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Potent P2Y12 Inhibitors and Bleeding Complications

Güçlü P2Y12 İnhibitörleri ve Kanama Komplikasyonları

LETTER TO THE EDITOR
EDİTÖRE MEKTUP

Dear Editor,

We read with interest the article by Akinci et al[1] that evaluates "In-Hospital Bleeding and Mortality in Acute Coronary Syndrome Patients Treated with Tirofiban and Potent P2Y12 Inhibitors". We appreciate the authors for their study describing the prognostic effects of in-hospital bleeding and mortality in patients with acute coronary syndrome (ACS) treated with tirofiban and potent P2Y12 inhibitors. However, we deem it essential to state additional notable points.

First, ticagrelor and prasugrel are potent and novel oral P2Y12 inhibitors.[2-4] Compared with clopidogrel, more rapid and consistent inhibitory effects on platelet aggregation are seen with these agents.[2,5] However, such benefit comes at the expense of increased bleeding rates with ticagrelor or prasugrel. Ticagrelor showed similar effects on platelet inhibition as prasugrel.The most common bleeding site in major randomized clinical trials (RCTs) of potent P2Y12 inhibitors was gastrointestinal tract, despite low rates of intracranial bleeding, the incidence was still higher for ticagrelor or prasugrel versus clopidogrel.[6] Therefore, for patients assessed as having a high risk for bleeding, potent antiplatelet agents must be used carefully to reduce bleeding risk.[6] Based on this hypothesis, the purpose of the clopidogrel with or without omeprazole in coronary artery disease (COGENT)-1 clinical trial was to determine the clinical efficacy of omeprazole in addressing the risk of gastrointestinal bleeding with clopidogrel.[7] In this RCT, 51 of 3761 patients developed bleeding complications. In the 6-month follow-up of the patients, bleeding events occurred in 1.1% of the omeprazole arm and 2.9% of the placebo arm, but due to insufficient financial support, the study was terminated earlier than the planned follow-up period. Although this is a major limitation of this study, no similar studies are currently available for potent P2Y12 inhibitors.[7] Therefore, according to this RCT, the proton pump inhibitor gastroprotection in patients at high risk of gastrointestinal bleeding on DAPT is recommended. Moreover, the concomitant use of potent P2Y12 inhibitors in patients taking oral anticoagulants has not been adequately studied, and therefore, these potent antiplatelet agents should be used cautiously given in patients using antithrombotic agents. The use of nonsteroidal anti-inflammatory agents (NSAIDs) after ACS must be avoided, and if it is mandatory, the shortest duration possible is recommended as it increases the risk of death. In a large Danish study comprising 61 971 post-ACS patients over 30 years of age, 34% of all total patients received 1 prescription of NSAID at least, and researchers pointed toward NSAIDs that significantly increase the risk of bleeding and cardiovascular events.[8] The readers may wonder whether medical treatment data such as anticoagulation, proton pump inhibitors, and NSAIDs that may increase or decrease bleeding complications in this study would affect the outcome of the study.

Second, pretreatment refers to the administration of a P2Y12 inhibitor prior to the invasive coronary angiography. Based on the data highlighting the increased bleeding risk without clear evidence preventing ischemic complications, routine pretreatment administration of a P2Y12 inhibitor before the assessment of coronary anatomy in patients undergoing early percutaneous coronary intervention is listed as a class III recommendation in the recent European Society of Cardiology (ESC) guidelines,[5] while the previous ESC revascularization guideline strongly recommended it.[9] In the method section of the article, the authors' statement regarding antiplatelet therapy is

Ahmet Güner
Ezgi Gültekin Güner
Serkan Kahraman
Fatih Uzun
Mehmet Ertürk

Department of Cardiology, Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Training and Research Hospital, Istanbul, Turkey

Corresponding author:
Ahmet Güner
✉ ahmetguner488@gmail.com

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given as follows: "Before or during the procedure, prasugrel was given 10 mg once daily after a 60 mg loading dose, ticagrelor 90 mg twice daily after a 180 mg loading dose, and clopidogrel 75 mg once daily after a 600 mg loading dose." From this statement of the authors, it appears that some patients were given P2Y12 inhibitors with preload and some during the procedure. Indeed, both the 2015 and 2020 ESC guidelines do not recommend pretreatment for prasugrel in patients with ACS (excluding ST-elevation myocardial infarction). It may be of interest to the readers if the authors provide more meticulous information on this subject. Because if there were patients who had pretreatment, it may affect the results of this research, and this may cause curiosity in the readers.

Declaration of Interests: The authors declare that they have no competing interest.

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