Spontano krvarenje tijekom terapije tikagrelorom – prikaz slučaja

Spontaneous bleeding during ticagrelor therapy – case report

Blanka Glavaš Konja^{*1},
Ivan Bitunjac²,
Zvonimir Ostojić¹,
Vlatka Rešković
Lukšić¹,
Joško Bulum¹,
Martina Lovrić Benčić¹,
Jadranka Šeparović
Hanževački¹,
Davor Miličić¹

¹Medicinski fakultet
Sveučilišta u Zagrebu,
Klinički bolnički centar
Zagreb, Zagreb, Hrvatska

²Opća bolnica "Dr. Josip
Benčević", Slavonski Brod,
Hrvatska

¹University of Zagreb School
of Medicine, University
Hospital Centre Zagreb,
Zagreb, Croatia

²General Hospital "Dr. Josip
Benčević", Slavonski Brod,
Croatia

KLJUČNE RIJEČI: tikagrelor, retroperitonealni hematoma, veliko krvarenje.

KEYWORDS: ticagrelor, retroperitoneal haematoma, major bleeding.

CITATION: Cardiol Croat. 2016;11(10-11):445. | DOI: <http://dx.doi.org/10.15836/ccar2016.445>

***ADDRESS FOR CORRESPONDENCE:** Blanka Glavaš Konja, Klinički bolnički centar Zagreb, Kišpatičeva 12, HR-10000 Zagreb, Croatia. / Phone: +385-1-2367-490 / E-mail: blanka.glavas@gmail.com

ORCID: Blanka Glavaš Konja, <http://orcid.org/0000-0003-1134-4856> • Ivan Bitunjac, <http://orcid.org/0000-0002-4396-6628> • Ivo Planinc, <http://orcid.org/0000-0003-0561-6704> • Vlatka Rešković Lukšić, <http://orcid.org/0000-0002-4721-3236> • Joško Bulum, <http://orcid.org/0000-0002-1482-6503> • Martina Lovrić Benčić, <http://orcid.org/0000-0001-8446-6120> • Jadranka Šeparović Hanževački, <http://orcid.org/0000-0002-3437-6407>

Davor Miličić, <http://orcid.org/0000-0001-9101-1570>

Prikaz slučaja: Muškarac, star 65 godina je hospitaliziran zbog spontanog retroperitonealnog hematoma. Anamnestički se saznaje tiroidektomija 1996. godine zbog papilarnog karcinoma, arterijska hipertenzija zadnjih 10 godina i kronična opstruktivna bolest pluća. Bolesnik je prebolio akutnog infarkta miokarda s ST-elevacijom kada je učinjena perkutana koronarna intervencija na D1 desnim transradikalnim pristupom. Zbog edema pluća tijekom akutne faze, bila je potrebna mehanička ventilacija i primjena bronhodilatatora i kortikosteroida. Ehokardiografski nalaz je ukazivao na reduciranu sistoličku funkciju lijeve klijetke (EF 30%). Bolesnik je bio otpušten 6. dan uz tikagrelol 2 x 90 mg, nebivolol 1,25 mg, acetilsalicilatnu kiselinu (ASK) 100 mg, furosemid 125 mg, spironolakton 50 mg, valsartan 2 x 160 mg, amiodaron 200 mg, atorvastatin 80 mg, pantoprazol 40 mg, metilprednizolon 16 mg, levotiroksin 150 µg i tiotropium bromid 18 µg. Nakon 22 dana je ponovno hospitaliziran zbog mučnine i omaglica uz pad hemoglobina s 136 na 82 g/L i uz povišene vrijednosti kalija. PV i APTV su bili urednih vrijednosti. Po nogama i lumbalnoj regiji su bili vidljivi brojni hematomi, a bez traume u anamnezi. Višeslojna kompjutorizirana tomografija (MSCT) je registrirala retroperitonealni hematoma lijevo od područja lijevog bubrega sve do lijeve ingvinalne regije 7,5 x 1,5 cm, 22 cm duljine. Tikagrelol i ASK su izostavljeni iz terapije. Agregometrijom (Multiplate® analyzer) se nalazi ekstremno snižena agregacija uz ASK (manje od 100 AUmin) i uz tiklopidin (234 AUmin). Primijene se dvije doze koncentriranih eritrocita. Hemoglobin ostaje stabilan, a kontrolni MSCT ne pokazuje progresije hematoma 7. dan hospitalizacije.

