Primljen/ Recived on:30.01.2015.
Revidiran/ Revised on:01.03.2015.
Prihvaćen/ Accepted on: 10.09.2015.

PRIKAZ SLUČAJA
CASE RAPORT
doi:10.5937/asn1572514S

PERIORALNI I SUBLINGVALNI HEMATOM-KOMPLIKACIJA ORALNE ANTIKOAGULANTNE TERAPIJE-PRIKAZ SLUČAJA

PERIORAL AND SUBLINGUAL HEMATOMA – ORAL ANTICOAGULATION THERAPY COMPLICATION – CASE STUDY

Milan Spasić[1,8], Miloš Tijanić[1,2], Dragan Nikolić[3], Simona Stojanović[2], Nikola Živković[4,2], Jelena Popović[5,2], Predrag Janošević[6,2], Miloš Trajković[7,8], Miloš Stojanović[7,8], Milica B.Petrović[8]

[1] KLINIKA ZA STOMATOLOGIJU, ODELJENJE ZA ORALNU HIRURGIJU, NIŠ, SRBIJA
[2] UNIVERZITET U NIŠU, MEDICINSKI FAKULTET, NIŠ, SRBIJA
[3] INSTITUT ZA JAVNO ZDRAVLJE NIŠ, SRBIJA
[4] CENTAR ZA PATOLOGIJU I PATOLOŠKU ANATOMIJU, NIŠ, SRBIJA
[5] KLINIKA ZA STOMATOLOGIJU, ODELJENJE ZA BOLESTI ZUBA I ENDODONCIJU, NIŠ, SRBIJA
[6] KLINIKA ZA STOMATOLOGIJU, ODELJENJE ZA ORTOPEDIJU VILICA, NIŠ, SRBIJA
[7] KLINIKA ZA STOMATOLOGIJU, ODELJENJE ZA MAKSILOFACIJALNU HIRURGIJU, NIŠ, SRBIJA
[8] UNIVERZITET U NIŠU, MEDICINSKI FAKULTET, STUDENT DOKTORSKIH STUDIJA

[1] CLINIC OF DENTISTRY, DEPARTMENT OF ORAL SURGERY, NIŠ, SERBIA
[2] UNIVERSITY OF NIŠ, FACULTY OF MEDICINE, NIŠ, SERBIA
[3] PUBLIC HEALTH INSTITUTE NIŠ, NIŠ, SERBIA
[4] CENTER FOR PATHOLOGY AND PATHOLOGICAL ANATOMY, NIŠ, SERBIA
[5] CLINIC OF DENTISTRY, DEPARTMENT OF OPERATIVE DENTISTRY AND ENDODONTICS, NIŠ, SERBIA
[6] CLINIC OF DENTISTRY, DEPARTMENT OF JAW ORTHOPEDICS, NIŠ, SERBIA
[7] CLINIC OF DENTISTRY, DEPARTMENT OF MAXILLOFACIAL SURGERY, NIŠ, SERBIA
[8] POSTGRADUATE .STUDENT, FACULTY OF MEDICINE ,UNIVERSITY OF NIŠ

Sažetak

Uvod. *Antikoagulantnu terapiju čine lekovi koji sprečavaju intravaskularno stvaranje i širenje tromba. U upotrebi su heparinski i dikumarinski preparati. Heparinski preparati se najćešće koriste kod potrebe za brzim antikoagulantnim efektom, daju se intravenski, deluju momentalno, vršeći inhibiciju aktiviranja tromboplastina, pretvaranja protrombina u trombin i delovanja trombina na fibrinogen. Oralnu antikoagulantnu terapiju (OAT) čine lekovi antagonisti vitamina K koji je odgovoran za sintezu faktora protrombinskog kompleksa II, VII, IX i X. Derivati su kumarina i inandiona. Jedan od najčešće korišćenih lekova iz grupe OAT je Varfarin. On je kompetitivni inhibitor vitamina K koji je potreban za karboksilaciju ostataka glutaminske kiseline faktora PK. Rezultati ove inhibicije vode neuspešnom formiranju gama karboksiglutaminske kiseline i produkciji funkcionalno inertnih koagulacionih proteina.*

Cij rada *bio je da se prikaže retka, ali opasna komplikacija neadekvatne primene oralne antikoagulantne terapije.*

Prikaz slučaja *Bolesnik S.S. muškog pola, starosti 79 godina, primljen je na Odeljenje za oralnu hirurgiju Klinike za stomatologiju Medicinskog fakulteta u Nišu 5.10.2012. godine zbog teškog opšteg stanja sa masivnim hematomom u predelu lica.Anamnestički su dobijeni podaci o tome da je u poslednjih nekoliko dana, svojevoljno, umesto propisane doze, uzimao celu tabletu Farina.Bolesniku je uvedena intravenska terapija niskomolekularnim heparinom (Fraxarin 0,3/12h) uz nastavak antibiotske terapije.Bolesnik je u narednom periodu svakodnevno kontrolisan. U narednih 7-10 dana hematom se resorbovao, a otok u potpunosti nestao.*

Ključne reči: *perioralni hematom, antikoagulantna terapija, Farin*

Corresponding author:
Milan Spasić
Clinic of Dentistry Niš
Bul. Zorana Djindjića 52, 18000 Niš
milan.s.spasic@gmail.com 063/8626663

Abstract

Introduction. *Anticoagulation therapy includes drugs which prevent intravascular formation and spreading of a thrombus. Heparin and dicoumarin preparation are in use.*

Heparin preparations are commonly used when a rapid anticoagulant effect is required, they are administered intravenously, act immediately performing the inhibition of thromboplastin activation, prothrombin to thrombin conversion, and the effect of thrombin to fibrinogen.

