoms; overuse; chronic obstructive pulmonary disease; acid rebound hypersecretion; gastroesophageal reflux disease.

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