Treatment with local hemostatic agents and primary closure after tooth extraction in warfarin treated patients

ROGER SVENSSON1, FREDRIK HALLMER1,2, CHARLOTTA SAHLSTRÖM ENGLESSON1, PETER J. SVENSSON3, JONAS P. BECKTOR1

Abstract
The aim of this retrospective study was to assess the frequency of postoperative bleeding in patients on warfarin after tooth removal followed by a complete soft tissue closure of the surgical site.

A total of 124 consecutive patients, 69 males and 55 females with a mean age of 71 years (range 28-95 years) were included in this study. Inclusion criteria were patients on warfarin with an INR ≤ 3.5 who were referred for tooth removal (single or multiple) during 2004-2009. After tooth extraction all sockets were packed with an absorbable haemostatic gelatin sponge or a collagen fleece and subsequently the sockets was primary closed with sutures.

5/124 (4%) patients returned with postoperative bleedings. All patients with a postoperative bleeding had received a surgical extraction in the posterior part of the maxilla. Consequently no patient had a postoperative bleeding in the mandible. None of the 124 patients returned to the clinic with a dry socket or postoperative pain. 3/124 (2%) patients returned with postoperative infection that required antibiotic treatment. All patients who bled were managed conservatively and none was admitted to hospital.

Conclusion: According to the protocol of this study (local hemostatic, primary closure, sutures and tranexamic acid) the risk of postoperative bleeding after tooth removal in patients on continued warfarin medication is low.

Key words
Anticoagulants, tooth extraction, warfarin

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Behandling med lokalhemostatika och primärslutning efter tandextraktion hos warfarin-behandlade patienter

Roger Svensson, Fredrik Hallmer, Charlotta Sahlström Englesson, Peter J. Svensson, Jonas P. Becktor

Sammanfattning

Avsikten med denna retrospektiva studie var att fastställa frekvensen av postoperativ blödning efter tandextraktion hos patienter som behandlas med warfarin och postoperativt erhållit lokalhemostatika och primärsuturering.


5/124 (4 %) av patienterna återvände med postoperativ blödning. Samtliga patienter med postoperativ blödning hade genomgått kirurgisk extraktion posteriort i överkäken. Inga patienter fick blödningar i underkäken som krävde återbesök. Ingen av de 124 patienterna återvände till kliniken med alveolit eller postoperativ smärta.

3/124 (2 %) av patienterna kom tillbaka till kliniken med en postoperativ infektion som krävde antibiotikabehandling. Samtliga patienter med blödningar behandlades konservativt och ingen krävde inläggning.

Slutsats: Om man ger lokalhemostatika, primärsuturerar och ger tranexamsyra efter tandextraktion är risken för blödning hos patienter som står på Warfarin låg.
Introduction

Since six decades warfarin is a widely used oral anticoagulant in the treatment and prevention of venous and arterial thrombosis (10). Warfarin inhibits vitamin K dependent clotting factors which results in the liver producing and excreting partially carboxylated and decarboxylated coagulation proteins (11).

Modification or interruption of warfarin treatment before a dental extraction and when the patient is in the recommended therapeutic interval (2,7), does no longer seem to be necessary. The risk of a thromboembolism is considered a greater problem for the patient than a postoperative bleeding after a dental extraction (8,9). There is no fatal bleeding reported in the literature in association with continuation of warfarin and a dental extraction. But some patients have died in relation to withdra- wal of anticoagulants before dental extractions and the risk of thromboembolism has been reported in up to 71% of cases (21).

There are several papers on how warfarin and tooth removal should be managed. Several authors have shown that there is no increase in postoperative bleeding in patients with warfarin treatment, when they continue with the medication and use a protocol of postoperative rinsing with tranexamic acid, often in combination with other local hemostatic agents, and compression (5,16,22). Recent studies have shown that postoperative compression with biting on a gauze soaked in a tranexamic acid solution, instead of rinsing for several days with or without a combination of a local hemostatic agent, is sufficient in preventing postoperative bleeding (2,7,18).

The uses of local hemostatic agents such as gelatin sponge or oxidised regenerated cellulose are common in patients taking warfarin at tooth removal. Several studies are repeated and show similar results of postoperative bleeding (6,18,22). Complete avoidance of hemostatics is unusual (7). There is no international consensus on proper preoperative, peroperative and postoperative care of patients on warfarin.