Oral anticoagulation therapy (OAT) includes drugs – antagonists of vitamin K, which is responsible for the synthesis of prothrombin complex factors – II, VII, IX and X. They are derived from coumarin and indandione. One of the most frequently used drugs from the OAT group is warfarin. It is a competitive inhibitor of vitamin K required for the carboxylation of the residues of PK factor glutamic acid. The results of this inhibition lead to the unsuccessful formation of gama carboxyglutamic acid and the production of functionally inert coagulation proteins.

The aim *of this study was to show a rare but dangerous complication of an inadequate application of oral anticoagulation therapy.*

Case study. *Patient S.S., male, aged 79, was admitted to the Oral Surgery Department, Clinic of Dentistry of the Faculty of Medicine in Niš on October 5, 2012 due to a severe general condition with massive hematoma in the facial area.*

Anamnestic data showed that during the previous couple of days, the patient was voluntarily taking a whole tablet of Farin instead of the prescribed dose.

The patient started receiving intravenous low-molecular-weight heparin therapy (Fraxarin 0.3/12h) along with the antibiotic therapy.

In the following period, the patient reported daily at the Oral Surgery Department for regular check-ups. The hematoma was absorbed and the swelling was completely gone within the next 7 to 10 days.

Key words: *perioral hematoma, anticoagulation therapy, Farin*

Uvod

Učestalost kardiovaskularnih bolesnika u opštoj populaciji je velika, što ovu grupu čini značajnom kategorijom u pogledu morbiditeta i mortaliteta. Jedan broj ovih bolesnika ima ugrađene veštačke srčane valvule, zbog čega su izloženi riziku za razvoj tromboembolijskih komplikacija i kao takvi se nalaze se na doživotnoj oralnoj antikoagulantnoj terapiji [1,2].

Antikoagulantnu terapiju čine lekovi koji sprečavaju intravaskularno stvaranje i širenje tromba. U upotrebi su heparinski i dikumarinski preparati [3,4].

1. Heparinski preparati se najčešće koriste kod potreba za brzim antikoagulantnim efektom, daju se intravenski, deluju momentalno, vršeći inhibiciju aktiviranja tromboplastina, pretvaranja protrombina u trombin i delovanja trombina na fibrinogen. Zbog intravenskog načina primene daju se više puta dnevno. Indikovani su kao uvodna terapija dikumarolskim preparatima koji se primenjuju per os. Koriste se i za profilaksu tromboze dubokih vena, kod akutne arterijske tromboze i nestabilne angine pektoris.

2. Oralnu antikoagulantnu terapiju (OAT) čine lekovi antagonisti vitamina K koji je odgovoran za sintezu faktora protrombinskog kompleksa- II, VII, IX i X. Derivati su Kumarina i Inandiona (retko se primenjuje). Najčešće su u upotrebi acenokoumarol (Sintrom-Novartis Switzerland), phenprocoumon (Marcumar, Marcoumar, Falithrom), ethyl biscoumacetate (Pelentan, Tromexan), varfarin (Farin-Galenika Srbija, Marivarin-Krka Slovenija)[5,6]. U stručnoj literaturi opisani su još ranih sedamdesetih godina[7]. Oni ne utiču na cirkulišuće faktore koagulacije, tako da je latentni period četiri dana, dok je početak dejstva već nakon 12-16 sati. Zato se kao uvodna terapija koristi heparin, dok se OAT uvodi narednog dana. Indikaciono područje OAT je profilaksa venske tromboze, apsolutna aritmija, veštački srčani zalisci, akutni infarkt miokarda itd. Za kontrolu nivoa OAT u krvi koristi se standardizovani INR test kojim se tačno određuje optimalan nivo za svakog bolesnika. Terapijske doze zavise od vrste oboljenja, tako da je za vensku profilaksu u opsegu od 1,5 do 2,5; za arterijsku od 2,5 do 4,5 i za veštačke srčane valvule od 3,0 do 5,0 [8].

Introduction

The incidence of cardiovascular patients in general population is large, which makes this group of patients a significant category in terms of morbidity and mortality. A number of these patients has built-in artificial heart valves which creates the risk of the development of thromboembolic complications, and as such, they receive a lifelong oral anticoagulation therapy [1,2].

Anticoagulation therapy includes drugs which prevent intravascular formation and spreading of a thrombus. Heparin and dicoumarin preparation are in use [3,4].

1. Heparin preparations are commonly used when a rapid anticoagulant effect is required, they are administered intravenously, act immediately performing the inhibition of thromboplastin activation, prothrombin to thrombin conversion and the effect of thrombin to fibrinogen. Due to intravenous administration, they are given several times a day. They are indicated as initial therapy using dicoumarol preparations which are used per os. Furthermore, they are used for the prophylaxis of deep veins thrombosis, in acute arterial thrombosis and unstable angina pectoris.

