Stručni rad / Professional article

Antiagregacijska terapija i stomatološki postupci u primarnoj zdravstvenoj zaštiti

Antiaggregation therapy and dental procedures in primary healthcare

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SAŽETAK: Široka uporaba intravaskularnih koronarnih stentova višestruko je povećala broj bolesnika na antiagregacijskoj terapiji acetilsalicilnom kiselinom i klopidogrelom. Uzimajući u obzir povišen rizik krvarenja kod ovih bolesnika raste i (ponekad pretjerana) zabrinutost prilikom planiranja manjih kirurških, pa tako i stomatoloških zahvata. Ista je rezultirala povremenim preuranjenim isključivanjem spomenute terapije što može, mada rijetko, imati i neželjene tromboembolijske komplikacije. Cilj ovog članka je iznijeti aktualne preporuke za postupak s bolesnicima na antiagregacijskoj terapiji kod kojih se planiraju stomatološki zahvati u sustavu primarne zdravstvene zaštite.

KLJUČNE RIJEČI: acetilsalicilna kiselina, klopidogrel, ekstrakcija zuba, hemostaza.

SUMMARY: Extensive use of intravascular coronary stents has multiply increased a number of patients receiving antiaggregation therapy with aspirin and clopidogrel. Taking into account an increased risk of bleeding, there is an increasing (sometimes excessive) concern of minor surgical and dental procedures in these patients. This has resulted in occasional premature exclusion of the above therapy, which can, albeit rarely, lead to adverse thromboembolic complications. The aim of this article is to present the current recommendations for the management of patients receiving antiaggregation therapy where dental procedures in primary healthcare system are planned.

KEYWORDS: aspirin, clopidogrel, tooth extraction, haemostasis.

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Svakodnevna i sve raširenija primjena perkutanih koronarnih intervencija (prema nekim navodima u SAD oko 1.000.000 intervencija godišnje), poglavito onih s implantacijama intrakoronarnih stentova rezultirala je velikim brojem bolesnika koji uz dobro definiranu terapiju statinima, ACE inhibitorima i beta blokatorima moraju uzimati i, najčešće dvojnu, antiagregacijsku terapiju acetilsalicilnom kiselinom (ASK) i klopidogrelom. Primjena navedene terapije povećala je broj posjeta bolesnika kardiološkim ambulantama s ciljem procjene rizika krvarenja i/ili odluke o prekidu anrtiagregacijske terapije prilikom planiranja manjih kirurških postupaka, uključujući i one u primarnoj stomatološkoj praksi. Klinički pokusi koji su ispitivali utjecaj dvojne antiagregacijske terapije na krvarenje kod ekstrakcije zuba relativno su malobrojni, najčešće su provođeni u jednom centru i na manjem broju bolesnika tako da se i aktualne smjernice u ovom području oslanjaju uglavnom na navedene studije i mišljenja stručnjaka.[1,2]

Najpotpunije preporuke o postupanju kod bolesnika na antiagregacijskoj terapiji kod kojih se planiraju stomatološki zahvati u primarnoj skrbi objavila je u kolovozu 2010. god. na svojim internetskim stranicama Britanska Nacionalna medicinska elektronička knjižnica (*National electronic Library for Medicines — NeLM*).[3] Prema navedenim preporukama,

Daily and increasingly widespread use of percutaneous coronary intervention (according to some sources there are around 1 million interventions per year in the U.S.A.), especially those with implantations of intracoronary stents resulted in a large number of patients who with well-defined therapy with statins, ACE inhibitors and beta blockers must most frequently receive antiaggregation therapy with aspirin and clopidogrel. The use of the above therapy has increased the number of patients' visits to cardiac outpatients department for the purpose of assessing the risk of bleeding and/or decision on discontinuation of antiaggregation therapy while planning on minor surgical procedures, including even those in primary dental practice. Clinical trials that have examined the impact of dual antiaggregation therapy on bleeding while performing tooth extraction are relatively few in number, they were usually conducted in one center and on a small number of patients, so that the current guidelines in this area mainly rely on these trials and expert opinions.[1,2]

