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Clopidogrel and Proton Pump Inhibitors: A Complete Audit Cycle of Prescribing in General Practice

Introduction: Clopidogrel is an oral antiplatelet drug commonly prescribed to at risk individuals to prevent myocardial infarction and ischaemic stroke. However, clopidogrel is a pro-drug which requires hepatic CYP2C19 for its activation. Proton pump inhibitors (PPI) inhibit this enzyme, an interaction which *in vitro* studies have demonstrated to attenuate clopidogrel's anti-platelet effect. However, *in vivo*, there are few randomised trials, and none comparing the effects of different PPIs in combination with clopidogrel. Consequently, the clinical significance of this interaction remains unclear. Despite this, current guidance recommends that patients taking clopidogrel should specifically avoid omeprazole and esomeprazole, which are more potent CYP2C19 inhibitors. (1) We aimed to evaluate adherence to this guidance in a general practice population.

Methods: Prescribing practice was analysed in East Quay Medical Centre, Bridgwater, using the practice software EMIS. A search was conducted over a six month period up to 25th September 2014 for patients taking clopidogrel in combination with a PPI. Data was then collected about the specific PPI prescribed. Results were presented at a practice meeting where recommendations were made. A re-audit using the same search criteria was conducted on 9th July 2015.

Results: In the first six month window, 120 patients were identified on a clopidogrel-PPI prescription. Of these, 86 (72%) were prescribed omeprazole, 3 (2%) esomeprazole, 29 (24%) lansoprazole, and 2 (2%) pantoprazole. Almost three quarters of patients were inappropriately co-prescribed omeprazole. We made recommendations as per local guidelines to 1) confirm a definite indication for a PPI; switching to ranitidine or stopping the prescription if possible, and to 2) prescribe lansoprazole if a PPI is absolutely necessary. Our re-audit identified 113 patients (86 from the previous cohort and 27 new patients). This time, 70 (62%) were prescribed omeprazole, 37 (33%) lansoprazole (7 of which had been switched from omeprazole since our initial audit), 5 (4%) esomeprazole, and 1 (1%) pantoprazole.

Discussion: Following our initial audit, 35patients taking clopidogrel had their PPI stopped and 7 patients originally on omeprazole were switched to lansoprazole. However, our re-audit identified 27 new patients on a clopidogrel-PPI prescription, 17 of which with co-prescribed omeprazole. The current issue appears to be the initiation of clopidogrel-omeprazole prescriptions in secondary care, which are not flagged up as an issue on repeat prescriptions issued in general practice. Further studies need to address whether the clopidogrel-PPI interaction is clinically significant, and if so, whether it should be considered a class effect or specific to omeprazole and esomeprazole. The drug tariff reveals little difference in cost between generic omeprazole, lansoprazole, and pantoprazole, (2) and as such, switching patients on omeprazole to lansoprazole or pantoprazole is a simple and practical clinical approach which may potentially reduce cardiovascular risk.

1. UK Medicines Information. *Do proton pump inhibitors reduce the clinical efficacy of clopidogrel?* http://bit.ly/1NjNAMe

2. NHS Business Services Authority. *Drugs for Dyspepsia – Prescribing Guidance and Discussion Points*. http://www.nhsbsa.nhs.uk/Documents/PPDPCTReports/pctreport_20101.pdf