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Source / Izvornik: **Acta clinica Croatica, 2006, 45, 101 - 104**

**Journal article, Published version**

**Rad u časopisu, Objavljena verzija rada (izdavačev PDF)**

Permanent link / Trajna poveznica: <https://um.nsk.hr/um:nbn:hr:220:975117>

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Download date / Datum preuzimanja: **2024-09-18**



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## DENTAL PROCEDURES IN PATIENTS RECEIVING ORAL ANTICOAGULANT THERAPY

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**SUMMARY** – There is a widespread belief among physicians and dentists that oral anticoagulant therapy must be discontinued before and for some time after dental procedures. This practice may increase the risk of potentially life-threatening thromboembolism. The present literature does not support routine discontinuation of anticoagulant therapy for dental patients. There is a theoretical risk of bleeding after dental surgery in patients at therapeutic levels of anticoagulation, however, it is minimal and may be greatly outweighed by the risk of thromboembolism upon anticoagulant therapy withdrawal. Thus, dental extractions can be performed without modification of oral anticoagulant therapy. In most patients local hemostasis with gelatin sponge, fibrin glue, sutures and/or mouthwash with tranexamic acid or ε-aminocaproic acid is sufficient to prevent postoperative bleeding.

**Key words:** *Anticoagulants – therapeutic use; Oral surgical procedures – adverse effects; Blood loss, surgical – prevention and control; Anticoagulants – contraindications; Thromboembolism – prevention and control; Oral hemorrhage – prevention and control*

### Introduction

The purpose of this article is to suggest how patients receiving oral anticoagulant therapy should be managed when dental procedures (single and multiple simple extractions, gingival surgery and alveolar surgery) are performed. Anticoagulant therapy is used to reduce the risk of thromboembolic events in patients with atrial fibrillation, mechanical heart valves, recent pulmonary embolism, deep vein thrombosis and hypercoagulable states.

### Oral Anticoagulants

Coumarins or vitamin K antagonists (VKAs) have been the mainstay of oral anticoagulant therapy for more than 50 years. Bleeding is the main complication of these drugs. Warfarin is the most common coumarin that is in clinical use. Its plasma half-life is about 37 hours<sup>1</sup> and

length of its effect 2-5 days<sup>2</sup>. Its metabolism occurs mainly in the liver, involving cytochrome P450, CYP2C9 isoenzyme in particular<sup>3</sup>. Warfarin effect is reversible with vitamin K<sup>4</sup>.

The coagulation status of patients taking VKAs must be evaluated on the day of invasive dental procedure or, if it is not possible, on the day before. Prothrombin time (PT) which responds to a reduction in vitamin K-dependent factors, and international normalized ratio (INR) are used as a measure of anticoagulation. The World Health Organization recommends the use of INR as a more reliable laboratory test to assess patient anticoagulation status than PT. INR is expressed as the patient PT to control PT ratio. In an individual with normal PT, INR is approximately 1. An INR of 2 to 3 is the usual therapeutic range in deep vein thrombosis, and INR of up to 3.5 is required in patients with prosthetic heart valves<sup>5</sup>.

### Warfarin and drug interactions

A number of drugs interact with warfarin by altering either protein binding or liver metabolism. The second-

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Received February 24, 2006, accepted March 31, 2006

and third-generation cephalosporins may augment the anticoagulation effect of warfarin by inhibiting cyclic interconversion of vitamin K<sup>6,7</sup>. Acetylsalicylic acid (ASA)<sup>8</sup>, nonsteroidal anti-inflammatory drugs (NSAIDs)<sup>9</sup> and penicillins in high doses<sup>10,11</sup> increase the risk of warfarin-associated bleeding by inhibiting platelet function. Doses of salicylates of >1.5 g *per* day<sup>12</sup> and acetaminophen<sup>13</sup> (paracetamol) may also augment the anticoagulant effect of warfarin, possibly by affecting the P450 cytochrome system (CYP2C9 enzyme). Cyclooxygenase inhibitors (rofecoxib and celecoxib) appear to have no major effect on platelets or INR<sup>1</sup>. Treatments with fluconazole, itraconazole and miconazole resulted in bleeding in dental patients<sup>1</sup>. Even topical miconazole gel potentiates warfarin anticoagulant activity<sup>14</sup>. Griseofulvin inhibits the anticoagulant effect of warfarin, whereas ketoconazole has no effect on hemostasis<sup>15</sup>. Some hypermetabolic states (fever, hyperthyroidism) increase warfarin responsiveness, probably by increasing the catabolism of vitamin K-dependent coagulation factors<sup>16,17</sup>. Liver disease potentiates the response to warfarin through the impaired synthesis of coagulation factors.