2. Oral anticoagulation therapy (OAT) includes drugs – antagonists of vitamin K, which is responsible for the synthesis of prothrombin complex factors – II, VII, IX, and X. They are derived from coumarin and indandione (rarely applicable). The most commonly used are acenocoumarol (Sintrom –Novartis Switzerland), phenprocoumon (Marcumar, Marcoumar, Falithrom), ethyl biscoumacetate (Pelentan, Tromexan), warfarin (Farin – Galenika Serbia, Marivarin –Krka Slovenia) [5,6]. These were described in the professional circles in the early seventies of the twentieth century [7]. They do not affect the circulating factors of coagulation, therefore the latent period is 4 days, whereas the onset of their action is after 12 to 16 hours. This is the reason why heparin is used as initial therapy, while OAT is introduced the next day. The OAT indication area is the prophylaxis of venous thrombosis, absolute arrhythmia, artificial heart valves, acute myocardial infarction, etc. In order to control the level of OAT in the blood, a standardised INR test is used to accurately determine the optimal level for each patient. Therapy dosages depend on the type of disease: for venous prophylaxis they range from 1.5 to 2.5, for arterial prophylaxis from 2.5 to 4.5, and for artificial heart valves from

Jedan od najčešće korišćenih lekova iz grupe1. OAT je varfarin. On je kompetitivni inhibitor vitamina K koji je potreban za karboksilaciju ostataka glutaminske kiseline faktora PK. Rezultati ove inhibicije vode neuspešnom formiranju gama karboksiglutaminske kiseline i produkciji funkcionalno inertnih koagulacionih proteina[9].

3.0 to 5.0 [8]. One of the most frequently used drugs from the OAT group is warfarin. It is a competitive inhibitor of vitamin K required for the carboxylation of the residues of PK factor glutamic acid. The results of this inhibition lead to the unsuccessful formation of gama carboxyglutamic acid and the production of functionally inert coagulation proteins[9].

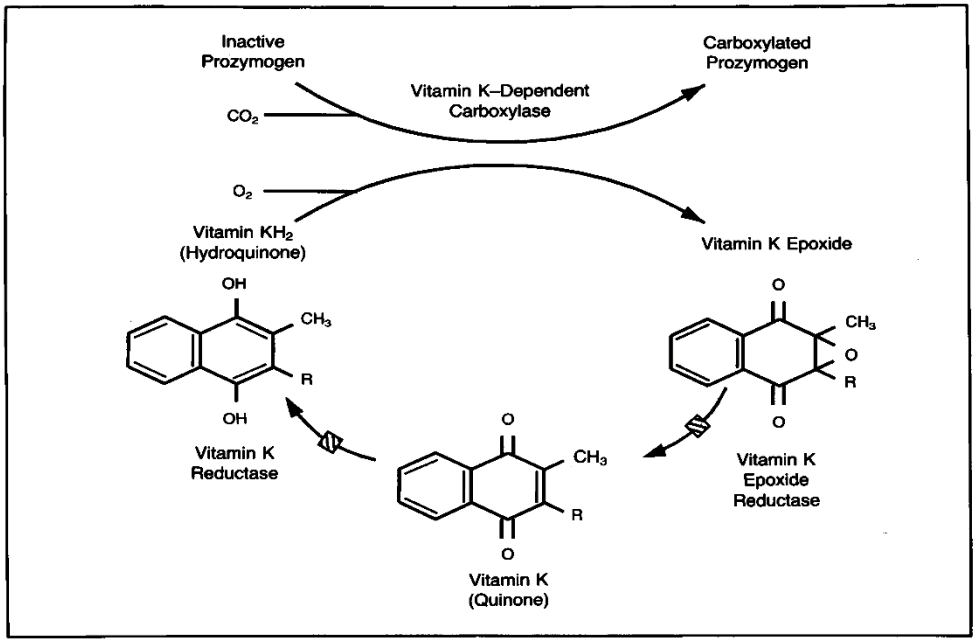


Figure 1. The Vitamin K Cycle and Its Inhibition by Warfarin.
Warfarin inhibits vitamin K epoxide reductase and vitamin K reductase (hatched box) and so blocks the conversion of vitamin K epoxide to vitamin KH_2. Vitamin KH_2 is a cofactor for the carboxylation of inactive proenzymes (factors II, VII, IX, and X) to the carboxylated proenzyme in a reaction that is catalyzed by vitamin K–dependent carboxylase and requires carbon dioxide and oxygen.

Postoji i nova generacija oralnih antikoagulantnih lekova Bayer Xarelto® (Rivaroxaban) za koje po preporuci proizvođača nije neophodna kontrola koagulacije. On je prvi dostupni visoko selektivni inhibitor faktora Xa. Ima dobru resorpciju iz creva, tako da maksilmalno dejstvo ispoljava četiri sata nakon primenjene terapije, efekti traju 8-12 sati, ali faktor Xa svoju aktivnost vraća u roku od 24 sata.

Jedna od retkih, ali mogućih komplikacija OAT je predoziranje, s obzirom da su ovi bolesnici pod stalnom kontrolom kardiologa i transfuziologa. Što je OAT intenzivnija, povećava se rizik od krvarenja [10].

Cij rada bio je da se prikaže retka, ali opasna komplikacija neadekvatne primene oralne antikoagulantne terapije.