The most comprehensive recommendations on the treatment of patients receiving antiaggregation therapy where dental procedures are planned in primary healthcare were published in August 2010 on its website *National electronic Library for Medicines — NeLM*.[3] According to these recom-

ocjena rizika krvarenja s jedne i tromboze u stentu s druge strane predstavlja odlučujući čimbenik prilikom odluke o nastavku ili prekidu antiagregacijske terapije. Poznato je da je ukupni rizik krvarenja povećan kod bolesnika na dvojnoj antiagregacijskoj terapiji. Uobičajeni test vremena krvarenja kojim se u grubo procjenjuje funkcija trombocita nije se pokazao učinkovitim u procjeni rizika.[4] Klinička evaluacija prije planiranih stomatoloških postupaka, odnosno pažljivo uzeta anamneza ključna je pri probiru bolesnika s povišenim rizikom krvarenja. S druge strane, bolesnici s ugrađenim intrakoronarnim stentovima imaju povišen rizik tromboembolijskih događanja, uključujući i trombozu stenta koja je najčešća prilikom preuranjenog prekida terapije klopidogrelom.[5,6]

Podaci o riziku krvarenja prilikom dentalnih procedura kod bolesnika na dvojnoj antiagregacijskoj terapiji ASK i klopidogrelom su oskudni, ali retrospektivne studije upućuju na zaključak da su približno slični riziku krvarenja bolesnika na monoterapiji.[7] Klinički značajno krvarenje nakon stomatološkog postupka definira se kao krvarenje na mjestu zahvata koje traje duže od 12 sati zbog kojeg se bolesnik ponovo javlja stomatologu ili hitnoj službi. Značajnim se krvarenjem smatra ono koje rezultira razvojem većeg hematoma ili ekhimoza unutar mekih tkiva ili ono koje zahtjeva transfuziju. Ipak, krvarenja prilikom stomatoloških postupaka imaju nekoliko ponekad i olakotnih okolnosti koje ih izdvajaju u usporedbi s onima kod drugih kirurških procedura. Gubitak krvi, čak i kod bolesnika na antiagregacijskoj terapiji je osjetno manji u usporedbi s onim kod gastrointestinalnih ili primjerice kardiotorakalnih operacija. Nadalje, krvarenje u ustima se lakše vizualizira i lokalni se hemostatski postupci jednostavnije primjenjuju nego u drugim operativnim zahvatima. Treba imati na umu i činjenicu da krvarenje ovisi o opsežnosti zahvata i da je prilikom ekstrakcija pojedinačnih zuba često i zanemarivo.

Kao što je navedeno, tromboembolijski incidenti, uključujući i one fatalne, koji se javljaju prilikom preuranjenog prekida antiagregacijske terapije dobro su dokumentirani u literaturi. S druge strane, u literaturi nije publiciran niti jedan slučaj nekontroliranog krvarenja u bolesnika na antiagregacijskoj terapiji koji su bili podvrgnuti različitim stomatološkim postupcima. Manje prospektivne kliničko istraživanje *Lillisa i sur.* iz 2011. god. (111 bolesnika na antiagregacijskoj terapiji), koji je prikazan i na Europskom kardiološkom kongresu, pokazao je da je uz adekvatne mjere hemostaze ekstrakcija zuba kod bolesnika na antiagregacijskoj terapiji sigurna i da se terapija ne treba prekidati neposredno pred zahvat.[8]

Slične su i preporuke NeLM[3] prema kojima se manji stomatološki zahvati mogu obavljati bez prekida antiagregacijske terapije u uvjetima primarne zdravstvene zaštite: jednostavna ekstrakcija jednog do tri zuba, manji zahvati na gingivi, postupci na zubnim krunama i mostovima. Ukoliko se planira ekstrakcija više od tri zuba, uputno je zahvate obaviti u ponavljanim posjetama stomatologu. Prilikom obavljanja spomenutih zahvata rizik krvarenja može se smanjiti uporabom lokalnog anestetika s vazokonstriktorom (adrenalinom). Zahvate trebaju provoditi iskusniji stomatolozi uz što manju traumu i primjenu lokalnih hemostatskih postupaka. S praktične strane, stomatološke postupke kod bolesnika na dvojnoj antiagregacijskoj terapiji treba planirati početkom radnog tjedna u jutarnjim satima u cilju bolje kontrole bolesnika i neposrednog rješavanja mogućih komplikacija. Bolesnike treba upozoriti da izbjegavaju manipulacije u usnoj šupljini (pranje zuba, jedenje čvršće hrane, pijenje vrućih napitaka) najmanje 24 sata po proceduri. U slučaju krvare-

mendations, the evaluation of the risk of bleeding on the one and stent thrombosis on the other hand is a determining factor when deciding on the continuation or discontinuation of antiaggregation therapy. It is well known that the overall risk of bleeding is increased in patients receiving dual antiaggregation therapy. The usual test of bleeding time which roughly estimates platelet function has proved to be effective in assessing the risk.[4] Clinical evaluation of previously planned dental procedures or carefully taken medical history is crucial in screening the patients who are at high risk of bleeding. On the other hand, patients with implanted intracoronary stents have an increased risk of thromboembolic events, including the stent thrombosis, which is the most common in premature discontinuation of clopidogrel therapy.[5,6]

