

## Dental management of patients receiving anticoagulant therapy

Nasser Nooh, BDS, MS, DSc, OMFS

عندما تتم جدولة المريض لإجراء عملية جراحية صغرى . يظهر السؤال التالي. ماذا يجب ان نفعّل بعلاج المضاد لتخثر الدم؟ نواجه صعوبه بين خطر وقف العلاج مما قد يؤدي الى حدوث تخثر للدم او الاستمرار بالعلاج وحدوث نزيف بعد العمليه. إن إيقاف العلاج قد يؤدي الى حالات وفات. واحتمال حدوثها ثلاث اضعاف عند المرضى الذين يوقفون علاج التخثر مقارنة بحالات النزيف إذا لم يوقف علاج مضاد للتخثر. هذه المقالة توضح كيفية علاج اسنان المرضى الذين يتعاطون علاج مضاد للتخثر.

When patient are scheduled for minor oral surgery procedure, a question is raised, what should we do with the Oral Anti Coagulant (OAC) therapy? We face the dilemma between the risk of discontinuing the medication and patient developing thrombosis or the continuation of the medication and patient bleeding postoperatively. Serious embolic complications, including death, were three times more likely to occur in patients whose anticoagulant therapy was interrupted than were bleeding complications in patients whose anticoagulant therapy was continued. This article reviews the dental management of patients on oral anticoagulant therapy.

### INTRODUCTION

Oral anticoagulant therapy (OAC) has been used to decrease the risk of thromboembolism. Dental treatment on anticoagulated patients has been controversial and physicians must weigh the risks of haemorrhage from the dental procedure against the risks of emboli from withdrawing anticoagulation treatment.<sup>1,2</sup> Warfarin is the main medication used in OAC therapy, ranked no. 29 among the top 200 prescribed medications in the USA.<sup>3</sup>

#### Warfarin

The discovery of warfarin goes back to the beginning of 1920 when a cattle farmer noticed that his cattle died because of unknown bleeding. In 1924, Schofield, a veterinarian, discovered that the cause of bleeding was the sweet clover which the animal ate.<sup>4</sup> In 1940, Karl Paul Link, a veterinarian from University of Wisconsin studied this sweet clover and they isolated the active compound and named it WARFARIN.

Warfarin stands for Wisconsin Alumina Research Foundation and they

added 'ARIN' to link it to Coumarin, because Warfarin is 4-hydroxycoumarin derivative. It is a vitamin K analogue, rapidly and completely absorbed one hour after ingestion with a half life of 36 hours. Warfarin is also known under the name Coumarin. It was approved to be used in humans in 1950 as oral anticoagulant therapy.

Warfarin is an antagonist of vitamin K, an element necessary for synthesis of clotting factors II, VII, IX and X, as well as the naturally occurring endogenous anticoagulant proteins C and S. These factors and proteins are biologically inactive without the carboxylation of certain glutamic acid residues. This carboxylation process requires a reduced vitamin K as a cofactor. Antagonism of vitamin K or a deficiency of this vitamin reduces the rate at which these factors and proteins are produced, thereby creating a state of anticoagulation.<sup>5</sup> Warfarin has two functions: anticoagulant activity and antithrombotic effect. Therapeutic doses of warfarin reduce the production of functional vitamin K dependent clotting factors by approximately 30 to 50 percent. A concomitant reduction in the carboxylation of secreted clotting factors yields a 10 to 40 percent decrease in the biologic activity of the clotting factors. As a result, the coagulation system becomes functionally deficient.<sup>5</sup>

Assistant Professor  
Department of Maxillofacial Surgery  
and Diagnostic Sciences  
College of Dentistry, King Saud University  
P.O. Box 60169, Riyadh 11545, Saudi Arabia

### International Normalized Ratio (INR)

The bleeding time, prothrombin time (PT) and activated partial thromboplastin time (APTT), have been the standards by which clinicians evaluate anticoagulation levels. Nevertheless, an international normalized ratio (INR) was introduced in 1983 by the World Health Organization Committee on Biological Standards to assess patients receiving anticoagulation therapy more accurately.<sup>6</sup>

INR is the patient prothrombin time (PT) divided by the standard prothrombin time of the laboratory, raised to the power of the international sensitivity index value (ISI).  $INR = (\text{patient PT} / \text{mean normal PT})^{ISI}$ . It is a more reliable and sensitive value for determining the level of anticoagulation because it depends on the patient's blood and on the sensitivity of the thromboplastin reagent and the assigned ISI value. Therefore, PT may not be the laboratory value of importance when evaluating the level of anticoagulation.<sup>6</sup>