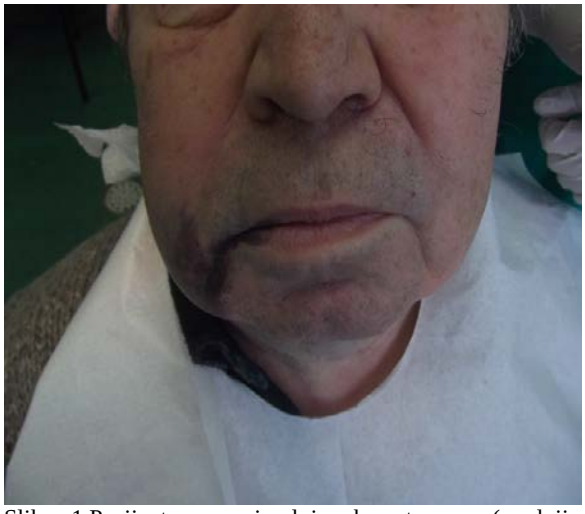
Furthermore, there is a new generation of oral anticoagulants Bayer Xarelto® (Rivaroxaban), which, according to the manufacturer, does not require coagulation control. It is the first available highly selective inhibitor of Xa factor. It has good absorption from the intestines and thus manifests its maximal effect four hours after the received therapy. The effects last for 8 to 12 hours, however, Xa factor restarts its activity within 24 hours.

One of the rare but possible complications of OAT is overdosing given that such patients are under constant supervision of cardiologists and transfusiologists. The risk of haemorrhage increases with OAT being more intensive [10].

The aim of this study was to show a rare but dangerous complication of an inadequate application of oral anticoagulation therapy.

Prikaz slučaja

Bolesnik S.S. muškog pola, star 79 godina, primljen je na Odeljenje za oralnu hirurgiju Klinike za stomatologiju Medicinskog fakulteta u Nišu 5.10.2012. godine zbog teškog opšteg stanja sa masivnim hematomom u predelu lica (slika 1,2).

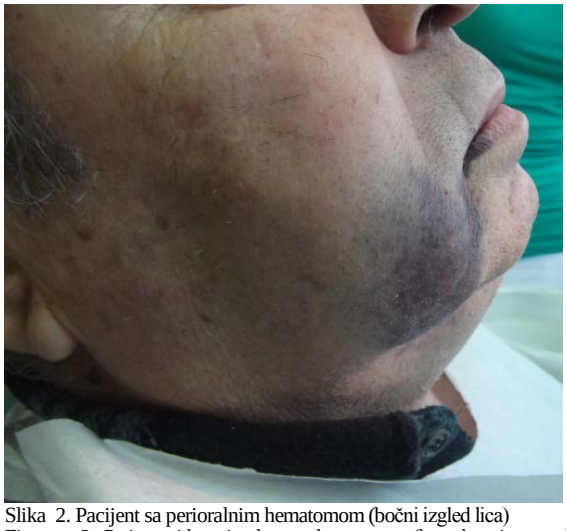


Slika 1.Pacijent sa perioralnim hematomom (prednji izgled lica)
Figure 1. Patient with perioral haematoma (anterior viewof the face)

Uvidom u medicinsku dokumentaciju utvrđeno je da pacijent boluje od angine pectoris, dijabetesa melitusa, hipertenzije, arrhytmia absolute, cicatrix myocardii par. inferioris i hyperlipidemije i da je pod konstantnom terapijom (Monizol, Lorist, Lopion, Tensec, Cornelin, Limeral, Glucophage, Lasix, Spironolacton i Nytroglicerin). Utvrđeno je da je na OAT *Farinom*, sa propisanom dozom ¼ tablete dnevno uz redovne kontrole, na koje, po sopstvenom priznanju, nije odlazio. Anamnestički su dobijeni podaci da je u poslednjih nekoliko dana, svojevoljno, umesto propisane doze, uzimao celu tabletu Farina. U toku noći je zubom povredio sluzokožu obraza sa desne strane, zbog čega je osetio blagu bol, ali nije bilo krvarenja. Ujutru je primetio otok i krvni podliv u predelu obraza sa desne strane koji se u toku dana povećavao. Kada su mu funkcije disanja i gutanja postale otežane, javio se lekaru na Odeljenju za oralnu hirurgiju Klinike za stomatologiju Medicinskog fakultreta u Nišu radi terapije.

Case study

Patient S.S., male, aged 79, was admitted to the Oral Surgery Department, Dentistry Clinic of the Faculty of Medicine in Niš on October 5, 2012 due to a severe general condition with massive hematoma in the facial area (Figure 1, 2).



Slika 2. Pacijent sa perioralnim hematomom (bočni izgled lica)
Figure 2. Patient with perioral haematoma (lateral view of the face)

After examining medical records, it was found that the patient suffered from angina pectoris, diabetes mellitus, hypertension, absolute arrhythmia, cicatrix myocardii par. inferioris and hyperlipidemia, and that he was receiving continuous therapy (Monizol, Lorist, Lopion, Tensec, Cornelin, Limeral, Glucophage, Lasix, Spironolacton and Nytroglicerin). It was also found that he was on OAT with *Farin*, with a prescribed dose of ¼ tablet a day with regular check-ups, to which, according to his own admission, he had never been. Anamnestic data showed that during the previous couple of days, the patient was voluntarily taking a whole tablet of Farin instead of the prescribed dose. During the night, he hurt the cheek mucosa on the right side, due to which he felt slight pain, but there was no bleeding. In the morning, he noticed a swelling and a hematoma on the right cheek, which increased in size throughout the day.

