EDITORIAL

Position paper of the Working Group of three Polish National Consultants in internal medicine, gastroenterology, and cardiology on prevention of gastrointestinal complications during antiplatelet treatment

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At the end of 2008, the experts of American College of Cardiology Foundation (ACCF), American Heart Association (AHA), and American College of Gastroenterology (ACG) published a joint position statement which encompassed the recommendations for reduction in gastrointestinal complications, particularly gastrointestinal hemorrhage, in patients on antiplatelet therapy.[1] Since no such document has been prepared by the European institutions, knowledge of the above recommendations appears highly important. Therefore, the members of the *ad hoc* Polish Working Group advise that the recommendations should be disseminated and implemented in Poland.

Numerous observations have confirmed the presence of patient groups at high risk of gastrointestinal complications during antiplatelet treatment. The major risk factor is a history of peptic ulcer disease, particularly with bleeding complications. The risk of gastrointestinal complications also increases with age, especially in subjects aged >60 years. It is also higher in patients with a prior history of bleeding from other sites than the gastrointestinal tract, in women, in patients with concomitant renal insufficiency, in patients on glucocorticosteroids and non-steroidal anti-inflammatory drugs, and in patients with dyspepsia or symptoms of gastroesophageal reflux disease. Complications occur far more frequently during combined therapy with an antiplatelet agent and an anticoagulant. It refers mostly to patients on intensive antiplatelet and anticoagulant therapy, including those with an acute coronary syndrome. Therefore, it is necessary that specialists in internal diseases, gastroenterology, and cardiology adopt a joint strategy to prevent gastrointestinal bleeding complications.

In most patients who are treated with acetylsalicylic acid (ASA) for the prevention of cardiovascular events, low doses of this drug should be administered. It has been demonstrated that 75–160 mg daily doses of ASA were as effective as higher doses. No further decrease in the risk of cardiovascular events was observed at higher doses of ASA, although there was a significant increase in complication rate. Therefore, the routine ASA administration of 75 mg/day for cardiovascular indications should be recommended. Proton pump inhibitors (PPIs) are the only recommended class of drugs with proven efficacy in the prevention of gastrointestinal complications. Easy dosage (once a day) and an extremely low rate of adverse effects contributed to widespread use of PPIs. The efficacy of PPIs has been shown in multiple studies designed to evaluate gastroscopic lesions and the incidence of gastrointestinal bleedings.

In a joint document, ACCF/AHA and ACG published an outline algorithm to prevent gastrointestinal complications in patients receiving antiplatelet therapy (FIGURE). The experts make prophylactic treatment dependent on the presence of risk factors. They recommend PPI administration as a preventive measure in patients with