The aim of this retrospective study was to assess the frequency of postoperative bleeding in patients on warfarin after tooth removal followed by a complete soft tissue closure of the surgical site.

Material and methods

Subjects

At the Department of Oral and Maxillofacial Surgery (OMFS), Skåne University Hospital, Malmö, Sweden, a total of 124 consecutive patients, 69 males and 55 females with a mean age of 71 years (range 28-95 years) were treated by the same oral and maxillofacial surgeon. Inclusion criteria were patients on warfarin with an International Normalized Ratio (INR) ≤ 3.5 who were referred for tooth removal (single or multiple) during 2004-2009. Patients with congenital bleeding disorders were excluded.

The INR value was measured within 24 hours before surgery. The INR mean value was 2.4 (range 1.0-3.5). The warfarin medication was not altered. In addition to warfarin 11 patients also received acetylsalicylic acid.

In total, 194 teeth were removed. Forty-eight patients had teeth removed because of advanced caries/apical periodontitis, 38 because of root rests/fractures and 28 because of marginal periodontitis. Medical data were collected from patient records and recorded on a standardised form.

Preoperative care

Xylocain® Dental adrenalin 20 mg/ml + 12.5 μg/ml was used for local anaesthesia. When the risk of endocarditis was increased 2g of amoxicillin or 600mg of clindamycin was given 1 hour preoperatively. The risk was considered increased when a patient had heart valve problems or an artificial heart valve, certain congenital heart defects or had a previous episode of infective endocarditis.

Peroperative care

The tooth removal was either a non-surgical procedure, not raising a flap, or a surgical procedure, raising a flap. Granulation tissue was thoroughly removed. Before suturing, one of two types of resorbable haemostatic dressings was placed in the alveolus. An absorbable haemostatic gelatin sponge (Spongostan®) was used in 64 patients and a hemostatic collagen fleece (TissuFleece E®) in 60 patients, subsequently the socket was closed with sutures (Vicryl Plus® 4/0).

When a non-surgical extraction was performed, the socket was closed with suturing of the adjacent soft tissue. If a primary closure was possible to obtain without raising a flap the socket was closed with suturing of the adjacent soft tissue. If primary closure was not achieved a mucoperiosteal flap was raised with or without a Rehrmann plasty (20) to cover the socket. In all cases where a mucoperiosteal flap was carried out, gauze soaked with tranexamic acid (Cyklokapron®, 1 g tablet dissolved in 10 ml of sterile saline) was placed under the flap for 5 minu-
After suturing. Twenty-seven patients received a Rehrmann plasty and the distribution of tooth removal and the number of teeth removed in the different tooth groups is presented in Tables 1 and 2. Consequently, all tooth removals were followed by a complete soft tissue closure of the surgical site.

Postoperative care
The patients were instructed to bite on gauze that was soaked in tranexamic acid for 60 minutes postoperatively. Paracetamol (acetaminophen) was recommended, when needed. The patients left the OMFS clinic after the surgery was completed. Patients were instructed to contact the hospital if uncontrolled bleeding would appear. As review appointments were not compulsory it is possible that minor bleedings might have occurred without being reported to the department of OMFS and consequently such bleedings are not included in this study.

Result
5/124 (4%) (95% CI 1.5-9.3) patients returned with postoperative bleedings. The group consisted of 3 males and 2 females with a mean age of 67 years. The bleedings occurred after 2, 4, 6, 7 and 10 days respectively after tooth removal. Patient number 5, (Table 3,) had 2 postoperative bleedings, the first on day 2 and the second on day 6 after tooth removal. In addition to warfarin two patients also medicated with acetylsalicylic acid.

Characteristics of the patients who returned with a postoperative bleeding are presented in table 3. All patients with a postoperative bleeding had received a surgical extraction in the posterior part of the maxilla, Table 3. Consequently no patient had a postoperative bleeding in the mandible. Three of the five patients with postoperative bleeding had multiple teeth removed. Furthermore, Rehrmann plasty was performed in 3 patients, where the bleeding in one patient was from the releasing incision.

None of the patients returned to the clinic with a dry socket or postoperative pain. 3/124 (2%) patients returned with postoperative infection that required antibiotic treatment. None of the patients in the present study had a postoperative bleeding that required hospitalisation, blood transfusions or drug administration. Local hemostatic measures were sufficient to stop the bleeding. No thromboembolic events were reported in any patient.