Rasprava: Veliko krvarenje nakon infarkta miokarda ima lošu prognozu. U PLATO studiji je tikagrelor u usporedbi s klopido-grelom bio povezan sa sličnim udjelom velikog krvarenja, no s učestalijim ne-CABG i ne-proceduralnim velikim krvarenjem u prvih 30 dana liječenja. Fatalno krvarenje je bilo rijetko i nije se razlikovalo između grupa. Europsko kardiološko društvo preporuča tikagrelor uz ASK u liječenju umjereno i visokorizičnog akutnog koronarnog sindroma. Postoji sumnja da je krvarenje u kliničkoj praksi gdje je više visoko rizičnih bolesnika, posebice žena starije dobi, češće nego u PLATO studiji.¹

Zaključak: Neophodno je brižno izvagati potrebu za snažnim trombocitnim inhibitornim učinkom i rizik krvarenja.

Case report: 65-years-old man has been admitted to hospital because of spontaneous retroperitoneal hematoma. Medical history and concomitant disease: 1996 thyroidectomy for papillary carcinoma, arterial hypertension for more than 10 years and chronic obstructive pulmonary disease. Patient had acute ST segment elevation myocardial infarction (STEMI) when percutaneous coronary intervention on D1 using right transradial approach was done. Because of pulmonary edema during acute phase, he needed mechanical respiratory support and application of bronchodilatory and corticosteroid therapy. Echocardiography showed reduced systolic function (EF 30%). Patient was discharge from hospital at the 6th day with prescription of ticagrelor 90 mg bid, nebivolol 1,25 mg, aspirin 100 mg, furosemid 125 mg, spironolactone 50 mg, valsartan 160 mg bid, amiodarone 200 mg, atorvastatin 80 mg, pantoprazole 40 mg, methylprednisolone 16 mg, levothyroxine 150 µg and tiotropium bromide 18 µg. 22 days after STEMI he was admitted again because of dizziness and light-headedness with drop of hemoglobin levels from 136 to 82g/L and high potassium levels. Prothrombin time and APPT was normal. Multiple hematomas on the legs and lumbar region were noticed with no anamnesis of trauma. Multislice computed tomography (MSCT) showed retroperitoneal hematoma on the left side from left kidney to the left inguinal region 7.5 x 10.5 cm, 22 cm in length. Ticagrelor and aspirin were stopped. Platelet function analysis (by Multiplate® analyzer) showed extremely depressed aggregation with aspirin (less than 100 AUmin) and with ticlopidin (234 AUmin). Two dose of concentrated erythrocyte were applied. Hemoglobin levels stayed stable and control MSCT showed no progression of hematoma 7 days after second admission.

Discussion: Major bleeding after myocardial infarction portends a poor outcome. In the PLATO trial ticagrelor compared with clopidogrel was associated with similar total major bleeding but increased non-CABG and non-procedure-related major bleeding, primarily after 30 days on study drug treatment. Fatal bleeding was low and did not differ between groups. There remains potential concern about bleeding in a "real world" population compromising more high risk patients; particularly more elderly and female, than those in PLATO.¹

Conclusion: A balance is required between potency of platelet inhibition and risk of bleeding.

LITERATURE

1. The Risk of Major Bleeding With Novel Anti-platelets: A Comparison of Ticagrelor With Clopidogrel in a Real World Population of 5000 Patients Treated for Acute Coronary Syndrome (ROBOT-ACS). <https://clinicaltrials.gov/ct2/show/NCT02484924>

RECEIVED:
September 28, 2016

ACCEPTED:
October 10, 2016