Data on the risk of bleeding during dental procedures in patients on dual antiaggregation therapy with aspirin and clopidogrel are scarce, but retrospective studies indicate their resemblance to the risk of bleeding in patients receiving monotherapy.[7] Clinically significant bleeding after a dental procedure is defined as bleeding at the place of surgical procedure that lasts longer than 12 hours as a consequence of which a patient again comes to a dentist's office or an emergency clinic. Significant bleeding is considered to be the one that results in development of a larger hematoma or ecchymosis within the soft tissues or the one requiring transfusion. However, bleeding during dental procedures show several, sometimes mitigating circumstances that distinguish them from those of other surgical procedures. The loss of blood, even in patients receiving antiaggregation therapy is significantly lower compared with the one in gastrointestinal or for instance, cardiothoracic operations. Furthermore, bleeding in the mouth is easier visualized and local hemostatic procedures are more easily applied than in other surgical procedures. We should bear in mind the fact that bleeding depends on the extensiveness of the procedure and that during the extraction of specific teeth it is often negligible.

As we have already mentioned, thromboembolic incidents, including the fatal ones, which occur during premature discontinuation of the antiaggregation therapy are well documented in the literature. On the other hand, not a single case of uncontrolled bleeding in patients receiving antiaggregation therapy who were subject to a variety of dental procedures has been publicized in the literature. Less prospective clinical trial by *Lillis et al.* conducted in 2011 (111 patients receiving antiaggregation therapy), which was presented at the European Society of Cardiology Congress as well, showed that with adequate homeostasis measures, tooth extraction in patients receiving antiaggregation therapy is safe and that the therapy should not be discontinued immediately before a surgical procedure.[8]

The NeLM[3] recommendations are similar according to which minor dental procedures can be performed without discontinuation of the antiaggregation therapy in terms of primary health care: a simple extraction of one to three teeth, smaller gingiva surgeries, procedures on a dental crown and bridges. If you are planning on extraction of more than three teeth, it is appropriate to perform the procedures in repeated visits to the dentist's office. When performing the above procedures, the risk of bleeding may be reduced by using local anesthetic with vasoconstrictor (adrenalin). Procedures should be conducted by more experienced dentists, with the least possible trauma and use of local hemostatic procedures. On the practical side, dental procedures in patients receiving dual antiaggregation therapy should be planned at

nja bolesnika treba uputiti da odmah komprimira mjesto krvarenja gazom (zagristi gazu kroz 20 minuta). Kod krvarenja koja se ne zaustave navedenim postupcima potrebna je ponovljena kontrola stomatologa i eventualno ponavljanje postupka hemostaze.

Bolesnici koji uzimaju antiagregacijsku terapiju, a kod kojih nije uputno obavljati stomatološke procedure u okvirima primarne zdravstvene zaštite zbog visokog rizika nekontroliranog krvarenja su: bolesnici s oštećenjem jetre ili kroničnim uzimanjem alkohola, bolesnici sa zatajenjem bubrega, bolesnici podvrgnuti terapijom citostaticima i hematološki bolesnici (trombocitopenija, poremećaji koagulacije). Navedene bolesnike je potrebno uputiti u centar sekundarne zdravstvene skrbi ili u posebno specijalizirane stomatološke klinike.

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the beginning of the workweek in the morning hours for the purpose of ensuring better control for the patients and immediate resolution of potential complications. Patients should be advised to avoid manipulation in the oral cavity (brushing teeth, eating more solid foods, drinking hot drinks) for at least 24 hours following the procedure. In case of bleeding, a patient should be instructed to immediately compress the bleeding spot with gauze (to bite the gauze for 20 minutes). Bleeding that cannot be stopped by these procedures requires repeated follow-up by a dentist and possibly repeated hemostasis procedure.

Patients receiving antiaggregation therapy, who are not advised to undergo dental procedures within primary healthcare because of a high risk of uncontrolled bleeding are: patients with liver impairment or patients who chronically abuse alcohol, patients with renal failure, patients undergoing treatment with cytostatics and hematology patients (thrombocytopenia, coagulation disorder). Such patients must be referred to secondary healthcare center or specialized dental clinics.

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