Inhibitori receptora P2Y₁₂ u liječenju koronarne bolesti srca – izazovi i perspektiva u optimizaciji antitrombotičnog liječenja

P2Y₁₂ receptor inhibitors in coronary artery disease – challenges and perspectives in optimizing antiplatelet therapy

Jure Samardžić*

Medicinski fakultet Sveučilišta u Zagrebu, Klinički bolnički centar Zagreb, Zagreb, Hrvatska

University of Zagreb School of Medicine, University Hospital Centre Zagreb, Zagreb, Croatia

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***ADDRESS FOR CORRESPONDENCE:** Klinički bolnički centar Zagreb, Kišpatićeva 12, HR-10000 Zagreb, Croatia. / Phone: +385-1-2367-467 / E-mail: jure.samardzic@gmail.com

Antitrombotični lijekovi imaju temeljnu ulogu u akutnoj i kroničnoj farmakoterapiji koronarne bolesti srca (KBS) jer smanjuju rizik od ishemijskih kardijalnih i cerebrovaskularnih događaja. Klopido­gre­l je najviše upotrebljavani inhibitor receptora P2Y₁₂, unatoč vrlo varijabilnom učinku na koji mogu utjecati različiti čimbenici. Razvojem i primjenom novih, snažnijih inhibitora receptora P2Y₁₂ s uniformnijim antitrombotičnim učinkom, kao što su prasugrel i ticagrelor, reducirana je stopa ishemijskih događaja u bolesnika s akutnim koronarnim sindromom (AKS), no uz cijenu povišenog rizika krvarenja. Proširenim izborom lijekova u blokadi receptora P2Y₁₂ liječnici nisu više suočeni samo s izazovom snižavanja ishemijskog rizika, već i s rizikom za nastanak jatrogenog krvarenja koji je nerijetko teško procijeniti jer se neki čimbenici rizika za ishemijske i krvareće incidente preklapaju.

U vremenu progresivnog individualiziranog pristupa liječenju i sve većeg značaja farmakoekonomike, potrebne su učinkovite, sigurne i dostupne strategije liječenja bolesnika s AKS-om kako bi se smanjio rizik za nove ishemijske događaje, a da se ne uveća rizik od krvarenja. Zadnjih nekoliko godina je ideja prilagođavanja antitrombotične terapije prema testovima reaktivnosti trombocita bila suočena s neuspjehom zbog negativnih rezultata velikih randomiziranih studija. Budući da su te studije uglavnom uključivale bolesnike sa stabilnom KBS, a znajući da je povišena ostatak reaktivnost trombocita snažnije povezana s neželjenim ishodima kod bolesnika s AKS-om, ispitivanje rutinske uporabe testova reaktivnosti trombocita u odlučivanju o antitrombotičnoj terapiji u akutnim aterotrombotskim događajima kao ideja još nije napuštena. Daljnja ispitivanja uporabe inhibitora receptora P2Y₁₂, testova reaktivnosti trombocita i personaliziranog pristupa u antitrombotičnom liječenju su nužna radi bolje procjene ishemijskog i krvarećeg rizika, optimizacije liječenja i poboljšanja ishoda bolesnika.

Antiplatelet drugs have a fundamental role in acute and chronic pharmacotherapy of coronary artery disease (CAD) as they reduce the risk of ischemic cardiac and cerebrovascular events. Clopidogrel is the most used P2Y₁₂ receptor inhibitor despite its very variable effect caused by different factors. Development of new, more potent P2Y₁₂ receptor inhibitors which produce more uniform antiplatelet effect, such as prasugrel and ticagrelor, has additionally reduced the rate of ischemic events in patients with acute coronary syndrome (ACS), but at the cost of increased bleeding risk. With expanded selection of P2Y₁₂ inhibitors physicians are no longer faced only with the challenge of lowering ischemic risk, but also with reducing the bleeding risk that is often difficult to assess as some risk factors for ischemic and bleeding events overlap.

In an era of progressive individualized approach to treatment and the growing importance of pharmacoeconomics, there is a need for effective, safe and available treatment strategies to reduce the risk of new ischemic events, without increasing the risk of bleeding in patients with ACS. In recent years the idea of antiplatelet therapy tailoring based on platelet function testing has faced setbacks as large randomized trials brought negative results. As these studies mostly enrolled patients with stable CAD, investigating whether routine use of platelet function tests to select antiplatelet therapy regimen might bring benefit in acute atherothrombotic events has not yet been abandoned since it is known that ADP induced high on-treatment platelet reactivity is strongly associated with adverse outcomes in ACS patients. Further studies on P2Y₁₂ receptor inhibitors, platelet function testing and personalized approach to antiplatelet treatment are warranted to enable better ischemic and bleeding risk assessment, optimize treatment and improve patient outcomes.

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