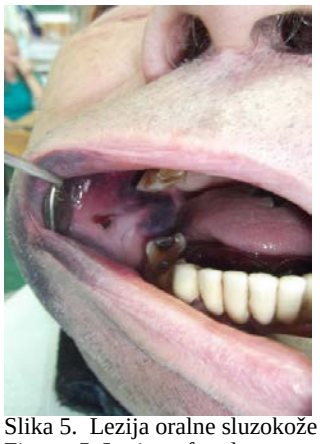
Kliničkim pregledom je ustanovljen otok i hematom desne strane lica koji se prostirao od donje ivice zigomatične kosti do donje ivice mandibule i od prednje ivice musculus masetera do ugla usana, zahvatajući i predeo donje i gornje usne sa te strane. Otok je bio tamnoljubičaste boje palpatorno elastičan, čvrst i bezbolan. Intraoralno se hematom prostirao od ugla usana do retromolarnog i parafaringealnog predela desne strane i od forniksa gornje vilice do poda usta u oba sublingvalna predela. Sublingvalne plike su bile edematozne, izdignute preko incizalnih ivica donjih zuba i tamnocrvene boje. Jezik je bio potisnut na gore i prema distalnim partijama usne duplje, ometajući disajni put i govor (slika 3,4). Zatvaranje i otvaranje usta kao i lateralne kretnje mandibule su bile blago ograničene. Uočen je i dekubitis sluzokože obraza u regiji prvog donjeg desnog molara (slika 5), kao i parcijalna krezubost sa neravnim i oštrim ivicama prisutnih zuba (slika 6).

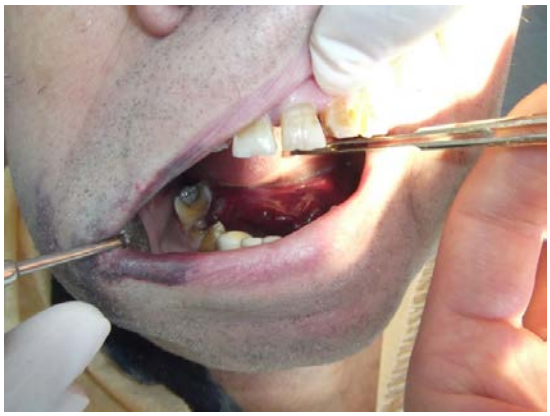
When breathing and swallowing became difficult, the patient saw a doctor at the Oral Surgery Department, Dentistry Clinic of the Faculty of Medicine in Niš for the appropriate therapy.

The clinical examination showed swelling and hematoma of the right side of the face, spreading from the lower edge of zygomatic bone to the lower edge of the mandible, and from the front edge of musculus masseter to the corner of the lips, including the area of the upper and lower lip on that side. The swelling was dark purple in colour, elastic to touch, hard and painless. Intraorally, the hematoma stretched from the corner of the lips to the retromolar and parapharyngeal area of the right side, and from the upper jaw fornix to the mouth floor, in both sublingual regions. The sublingual folds were edematous, raised over the incisal edges of lower teeth, dark red in colour. The tongue was pushed upwards and towards the distal parts of the oral cavity, obstructing the airway and speech (Figure 3, 4). Closing and opening of the mouth, as well as lateral mandibular movements, were slightly limited. In addition, cheek mucosa decubitus was noticed in the lower right first molar region (Figure 5), as well as partial edentulism with uneven and sharp edges of the existing teeth (Figure 6). In addition, cheek mucosa decubitus was noticed in the lower right first molar region (Figure 5), as well as partial edentulism with uneven and sharp edges of the existing teeth (Figure 6).

Slika 3. Sublingvalni hematom – prednji pod usta
Figure 3. Sublingual hematoma – anterior floor of the mouth

Slika 4. Sublingvalni hematom koji se širi u obraznu regiju
Figure 4. Sublingual hematoma spreading in to the cheek area


Slika 5. Lezija oralne sluzokože
Figure 5. Lesion of oral mucosa


Slika 6. Oštre ivice gleđi prisutnog zuba
Figure 6. Scharp enamel edges of the present teeth

Ortopan tomografski snimak je potvrdio kliničke nalaze u vezi oštrih ivica i krezubosti (slika 7).

Nakon obavljenog kliničkog pregleda, bolesnik je smešten na Odeljenju intenzivne nege, gde mu je ordinirana antibiotska terapija: amp. Nilacef 1.5 g/12 h; Sol.Orvagil 400 mg/8h. Hitno je urađena kompletna krvna slika, laboratorija i skrining test koagulacije. S obziron na to da je bio u pitanju srčani bolesnik, pregledan je od strane kardiologa.

Prvi rezultati krvi pokazali su vrednost INR>8, glukoza 11,8 mmol/l, CRP 28,3, HCT 35,4 %.