A patient with a normal coagulation profile would have an INR of 1.0. It is recommended that a patient undergoing invasive treatment should have a PT within 1.5 to 2.0 times the normal value, and this corresponds to an INR of 1.5 to 2.5 when the ISI is 1.0.<sup>5</sup> In patients with anticoagulant therapy, an INR between 2.0 and 3.0 is recommended for most indications. Thus, an INR of 2.5 (range 2.0 to 3.0) minimizes the risk of either haemorrhage or thromboembolism.<sup>5</sup> Optimal therapeutic ranges for anticoagulation were established in the late 1980s and recommended that the INR value be between 2.0 and 3.0 for most anti-coagulation regimens, and in the range of 3.0 to 4.0 for patients with mechanical heart valves and/or a history of recurrent embolism.<sup>7,8</sup>

Many physicians recommend interrupting continuous anticoagulant therapy for dental surgery to prevent haemorrhage. In reviewing the available

literature, there are no well-documented cases of serious bleeding problems from dental surgery in patients receiving therapeutic levels of continuous warfarin sodium therapy, but there were several documented cases of serious embolic complications in patients whose warfarin therapy was withdrawn for dental treatment.<sup>9</sup> Many authorities state that dental extractions can be performed with minimal risk in patients who are at or above therapeutic levels of anticoagulation. Although, there is a theoretical risk of haemorrhage after dental surgery in patients who are at therapeutic levels of anticoagulation, the risk appears to be minimal, the bleeding usually can be easily treated with local measures, and this risk may be greatly outweighed by the risk of thromboembolism after withdrawal of anticoagulant therapy.<sup>10,11</sup>

In the past, haematologist used to recommend stopping warfarin for 3 days and starting the patient on heparin to deliver any minor oral surgical procedure. In January 2006, the National Patient Safety Agency (NPSA) published a risk assessment of oral and injectable anticoagulant therapy. They suggested that dental management of patient as one of the risk of OAC therapy and advocated the dentists to follow the recommended guidelines.<sup>12</sup>

A question always comes up, what type of dental works are considered minor oral procedure? Some have recommended the following, extraction up to three teeth, endodontic, gingival surgery and scaling, and surgical removal of a tooth. The subgingival debridement may cause significant bleeding.<sup>13</sup>

### Anticoagulation Therapy and Oral Surgery

The risk of stopping warfarin is greater than the complications that may arise from continuing it during minor surgical procedures. Wahl<sup>14</sup> showed that 1% of the

patient who stopped warfarin died because of embolic complications. In a survey among 950 patients receiving continuous anticoagulant therapy who underwent more than 2,400 surgical procedures, only 12 (1.3%) needed more than local measures to control haemorrhage.<sup>2</sup>

Many authors have suggested that stopping warfarin may lead to rebound coagulation effects.<sup>15,16</sup>

In a clinical study, Devani *et al.*<sup>17</sup> compared the effect of short term (2-3 days) stopping of warfarin on dental extractions with an average INR 1.6 with the control group who continued warfarin with an average INR 3. They found that only one patient from each group had bleeding which was not fatal. This showed that when patient stopped warfarin, the outcome was similar to the group which continued the warfarin.

Evans *et al.*<sup>18</sup> had two groups of patients who underwent dental extraction. Group one (57 patients) continued the medication with INR average of 2.5. Group two (52 patients) stopped OAC with INR average 1.6. There were no significant difference between the two groups, only two patients from group one required hospital visit and none were fatal. Beirne and Koehler<sup>19</sup> concluded that with proper local measures, teeth can be extracted safely for patients taking OAC therapy. Sindet-Pederson *et al.*<sup>20</sup> studied the hemostatic effect of tranexamic acid mouthwash after oral surgery in 39 patients receiving anticoagulant agents because of the presence of cardiac valvular stenosis, a prosthetic cardiac valve, or a vascular prosthesis. Out of the 39 patients with INR 2.5 - 4.8, only one patient had bleeding which could be stopped by local measures and none was fatal.

Campbell *et al.*<sup>21</sup> examined 12 patients with INR 1.2 - 2.9, only one patient had bleeding and was controlled by local measures. Zanone *et al.*<sup>11</sup> observed among 250 patients with INR 1.8-4, only

4 patients bleed and they were controlled by local measures. Cannon *et al.*<sup>22</sup> have 35 patients INR 2-4 only two patient bleed and it was controlled by local measures.

Sacco *et al.*<sup>23</sup> had 65 patients who underwent dental extraction with INR ranging from 2.5 - 3.3, only six patients had bleeding and were all controlled. Blinder *et al.*<sup>24</sup> performed 543 extractions on 249 patients which were divided according to the INR level (Table 1).

