

Prescription behaviour for gastroprotective drugs in new users as a result of communications regarding clopidogrel- proton pump inhibitor interaction

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Background

- In 2008-2011 clopidogrel was mainly used for patients with acute coronary syndromes or undergoing percutaneous coronary intervention.
- Clopidogrel is associated with increased risk of gastro intestinal bleeding.
- Safety concerns of concomitant use of clopidogrel and proton pump inhibitors (PPIs) were published in 2009 and 2010 by medicines regulatory agencies, including direct healthcare provider communication.
- The impact of safety communications by regulatory authorities is not always self-evident and healthcare professionals do not always act upon it.

Results

- Demographics and use of gastroprotective drugs are presented in Table 1.
- After January 2009 15.5% (95% CI 7.8, 23.4) more patients started concomitantly with (es)omeprazole and 13.8% (95% CI 6.5, 21.2) less with other PPIs (Figure 1).
- Directly after the first statement in June 2009, we found a steep increase in histamine 2-receptor antagonists (H2RA) peaking at 25%, placing those patients at risk for gastrointestinal events (Figure 1).
- This effect for H2RA faded away after a few months (Figure 1).
- In February 2010 when the official advice via an adjusted statement was to avoid (es)omeprazole, we found a decrease of 11.9% (95% CI 5.7, 18.2) for (es)omeprazole and an increase for other PPIs of 16.0% (95% CI 10.3, 21.7). Still 22.6% (95% CI 19.5, 25.7) of patients started on (es)omeprazole in February 2010, placing them at risk for cardiovascular events (Figure 1).

Objective

We examined the association between various safety statements on the combined use of clopidogrel and PPIs and prescription behaviour for gastroprotective drugs in naïve patients in the Netherlands in the years 2008-2011.

Methods

- Data from the PHARMO Database Network were analysed and dispensings from the Out-patient Pharmacy Database were used as a proxy variable for prescription behaviour.
- The studyperiod was divided into four separate periods: Jan 2008 – Jan 2009, Feb 2009-May 2009, June 2009- Feb 2010 and March 2010 -Dec 2011.
- Dispensings were clustered into episodes of continuous use of the same chemical entity.
- Demographic characteristics and use were determined in each calendar year.
- Interrupted time series analyses were used to estimate the impact of each communication on the dispensing of gastroprotective drugs.

Table 1. Demographic characteristics and use of gastroprotective drugs

	2008 N = 9,717	2009 N = 10,261	2010 N = 10,010	2011 N = 9,508	Total N = 39,496
Number of patients starting clopidogrel					
age - year (SD)	66.1 (12.4)	66.3 (12.6)	66.9 (12.6)	67.3 (12.5)	66.6 (12.6)
male - %	63.7%	64.5%	64.0%	63.4%	63.9%
patients without gastroprotective drugs at the start of clopidogrel	55.4%	53.2%	49.7%	42.1%	50.2%
patients on gastroprotective drugs the moment they start clopidogrel	44.6%	46.8%	50.3%	57.9%	49.8%
of whom using histamine 2-receptor antagonists	1.4%	3.8%	2.2%	1.5%	2.3%
of whom using (es)omeprazole	20.7%	21.0%	14.5%	15.1%	17.8%
age ≥ 60 years	69.6%	70.0%	71.2%	72.7%	70.9%
of whom without gastroprotective drugs	52.8%	49.9%	46.0%	37.9%	46.6%
age ≥ 70 years	41.9%	42.5%	44.2%	45.8%	43.6%
of whom without gastroprotective drugs	48.8%	46.8%	42.1%	33.4%	42.7%
age ≥ 80 years	15.1%	16.4%	17.8%	18.3%	16.9%
of whom without gastroprotective drugs	45.1%	43.6%	37.8%	29.0%	38.6%

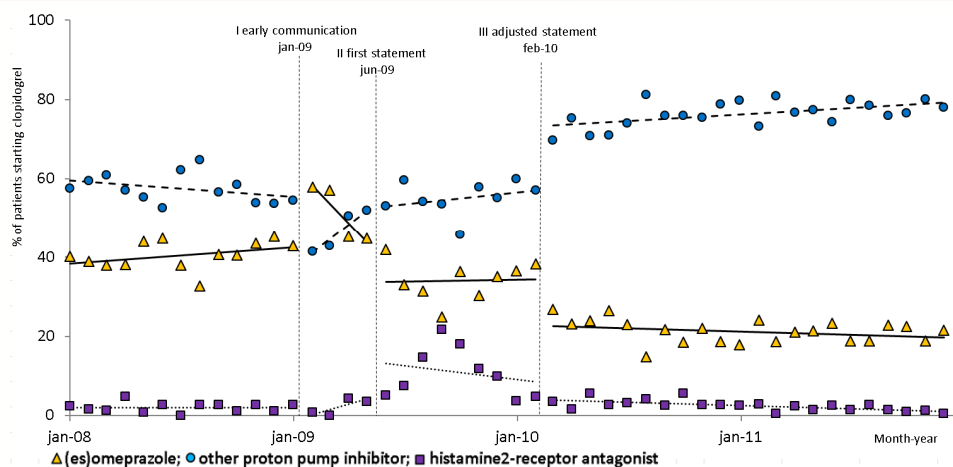


Figure 1. Choice of gastric protection pump in patients starting concomitantly with clopidogrel

Conclusion

This study describes an association between the various safety communications on the prescribing behaviour of gastroprotective drugs. Advices of regulatory authorities were followed, however reluctantly and not fully, probably partly because of the existing scientific doubt about the interaction. As a result, a considerable part of the patients was placed at risk for gastrointestinal or cardiovascular events.