Bolesniku je hitno aplikovana sveža zamrznuta plazma i ukinuta terapija Farinom. Po stabilizovanju opšteg stanja, urađena je detaljna pretraga uzroka dekubitisa i konzervativna sanacija zuba, kako bi se izbeglo ponovno povređivanje. Sledećeg dana rezultati su se popravili (INR 3,2). Uvedena je intravenska terapija niskomolekularnim heparinom (Fraxarin 0,3/12h) uz nastavak antibiotske terapije. Otok se blago povlačio. Trećeg dana rezultati su bili još stabilniji. INR je iznosio 2,6, što je u terapijskim granicama za njegovu bolest. Četvrtog dana je prekinuta intravenska terapija Fraxarinom i pacijent je ponovo prebačen na OAT Farinom. Stabilnog opšteg stanja i sa hematomom u fazi regresije bolesnik je otpušten na kućno lečenje (Th: tbl. Clindamycin 600mg/12h).

Bolesnik se u narednom periodu svakodnevno javljao na Odeljenje oralne hirurgije radi kontrole. U narednih 7-10 dana hematom se resorbovao, a otok u potpunosti nestao.

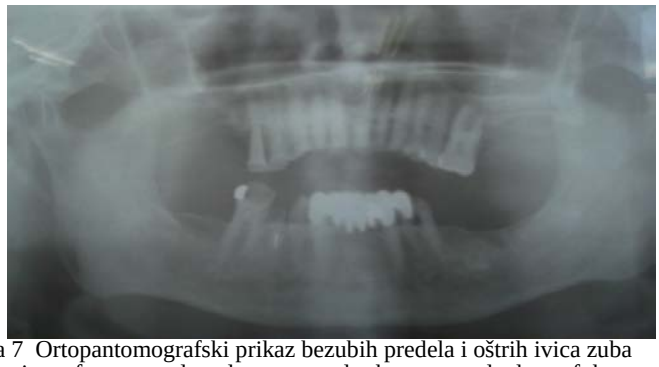
The orthopantomographic image confirmed the clinical findings related to sharp edges and edentulism (Figure 7).

After the clinical examination had been done, the patient was placed in the intensive care unit where he received antibiotic therapy: amp. Nilacef 1.5g/12h; Sol.Orvagil 400mg/8h. An urgent complete blood count, laboratory and coagulation screening test were done. Since the patient was a heart patient, he was also examined by a cardiologist.

The first blood tests showed the values INR>8, glucose 11.8 mmol/l, CPR 28.3, HTC 35.4%.

The patient immediately received fresh frozen plasma and his therapy with Farin was cancelled. As his general condition was stabilized, a detailed examination of the cause of decubitus was performed, as well as the conservative tooth repair to avoid further injuries. The following day the patient's results were better (INR 3.2). The patient started receiving intravenous low-molecular-weight heparin therapy (Fraxarin 0.3/12h) along with the antibiotic therapy. The swelling was slowly receding. The results were even more stable on the third day. The value of INR amounted to 2.6, which was within the therapeutic range considering his disease. On the fourth day, the intravenous Fraxarin therapy was cancelled and the patient was again receiving OAT with Farin. With the general condition being stable and the hematoma in the regression phase, the patient was discharged from hospital for home treatment (Th: tbl. Clindamycin 600mg/12h).

In the following period, the patient reported daily at the Oral Surgery Department for regular check-ups. The hematoma was absorbed and the swelling was completely gone within the following 7 to 10 days.



Slika 7 Ortopantomografski prikaz bezubih predela i oštrih ivica zuba
Figure 7 Panoramic view of present edentulousness and scharp enamel edges of the present teeth

Diskusija

U prošlosti je bilo mnogo kontroverzi u vezi sa stomatološkim procedurama kod bolesnika na OAT. Najviše hemoragijskih komplikacija kod njih javljalo se do standardizacije oralne antikoagulantne kontrole, tj. do razvoja i uvođenja INR-a 1983. godine[11,3]. Preovladavali su stavovi da se pre vađenja zuba, a naročito pre oralno-hirurških intervencija, mora obustaviti ili redukovati OAT kako bi se smanjio rizik od krvarenja. Takve stavove pravdali su pojavom profuznog krvarenja nakon vađenja zuba kod nekoliko bolesnika na terapiji Dikumarolom[12].

Ogiuchi i saradnici su 1985. godine objavili da privremeno prekinuta OAT nosi povećani rizik od tromboembolizma, posebno kod bolesnika sa veštačkim valvulama[13]. Wahl je 1998. prikazao pojavu nekoliko slučajeva ozbiljnih embolijskih komplikacija kod bolesnika sa ukinutom antikoagu-lantnom terapijom pre hirurške intervencije. Britanski komitet za standard i hematologiju, u svojoj praktičnoj preporuci za tretman bolesnika na OAT kod kojih je neophodna stomatološka procedura, navodi da je rizik od značajnijeg krvarenja kod bolesnika na OAT sa INR-om u terapijskoj granici veoma mali, dok se rizik od pojave tromboze povećava kod privremeno prekinute OAT [14].

Prospektivna randomizirana studija sprovedena u Španiji je pokazala da nakon hirurške intevencije nije bilo razlike u učestalosti hemoragijkih komplikacija kod bolesnika sa preoperativno smanjenom dozom i onih kod kojih je doza oralnih antikoagulanasa bila na terapijskom nivou[15].