Discussion
This study supports other studies in the findings that warfarin does not have to be suspended when

<table>
<thead>
<tr>
<th>Patient</th>
<th>Gender</th>
<th>INR preoperative</th>
<th>ASA</th>
<th>Teeth removed</th>
<th>Tooth diagnosis</th>
<th>Type of tooth removal</th>
<th>Localisation of bleeding (tooth)</th>
<th>Rehrmann plasty (Yes/No)</th>
<th>Day of postoperative bleeding</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>Male</td>
<td>2.1</td>
<td>No</td>
<td>Teeth 37,12,15</td>
<td>Caries/Apical periodontitis</td>
<td>Surgical extraction</td>
<td>15</td>
<td>No</td>
<td>10</td>
</tr>
<tr>
<td>2</td>
<td>Female</td>
<td>2.8</td>
<td>No</td>
<td>Tooth 17</td>
<td>Marginal periodontitis</td>
<td>Surgical extraction</td>
<td>17</td>
<td>Yes</td>
<td>4</td>
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<tr>
<td>3</td>
<td>Female</td>
<td>2.8</td>
<td>No</td>
<td>Teeth 32,33,25,26</td>
<td>Caries/Apical periodontitis</td>
<td>Surgical extraction</td>
<td>25</td>
<td>No</td>
<td>6</td>
</tr>
<tr>
<td>4</td>
<td>Male</td>
<td>3.0</td>
<td>Yes</td>
<td>Tooth 28</td>
<td>Caries/Apical periodontitis</td>
<td>Surgical extraction</td>
<td>28</td>
<td>Yes</td>
<td>7</td>
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<tr>
<td>5</td>
<td>Male</td>
<td>2.5</td>
<td>Yes</td>
<td>Tooth 16,24</td>
<td>Caries/Apical periodontitis</td>
<td>Surgical extraction</td>
<td>16</td>
<td>Yes</td>
<td>2</td>
</tr>
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Table 4. Examples of variation of different local hemostatic measures and postoperative bleeding

<table>
<thead>
<tr>
<th>Authors</th>
<th>Type of study design</th>
<th>Test group</th>
<th>Control group</th>
<th>Test group</th>
<th>Control group</th>
<th>Test group</th>
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<th>Control group</th>
<th>Test group</th>
<th>Control group</th>
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<tbody>
<tr>
<td>Devani et al. 1998</td>
<td>Prospective, CCT</td>
<td>33/69</td>
<td>32/64</td>
<td>33/69</td>
<td>32/64</td>
<td>33/69</td>
<td>32/64</td>
<td>33/69</td>
<td>32/64</td>
<td>33/69</td>
<td>32/64</td>
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<tr>
<td>Evans et al. 2002</td>
<td>RCT</td>
<td>57/2/pat</td>
<td>52/3/pat</td>
<td>57/2/pat</td>
<td>52/3/pat</td>
<td>57/2/pat</td>
<td>52/3/pat</td>
<td>57/2/pat</td>
<td>52/3/pat</td>
<td>57/2/pat</td>
<td>52/3/pat</td>
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<td>Ferrieri et al. 2007</td>
<td>Case series</td>
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<td>255/n/a</td>
<td>255/n/a</td>
<td>255/n/a</td>
<td>255/n/a</td>
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<td>255/n/a</td>
<td>255/n/a</td>
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<td>Carter et al. 2003</td>
<td>Prospective, RCT</td>
<td>43/97</td>
<td>42/104</td>
<td>43/97</td>
<td>42/104</td>
<td>43/97</td>
<td>42/104</td>
<td>43/97</td>
<td>42/104</td>
<td>43/97</td>
<td>42/104</td>
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<tr>
<td>Sacco et al. 2007</td>
<td>Prospective, RCT</td>
<td>65/511</td>
<td>66/511</td>
<td>65/511</td>
<td>66/511</td>
<td>65/511</td>
<td>66/511</td>
<td>65/511</td>
<td>66/511</td>
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<tr>
<td>Blinder et al. 1999</td>
<td>Prospective, CCT</td>
<td>50/119</td>
<td>50/117</td>
<td>50/119</td>
<td>50/117</td>
<td>50/119</td>
<td>50/117</td>
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<td>50/117</td>
<td>50/119</td>
<td>50/117</td>
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</table>

Table 4. Examples of variation of different local hemostatic measures and postoperative bleeding