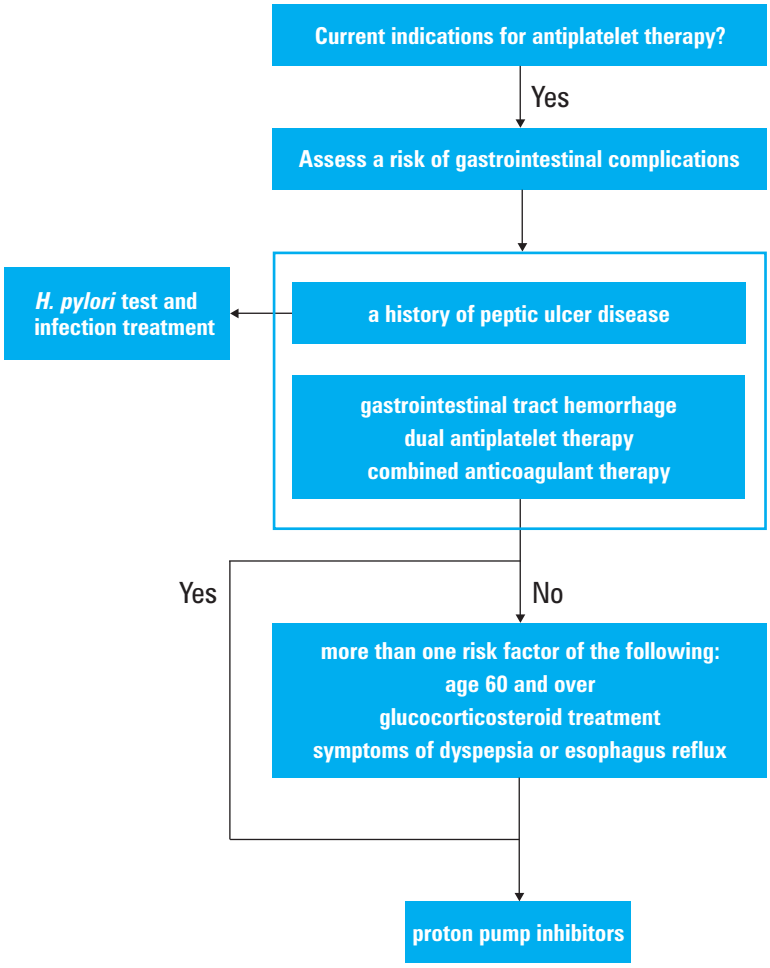

FIGURE Prevention of gastrointestinal complications – outline scheme. Recommended by the Polish Working Group based on the ACCF/AHA/ACG recommendations.

a prior history of peptic ulcer; in patients with gastrointestinal bleeding; in patients on double antiplatelet treatment; and in those receiving oral anticoagulant therapy. Moreover, patients with a prior history of peptic ulcer should be tested for *Helicobacter pylori* (provided that they have not undergone the test previously), and if the test is positive an eradication treatment should be administered. Efficacy of eradication treatment is not an indication for PPI discontinuation. PPI administration as a preventive measure is recommended in patients with at least two of the following risk factors: age ≥60 years, glucocorticosteroid therapy, signs or symptoms of dyspepsia or gastroesophageal reflux disease.

The choice of a specific PPI for the above indications is a significant therapeutic challenge. Recently, a series of reports have been published showing that omeprazole and other PPIs decrease antiplatelet effect of clopidogrel. No such effects have been reported with regard to esomeprazole and pantoprazole. This is most often linked with competitive metabolism of some PPIs and clopidogrel mediated by cytochrome P450 2C19 (CYP2C19) isoenzyme and possibly by other isoforms of this cytochrome.[2-7]

In light of the above reports and results of the latest clinical trials, the Polish Working Group presents the recommendations as listed below.

1 In patients who are treated with ASA, PPIs should be administered in the case of:

A a history of peptic ulcer disease

B a history of prior gastrointestinal hemorrhage

C dual antiplatelet therapy (acetylsalicylic acid and clopidogrel)

D combined anticoagulant and antiplatelet treatment (combined treatment with an antiplatelet agent and an anticoagulant or triple therapy with two antiplatelet agents and an anticoagulant)

E coexistence of at least two of the following risk factors: age ≥60 years, glucocorticosteroid therapy, signs or symptoms of dyspepsia or gastroesophageal reflux disease.

2 Other risk factors which have not been included in the American consensus report, such as chronic renal insufficiency, female sex, long-term administration of non-steroidal anti-inflammatory drugs, should also be considered while making individual decisions on preventive PPI administration.

3 Preventive PPI administration should be continued as long as the risk factor specified in the FIGURE is present (e.g. PPI administration in patients with acute coronary syndrome is continued for the duration of the combined treatment with ASA and clopidogrel).

4 Esomeprazole and pantoprazole are preferred PPIs in patients treated with clopidogrel while other PPIs, particularly omeprazole, are not recommended due to a risk of significant interactions with clopidogrel.

Notice This position paper has been submitted to a number of Polish journals of internal diseases, gastroenterology and cardiology with a request for publication. It is also available on the websites of National Consultants in the appropriate disciplines.

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