Discussion

There were numerous controversies in the past related to dental procedures in patients receiving OAT. The largest number of haemorrhagic complications in such patients appeared prior to the standardization of oral anticoagulant control, that is, prior to the development and introduction of INR in 1983 [11,3]. Attitudes that prior to tooth extraction and especially prior to oral surgical interventions OAT must be suspended or reduced to decrease the risk of haemorrhage, prevailed. Such attitudes were justified by the appearance of profuse bleeding after tooth extraction in several patients receiving dicoumarol therapy [12].

In 1985, Ogiuchi et al. reported that temporarily cancelled OAT bears an increased risk of thromboembolism, especially in patients with artificial valves [13]. In 1998, Wahl presented several cases of severe embolic complications in patients with revoked anticoagulant therapy prior to a surgical intervention. The British Committee for Standards in Haematology, in their practical guidelines for the treatment of patients receiving OAT and requiring necessary dental procedures, state that the risk of significant bleeding in patients receiving OAT with INR is very small in the therapeutic range, whereas the risk of thrombosis increases in temporarily cancelled OAT [14].

A prospective, randomized study carried out in Spain showed that after a surgical intervention there were no differences in the incidence of haemorrhagic complications in patients with a preoperatively reduced dose and the ones with a therapeutic

Do sličnih rezultata je došao i Đovani sa saradnicima kod koga su bolesnici i u kontrolnoj i u studijskoj grupi bili bez krvarenja u periodu praćenja, u prvih 30 minuta nakon ekstrakcije zuba, kao i u prva 24 sata [16].

Objavljena je i metaanaliza o 774 bolesnika na konstantnoj terapiji Farinom, sa INR- om manjim od 4, kod kojih je sprovedeno 2014 stomatoloških procedura, u kojoj u više od 98 % bolesnika nije bilo ozbiljnijeg krvarenja [5].

Danas se smatra, što je i doktrinarni stav Klinike za stomatologiju u Nišu, da zbog presudnog značaja za kardiovaskularne bolesnike OAT ne treba prekidati za ekstrakcije zuba i oralno-hirurške intervencije manjeg obima. Neophodna je redovna laboratorijska kontrola kako bi se vrednost INR održavala u terapijskom opsegu. Za obimnije operacije OAT se prekida 24-48 sati pre intervencije i istovremeno prelazi na intravensko davanje niskomolekularnog heparina (fraksarin). Nakon 4-5 dana, vrši se preklapanje sa oralnim antikoagulansima do postizanja odgovarajućeg nivoa INR-a, kada se ukida fraksarin[8].

U toku lečenja na Klinici za stomatologiju našem bolesniku je svakodnevo kontrolisan INR, što odgovara i preporukama Britanskog udruženja hematologa[14].

Bolesnik koji je prikazan samoinicijativno je, iz samo njemu znanih razloga, četiri puta povećao svoju dozu OAT. To je drastično smanjilo koagulabilnost krvi (INR>8), što je uz minimalnu traumu tkiva (dekubit) bukalne sluzokože, prouzrokovane oštrim ivicama prvog donjeg desnog molara, izazvalo drastično krvarenje i formiranje obimnog hematoma.

U startu je ordinirana sveže zamrznuta plazma kako bi se nadoknadila izgubljena krv zbog hematokrita koji je na to ukazivao. Sveža zamrznuta plazma sadrži sve stabilne i labilne činioce sistema koagulacije, fibrinolize i komplemenata, uz efikasne proteine i imunoglobuline. Koristi se uglavnom kod bolesnika sa deficitom više činilaca koagulacije, nekada i kod deficita pojedinih činilaca kada nedostaju koncentrovani preparti[6,17]. Primenjuje se i kod bolesnika sa oštećenom funkcijom jetre ili deficitom vitamina K, odnosno u slučajevima predoziranja njegovim antagonistima što pokazuje i prikazani slučaj.

dose level of oral anticoagulants [15]. Similar results were obtained in a study by Giovanni et al. in which patients in both the control and study group did not exhibit bleeding within the monitoring period, in the first 30 minutes after tooth extraction, as well as within the first 24 hours [16].

Moreover, meta-analysis was done on 774 patients on continuous therapy with Farin, with INR less than 4, on whom 2014 dental procedures were performed in which 98% of the patients exhibited no serious bleeding [5].

Nowadays, it is considered that due to crucial significance for cardiovascular patients, OAT should not be suspended for tooth extraction and smaller oral surgical interventions, and this approach is in accordance with the doctrinal approach of the Clinic of Dentistry in Niš. Regular laboratory control tests are necessary to keep the INR value in the therapeutic range. For more serious surgical interventions, OAT is suspended 24 to 48 hours prior to the intervention and the intravenous administration of low-molecule-weight heparin (fraxarin) is simultaneously introduced. After 4 to 5 days, there is an overlapping with oral coagulants until the adequate level of INR has been achieved, when the use of fraxarin is terminated [8].

During the treatment at the Clinic of Dentistry, our patient had the INR controlled on a daily basis, which is in accordance with the recommendations of the British Association of Haematologists [14].

The presented patient had previously increased the dose of OAT four times, on his own initiative. Consequently, the blood coagulation ability (INR>8) decreased drastically, which, along with minimal buccal mucosa tissue trauma (decubitus) provoked by sharp edges of the lower right first molar, caused considerable bleeding and the formation of a large hematoma.