### *Dental management and warfarin*

Until recently it was standard practice to discontinue anticoagulant therapy before dental extractions or similar procedures. The discontinuation of warfarin exposes the patients, especially those with artificial heart valves, to the risk of thromboembolism<sup>18</sup>. In 542 documented cases in 493 patients exposed to anticoagulant therapy withdrawal specifically for dental procedures, five patients (1.0% of patients; 0.9% of cases) had serious embolic complications (including 4 deaths)<sup>19</sup>. There are no well-documented cases of serious bleeding problems after dental surgery in patients therapeutically anticoagulated with warfarin. A comprehensive review of more than 2014 dental surgical procedures (including more than 1964 dental extractions in 774 patients receiving continuous oral anticoagulant therapy) from 26 case reports and studies has revealed that in most cases no change in the intensity of anticoagulant therapy was needed<sup>19</sup>. These procedures included both single and multiple extractions, surgical extractions and alveolectomies. The risk of bleeding after dental surgery in patients on therapeutic levels of anticoagulation is minimal<sup>19,20</sup>. The value of INR at therapeutic dose does not significantly influence the incidence of post-

operative bleeding<sup>21,22</sup>. Local measures (Table 1) are important to protect the soft tissues and operative area, and to minimize the risk of bleeding. If there is the need to control local bleeding, inhibitors of fibrinolysis such as tranexamic acid mouthwash or *e*-aminocaproic acid mouthwash have been successfully used without anticoagulant therapy discontinuation<sup>23,24</sup>. The efficacy of gelatin sponge<sup>25</sup>, sutures<sup>26</sup> and fibrin glue<sup>27,28</sup> has also been reported. Suturing is desirable to stabilize gum flaps and to prevent postoperative wound irritation by eating<sup>29</sup>.

*Table 1. Local measures to control bleeding after dental procedures in patients receiving oral anticoagulant therapy*

Local pressure with gauze packs
Gelatin sponge
Fibrin glue
Sutures
Tranexamic or <i>e</i> -aminocaproic acid

### *Antiplatelet Drugs*

ASA is the most widely used therapeutic agent in the prevention of vascular ischemic events. ASA irreversibly decreases platelet aggregation by inhibition of thromboxane A<sub>2</sub> (TXA<sub>2</sub>). In patients receiving up to 100 mg ASA, there are no significant bleeding problems.

Adenosine diphosphate (ADP) receptor antagonists (clopidogrel and ticlopidine) are orally administered thienopyridine derivatives that inhibit platelet function by inhibiting the binding of ADP to one of its receptors<sup>30,31</sup>. Neither clopidogrel nor ticlopidine prolong the bleeding time, and they have little effect on postoperative bleeding<sup>32</sup>. Patients taking these drugs may undergo invasive dental procedures without altering the dosage<sup>33</sup>. If major oral surgery is planned and excessive bleeding is anticipated, clopidogrel should be discontinued for 7 days prior to surgery<sup>34</sup>.

### **Conclusion**

Many physicians and dentists recommend interrupting continuous oral anticoagulant therapy for a few days before dental surgery to prevent bleeding. There are several documented cases of thromboembolic events, including deaths, in patients whose anticoagulant therapy was withdrawn for dental treatment. On the other hand, although theoretically possible, there are no well-

documented cases of serious bleeding complications after dental surgery in patients receiving oral anticoagulant therapy within therapeutic range.

Current data suggest that in patients on therapeutic levels of anticoagulation dental surgery can be safely managed without stopping or altering their anticoagulant therapy. The procedure should be done with as little trauma as possible and by minimizing the necessity of multiple extractions. Local hemostasis with tranexamic acid or  $\epsilon$ -aminocaproic acid, gelatin sponge, fibrin glue and/or sutures appears to be sufficient if excessive post-operative bleeding occurs.

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### Sažetak

#### STOMATOLOŠKI ZAHVATI U BOLESNIKA LIJEČENIH PROTUZGRUŠAVAJUĆOM TERAPIJOM

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Prošireno je mišljenje među liječnicima i stomatolozima da se oralna protuzgrušavajuća terapija mora prekinuti prije i kroz neko vrijeme nakon stomatoloških zahvata. Ova navika može povećati rizik od moguće za život ugrožavajuće tromboembolije. Sadašnja literatura ne podupire rutinski prekid protuzgrušavajuće terapije u stomatoloških bolesnika. U bolesnika na protuzgrušavajućoj terapiji u terapijskim vrijednostima nakon zubnog zahvata teorijski postoji minimalan rizik od krvarenja, dok prekidom protuzgrušavajuće terapije rizik može biti znatno veći zbog moguće tromboembolije. Stoga se vađenje zuba može izvesti bez promjene protuzgrušavajuće terapije. U većine bolesnika je lokalna hemostaza želatinoznom spužvom, fibrinskim ljepilom, šavovima i/ili ispiranje usne šupljine traneksamičnom ili epsilon amino kaproičnom kiselinom dostatno da spriječi poslijeoperacijsko krvarenje.

*Ključne riječi: Antikoagulansi – terapijska primjena; Stomatološki zahvati – štetni učinci; Gubitak krvi, kirurški – prevencija i kontrola; Antikoagulansi – kontraindikacije; Tromboembolija – prevencija i kontrola; Oralno krvarenje – prevencija i kontrola*