Clinical Study Report Synopsis

Drug Substance	Esomeprazole
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ASSOCIATION BETWEEN LOW DOSE ACETYLSALICYLIC ACID (ASA) AND PROTON PUMP INHIBITORS AND RISK OF ACUTE MYOCARDIAL INFARCTION OR CORONARY HEART DISEASE DEATH

Nested case control analyses in a cohort of first-time users of low dose ASA for secondary prevention of cerebrovascular and cardiovascular outcomes

Study dates:	Study start date: June 2011 Study completion date: December 2011
Phase of development:	Therapeutic use
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This study was performed in compliance with Good Pharmacoepidemiology Practice, including the archiving of essential documents.

Study centre(s)

UK

Publications

Abstract presented at the European Society of Cardiology Congress August 2012 (Garcia Rodriguez et al 2012).

Objectives

To estimate the risk of MI/CHD death associated with use of monotherapy low dose ASA (single antiplatelet) as well as concomitant use of monotherapy low dose ASA and proton pump inhibitors (PPIs).

Study design

Retrospective cohort study with nested case–control analyses

Study population

Using data from The Health Improvement Network, all individuals aged 50–84 years with a first ever prescription of low-dose ASA (defined as 75–300 mg/day) for the secondary prevention of cardiovascular or cerebrovascular events (defined as any previous ischemic cerebrovascular event or ischemic heart disease) from 1 January 2000 to 31 December 2007 were identified (n= 39 513).

All individuals in the study cohort were followed up from the day after their first prescription of low-dose ASA (start date) until the first of the following endpoints: first recorded diagnosis of MI (myocardial infarction), cancer, alcohol abuse, reaching the age of 85 years, death, or the end of the study period (31 December 2007). Mean follow-up time was 3.2 years. New cases of non-fatal MI or coronary heart disease (CHD) death (n = 1222) were identified and compared with age- and calendar-date-matched controls (n = 5 000) sampled from the original study cohort of 39 513 patients. All cases of MI or CHD deaths were manually reviewed with free text comments to define final case status.

Exposure definition

All prescriptions issued by the primary care physician are recorded in the database and a coded drug dictionary (Multilex) is used to record prescribed medicines. Use of low-dose ASA and of PPIs was established for every day of each patient's individual follow-up period. For both low-dose ASA and PPIs, current use was defined as use of the respective drug on the index date (CHD event date for cases and a random date for controls). Non-use was defined as no prescription for the drug within the year prior to the index date.

Patients were considered continuous low-dose ASA or PPI users if they were exposed to the relevant drug, from initiating the treatment until the index date (with a maximum gap in treatment of 30 days).

Statistical methods

Multivariate adjusted unconditional logistic regression analyses were performed to estimate the relative risk (RR) of non-fatal MI/CHD death associated with current continuous use of both low-dose ASA mono-therapy and a PPI, compared with current continuous low-dose ASA therapy without PPI therapy.

Summary of results

Mean age at index date (date of MI or CHD death) among cases was 71.6 (95% CI: 71.2-72.2) years and 71.2 (95% CI: 70.9-71.4) among controls, respectively. Overall (cases and controls), the majority of patients were men (64.4% men, 35.6% women). The most frequent low dose ASA indication was for IHD while controls were more likely to have received low dose ASA for cerebrovascular disease (31.3 % among controls vs. 21.8% among cases) and cases for MI (31.8% among cases vs. 20.6 % among controls).

Cases were more likely to be smokers than controls (21.2% vs. 14.5%) while the distribution among BMI and alcohol consumption was similar across both groups. With regards to co-morbidities, cases more often presented a history of heart failure (11.8% vs. 5.4% among controls) and diabetes (17.8% vs.12.9% respectively) while the distribution of hypertension and hypercholesterolemia was similar among both groups. Cases utilized more health care services than controls such as being hospitalized in the year before the index date (31.8% among cases vs. 17.3% among controls).

Overall, a total of 2796 patients (44.9%) were current continuous users of low dose ASA on the index date, a total of 2,292 controls (45.8%) and 504 cases (41.2%) during the study period. Compared with non-use of low-dose ASA, there was a suggestion of a decreased risk of coronary events associated with current continuous use of low-dose ASA monotherapy (RR: 0.78; 95% CI: 0.60–1.02). The majority of current low-dose ASA users received a daily dose of ASA of 75 mg: 3416 (90.3%) among controls and 780 (88.9%) among cases,

In current continuous users of low-dose ASA mono-therapy, current continuous use of a PPI was not associated with a statistically significant increase in the risk of coronary events compared with non-use of a PPI (RR: 1.15; 95% CI: 0.80–1.66). No statistically significant increase in risk were seen either regardless of whether PPI use was started at or before the time of low-dose ASA initiation (RR: 1.03; 95% CI: 0.68–1.55) or at any time after low-dose ASA initiation (RR: 1.44; 95% CI: 0.79–2.65).

In this population-based cohort study with nested case-control analyses among first-time users of low-dose acetylsalicylic acid (ASA) the relative risk of non-fatal MI or death due to coronary heart disease associated with current continuous low-dose ASA use (irrespective of proton pump inhibitor [PPI] use) compared with non-use of ASA was 0.78 (95% confidence interval [CI]: 0.60–1.02). Current continuous use of both low-dose ASA mono-therapy and a PPI was not statistically associated with an increase in the risk of coronary events compared with current continuous low-dose ASA use without concomitant PPI therapy (RR: 1.15; 95% CI: 0.80–1.66).

Reference

García Rodríguez LA, Cea Soriano L, Johansson S. Use of proton pump inhibitors and the risk of coronary events in patients receiving low-dose acetylsalicylic acid in UK primary care. European Society of Cardiology Conference, Munich, Germany 2012; P1834.