At first, the patient received fresh frozen plasma to replenish the blood lost due to the haematocrit which was suggestive of that. Fresh frozen plasma contains all stable and unstable factors of the system of coagulation, fibrinolysis and complements, along with effective proteins and immunoglobulins. It is mainly used in patients with many coagulation factors deficiencies, sometimes with deficiencies of certain factors when concentrated preparations are missing [6,17]. It is also used in patients with an impaired liver function or vitamin K deficiencies, that is, in cases of overdosing with its antagonists, which was the case with our patient.

Antibiotici su ordinirani da bi se sprečio nastanak infekcije, jer izlivena krv predstavlja pogodno mesto za nastanak i razvoj infekcije.

Ukidanjem OAT i prelaskom na Fraxarin u ciljanim dozama uticalo se na poboljšanje opšteg stanja i smanjenje hematoma, što je na kraju rezultiralo potpunim izlečenjem. Obradom oštrih ivica svih zuba, a posebno zuba uzročnika dekubitisa, eliminisani su potencijalni uzroci daljih oštećenja bukalne sluzokože.

Zaključak

Redovna laboratorijska kontrola OAT preko INR testa je obavezna kako bi se na vreme uočilo smanjenje ili povećanje nivoa leka i održala njegova ciljana vrednost. Pri tom, veliku ulogu ima i edukacija bolesnika. Kako se vrlo često radi o starim i neprosvećenim bolesnicima, na lekaru je da detaljno objasni opasnost od OAT u smislu smanjenja doze i rizika za pogoršanje osnovne bolesti, kao i predoziranja i rizika od iznenadnog krvarenja. U oba slučaja mogu nastati komplikacije koje nekada mogu i životno da ugroze bolesnika.

Antibiotics were administered to prevent the occurrence of an infection given that the blood which poured out represents a suitable medium for the appearance and development of an infection.

The suspension of OAT and switching to Fraxarin in target doses affected the improvement of the general condition and the reduction of the hematoma, which eventually resulted in complete recovery. The treatment of the sharp edges of all teeth, especially teeth that caused decubitus, excluded potential causes of further buccal mucosa damage.

Conclusion

Regular laboratory control of OAT via the INR test is mandatory in order to spot a decrease or increase in drug levels in time and maintain its target value. In addition, patient education plays a crucial role. Since doctors are very often dealing with old and uninformed patients, they have to explain thoroughly the dangers of OAT in terms of dose reduction and risks of worsening the underlying disease, as well as the dangers of overdosing and risks of sudden bleeding. Complications, which can sometimes be life-threatening, may arise in both cases.

LITERATURA / REFERENCES

1 Stein PD, Collins JJ, Kantrowitz A: Antithrombotic therapy in mechanical and biological prosthetic heart valves and saphenous vein bypass grafts. Chest 1986 (suppl 2) 89:46.
2. Levine HJ, Pauker SG, Salzman EW: Antithrombotic therapy in valvular heart disease. Chest 1986 (suppl 2) 89:36.
3. Kirkwood TB. Calibration of reference thromboplastins and standardisation of the prothrombin time ratio. Thromb Haemost 1983;49(3):238-44.
4. Stroke Prevention in Atrial Fibrillation Investigators. Warfarin versus aspirin for prevention of thromboembolism in atrial fibrillation: Stroke Prevention in Atrial Fibrillation II Study.Lancet1994;343,687-691.
5. Vujičić B, Mačukanović-Golubović L. Krvarenje i hemostaza u oralnohirurškoj praksi. Kosovska Mitrovica, 2009.
6. WHO (2014). World Health Organization, http://www.who.int, preuzeto 9.6.2014.
7. Deykin D. Warfarin therapy. N Englen J Med 1970; 283:691-4.
8. Devani P, Lavery KM, Howell CJ. Dental extractions in patients on warfarin: is alteration of anticoagulant regime necessary? Br J Oral Maxillofac Surg 1998;36(2):107-11.
9. Davies JA, Tuddenham EGD. Haemostasis and thrombosis.In: Weatherall DJ, Ledinghman JGG, Warrell DA, eds: Oxford Textbook of medicine, 2nd Edition. Oxford Mwdical Publications, 1988; 19:228-229.
10. Hirsch J: Oral anticoagulant drugs. N Engl J Med 1991; 324:1865.
11. Ziffer AM, Scopp IW, Beck J, Baum J, Berger AR. Profound bleeding after dental extractions during dicumarol therapy. N Engl J Med 1957;256(8):351-3.
12. Ziffer AM, Scopp IW, Beck J, et al: Profound bleeding after dental extractions during dicumarol therapy. N Engl J Med 1957; 256:351.
13. Ogiuchi H,Ando T, Tanaka M: Clinical reports on dental extraction from patients undergoing oral anticoagulant therapy. Bull Tokyo Dent Coll 1985;26:205.
14. Wahl MJ. Dental surgery in anticoagulated patients. Arch Intern Med 1998;158(15):1610-6.
15. Souto J.C., Oliver A, Zuazu-Jausoro, Vives A., Foncuberta J. Oral Surgery in Anticoagulated Patients Without Reducing the Dose of OraI Anticoagulant: A Prospective Randomized Study. J Oral Maxillofac Surg 1996;54:27-32.
16. British Committee for Standards in Haematology. Guidelines for the management of patients on oral anticoagulants requiring dental surgery, September 2011.
17. Perović J. Hemostaza u stomatološkoj praksi. Beograd,2002.