**Table 1.** Dental extractions in patients maintained on oral anticoagulant therapy: Comparison of INR value with occurrence of postoperative bleeding (Adopted from Blinder *et al.*<sup>24</sup>)

Groups	INR level	Patients number	Bleeding incidence
Group 1	1.5-1.99	59	3 patients
Group 2	2.0-2.49	78	10 patients
Group 3	2.5-2.99	59	9 patients
Group 4	3.0-3.49	80	5 patients
Group 5	Above 3.5	23	3 patients

Morimoto *et al.*<sup>25</sup> examined 270 patients with oral antithrombotic therapy. Out of the 513 extractions of teeth, only 7 patients had bleeding which can be controlled by local measures. They recommended to do extraction if INR is less than 3. Ferrieri *et al.*<sup>26</sup> had 255 patients with INR less than 5.5, only five patients bleed, one patient started bleeding five days postoperatively. Salam *et al.*<sup>27</sup> studied the incidence of bleeding after dental extractions in subjects taking warfarin continuously before and after extractions whose INR was below 4.0 at the time of extraction. One hundred fifty patients underwent dental extractions. The first group had 101 patients with INR less than 2.5 and the second group with INR more than 2.5. Five patients in each

group had bleeding which was managed conservatively and was not fatal.

Several studies<sup>11,17,20,28,29</sup> recommended that extractions can be carried out with an INR less than 4. However, Barrero *et al.*<sup>30</sup> and Al-Mubarak *et al.*<sup>31,32</sup> recommended INR to be less than 3. Majority of the studies<sup>33,34</sup> recommended that warfarin may be continued during dental extraction. Lim *et al.*<sup>35</sup> did a survey of oral/maxillofacial surgeons and haematologist in Canada and found that 70% of haematologist will discontinue warfarin 4.4 days preoperatively and only 37% of the maxillofacial surgeons will stop it 3.2 days preoperatively. Malden *et al.*<sup>36</sup> examined the INR before and after dental surgery in 71 patients and found that an increase in the INR postoperatively averaged 0.21.

### Recommendations

The new recommendation calls for continuing the OAC therapy and continuing the dental extraction. All studies agreed that the INR could be less than 3. However, some studies recommended the INR to be less than 4. All authors agreed that the most important was the local measures. A traumatic dental procedure combined with instructing the patient to apply pressure on the surgical site is essential. Suturing of the site, if needed, will add to control the bleeding and the application of surgical or collagen sponge or the use of 5% tranexamic acid mouthwash 4 times a day for two days was also recommended. In case of giving the patients one dose of prophylactic antibiotic, it is ok to continue the treatment and OAC therapy. In all patients, the INR must be checked preoperatively. Patients who are taking warfarin must not take Non Steroidal Anti Inflammatory Drugs (NSAID) and they should not take COX-2 inhibitor as analgesia.

If patients take warfarin and have liver impairments, renal failure,

thrombocytopenia, haemophilia or receiving cytotoxic medication, they should be investigated before any dental procedures. Most authors suggested that the risk of continuing the medication is far less than the risk of stopping it. Patients with unstable INR should be discussed with their INR managing team. If patients are to be given a course of antibiotic, their INR must be measured 2 - 3 days after they start the antibiotics.<sup>32</sup> Dental practitioners may prescribe prophylactic or therapeutic antibiotics only when it is absolutely necessary for the patients, particularly those receiving continuous anticoagulant therapy. Concomitantly administered antibiotics may interact with continuously administered anticoagulants, thus increasing patients' level of anticoagulation. This is especially true with multidose antibiotic therapy.

Dentists should advice their patients to continue therapeutic levels of anticoagulation, but if the patient and physician insist, then it should be the physician who withdraws the anticoagulant therapy and the dentist who performs the dentistry. Similarly, if more than local measures are required to control bleeding after dental surgery, the physician should be involved. Good surgical technique and appropriate local measures to control bleeding are important for all dental patients, especially those receiving continuous anticoagulant therapy.<sup>14</sup>

### CONCLUSIONS

Patients with a variety of medical conditions often receive continuous anticoagulant therapy with a vitamin K antagonist such as warfarin sodium to prevent complications from atrial fibrillation, thromboembolisms or stroke. Although continuous anticoagulant therapy can be lifesaving, it can also put patients at greater risk of experiencing haemorrhage after dental surgery.

Therefore, a decision must be made whether to interrupt or continue anticoagulant treatment in patients undergoing various dental procedures. It can be concluded that the optimal INR value for dental surgical procedures is 3 because it minimizes the risk of either haemorrhage or thromboembolism. Published data suggests that minor dental surgical procedures can be safely carried out on patients with an INR  $\leq$  4.0. The consensus from reviews on the management of dental patients taking warfarin was that minor dental surgical procedures should be carried out without alteration to the patient's warfarin therapy if the INR is within the therapeutic range (INR 2.0 – 4.0).

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