

# Prescribing of antisecretory medication in general practice

**Defended:** 02-02-2016

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## English summary:

### Background

Antisecretory drugs are designed to reduce the production of gastric acid. They are quite effective and well tolerated and they have improved treatment of acid related disorders such as peptic ulcer and gastrooesophageal reflux disease substantially. However, during the past decades the prescribing of antisecretory medication has increased dramatically without an apparent corresponding increase in frequency of indications for antisecretory treatment. As a respond clinical guidelines have been introduced and regulatory actions of eligibility for reimbursement of antisecretory drugs have been taken. The effects on prescribing patterns have, however, not been evaluated.

A possible explanation for the increasing prescribing of antisecretory medication could be that it is used as a diagnostic tool in management of dyspepsia in general practice. Dyspepsia is a complex of symptoms thought to origin from the upper gastrointestinal tract. A recent study has shown that 15% of the adult Danish population has experienced dyspeptic symptoms within a four week period (ref. overlap), and that dyspepsia is a common reason for consultation with a general practitioner (GP) (ref lægesøgningsartiklen). A clinical diagnosis of the cause of dyspepsia has been proven unreliable, but only in approximately 40% of the patients presenting with incident dyspepsia in general practice is it possible to establish a structural diagnosis at endoscopy, meaning that functional dyspepsia is the most common cause of the symptoms. A management strategy for dyspepsia in primary care comprising empirical treatment with antisecretory medication targeting secretion of gastric acid has been suggested. If the symptoms are relieved after antisecretory treatment the symptoms are thought to be acid related.

However, this strategy may lead to overtreatment with antisecretory medication. Firstly, symptoms in patients with functional dyspepsia are fluctuating, meaning that symptom relief in a patient with functional dyspepsia during treatment with antisecretory medication might not be caused by the inhibition of gastric acid secretion. The observed improvement might be a natural part of the course of the disease or it might be due to a placebo response. Secondly, recent studies have demonstrated that withdrawal of antisecretory therapy after a few weeks of treatment can induce rebound acid hypersecretion and acid related symptoms in previous asymptomatic patients. Hence, initiating empirical antisecretory treatment for an uncertain indication for more than a few weeks may lead to unnecessary use. Patients with ambiguous symptoms that are not truly acid-related might develop truly acid-related symptoms when discontinuing treatment, necessitating continuous antisecretory therapy and impeding discontinuation.

Therefore, this thesis aims to analyse changes in prescribing of antisecretory medication in Denmark over the past decade, to analyse possible factors that might influence the prescribing and to assess the feasibility of discontinuation of long-term antisecretory treatment.

### Methods

Corresponding to the four aims four studies were performed, three nationwide register-based studies and a systematic literature review.

For the register-based studies data from several national registers were linked and analysed. The data comprised information on patients redeeming prescriptions for antisecretory medication, their comedication, diagnoses and socioeconomic and demographic variables. For the doctors prescribing antisecretory medication the retrieved data comprised information on specialty, practice characteristics and demographic variables.

For the systematic review the databases MedLine, EMBASE and Cochrane Library were searched for relevant studies on discontinuation of antiseecretory medication. The literature search and selection of studies were guided by the PRISMA and AMSTAR guidelines for conducting a systematic review.

## Results

The analyses of changes in prescribing of antiseecretory medication in Denmark demonstrates a 213% increase in total prescribing from 2001-2011. After the changes in reimbursement of antiseecretory medication were made, the prescribing of subtypes of antiseecretory drug changed correspondingly, but the continuous growing overall prescribing remained apparently unaltered.

The number of patients treated on long-term basis (defined as treatment for more than two out of six months) increased by 224% from 2001-2011, demonstrating that increasing long-term prescribing is an important cause of the increasing total prescribing. In 2011 68% of the patients redeeming a prescription for antiseecretory medication met the criteria for long-term use. The long-term users were to larger extent comedicated in 2011 compared to 2001. However, in 2011 fewer of the long-term users had a medical history of peptic ulcer or diagnosed gastrooesophageal reflux disease (GORD) compared to 2001.

During the decade from 2001-2011 some characteristics of the incident user of antiseecretory medication changed. The frequency of comedication with non-steroidal anti-inflammatory drugs (NSAIDs) rose. Fewer patients had a medical history of peptic ulcer or diagnosed GORD prior to the first prescription of antiseecretory medication. Approximately 70% of the incidents prescriptions came from a GP.

Socioeconomic variables did not turn out to be important factors for duration of treatment with antiseecretory medication.

The literature review of discontinuation strategies for antiseecretory medication identified six clinical studies of the topic. In all six studies it was possible for the authors to identify a substantial number of long-term treated patients without a clear indication for treatment. The discontinuation regimens tested were quite heterogeneous, but all studies found discontinuation to be feasible in a clinical setting. A substantial number of patients treated without a clear indication can safely reduce or discontinue treatment. Tapering seems to be the most effective way of doing this.

## Conclusions

Prescribing of antiseecretory medication in Denmark has increased substantially. Increasing prescribing of long-term treatment is an important cause. Most of the patients do not have a medical history of peptic ulcer or diagnosed GORD. Almost half of the long-term treated patients are comedicated with NSAIDs. This could indicate an increasing awareness of peptic ulcer prophylaxis among GPs.

The results of this thesis indicate that it is not possible to identify a clear indication for antiseecretory medication in a substantial number of patients.

## Related publications (links):

Rapidly increasing prescribing of proton pump inhibitors despite interventions: a nationwide observational study <http://www.tandfonline.com/doi/full/10.3109/13814788.2014.905535#.Vw9iaE1-PIU>

Strategies for discontinuation of proton pump inhibitors: a systematic review  
<http://fampra.oxfordjournals.org/content/31/6/625.long>

Medical and non-medical predictors of initiating long-term use of proton pump inhibitors: a nationwide cohort study of first-time users during a 10-year period  
<http://onlinelibrary.wiley.com/doi/10.1111/apt.13649/abstract;jsessionid=FB02EAF5F31AB1CC93FECDFAF48831F.f01t01>

General practice variation when initiating long-term prescribing of proton pump inhibitors: a nationwide cohort study <http://bmcfampract.biomedcentral.com/articles/10.1186/s12875-016-0460-9>

Updated: 18-08-2016