<table>
<thead>
<tr>
<th>Authors</th>
<th>Type of study design</th>
<th>Patients</th>
<th>Teeth extracted</th>
<th>INR (mean)</th>
<th>Age (mean)</th>
<th>Local haemostatic agent</th>
<th>Sutures</th>
<th>Tranexamic acid</th>
<th>Compression</th>
<th>Bleeding (patients)</th>
<th>Day of postoperative bleeding after dental extraction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Devani et al. 1998</td>
<td>Prospective, CCT</td>
<td>Test group</td>
<td>33/69</td>
<td>2.2-3.9</td>
<td>30-82</td>
<td>Surgicel</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>1 (3.0%)</td>
<td>2</td>
</tr>
<tr>
<td>Zanon et al. 2003</td>
<td>Prospective, CCT</td>
<td>Test group</td>
<td>250/525</td>
<td>1.8-4.0</td>
<td>44-88</td>
<td>Spongostan</td>
<td>Yes</td>
<td>For postoperative compression 30-60min</td>
<td>Yes</td>
<td>4 (1.6%)</td>
<td>2</td>
</tr>
<tr>
<td>Evans et al. 2002</td>
<td>RCT</td>
<td>Test group</td>
<td>57/2/pat</td>
<td>2.5-4.7</td>
<td>36-92</td>
<td>Surgicel</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>15 (26%)</td>
<td>n/a</td>
</tr>
<tr>
<td>Ferrieri et al. 2007</td>
<td>Case series</td>
<td>Test group</td>
<td>255/n/a</td>
<td>1.3-5.4</td>
<td>27-89</td>
<td>In some cases for postoperative compression</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>5 (2.0%)</td>
<td>12 hours-5 days</td>
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<tr>
<td>Bacci et al. 2010</td>
<td>Prospective, CCT</td>
<td>Test group</td>
<td>451/921</td>
<td>1.8-4.0</td>
<td>38-89</td>
<td>Oxidised cellulose</td>
<td>Yes</td>
<td>For postoperative compression 30-40min</td>
<td>Yes</td>
<td>7 (1.6%)</td>
<td>2-6</td>
</tr>
<tr>
<td>Carter et al. 2003</td>
<td>Prospective, RCT</td>
<td>Test group</td>
<td>43/97</td>
<td>2.7-4.0</td>
<td>21-77</td>
<td>Surgicel</td>
<td>Yes</td>
<td>4.8% Rinsing 2 days postoperative</td>
<td>n/a</td>
<td>2 (4.7%)</td>
<td>0-2</td>
</tr>
<tr>
<td>Carter et al. 2003</td>
<td>Prospective, RCT</td>
<td>Test group</td>
<td>42/104</td>
<td>2.8-4.0</td>
<td>26-86</td>
<td>Surgicel</td>
<td>Yes</td>
<td>4.8% Rinsing 5 days postoperative</td>
<td>n/a</td>
<td>1 (2.4%)</td>
<td>0-2</td>
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<td>Carter et al. 2003</td>
<td>Prospective, RCT</td>
<td>Test group</td>
<td>26/71</td>
<td>3.0-4.0</td>
<td>24-85</td>
<td>Surgicel</td>
<td>Yes</td>
<td>4.8% Rinsing 7 days postoperative</td>
<td>n/a</td>
<td>0</td>
<td>n/a</td>
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<tr>
<td>Sacco et al. 2007</td>
<td>Prospective, RCT</td>
<td>Test group</td>
<td>65/511</td>
<td>2.89-4.2</td>
<td>29-86</td>
<td>Gelatin/ oxidized cellulose sponges</td>
<td>Yes if indicated</td>
<td>Yes</td>
<td>6 (9.2%)</td>
<td>2-3</td>
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<tr>
<td>Blinder et al. 1999</td>
<td>Prospective, CCT</td>
<td>Test group 1</td>
<td>50/119</td>
<td>1.5-4.0</td>
<td>40-86</td>
<td>Gelatin sponge</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>10 (15.1%)</td>
<td>2</td>
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<tr>
<td>Salam et al. 2007</td>
<td>Retrospective, Case series</td>
<td>Test group</td>
<td>150/279</td>
<td>0.9-4.2</td>
<td>33-92</td>
<td>Surgicel</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>10 (6.7%)</td>
<td>n/a</td>
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<tr>
<td>Morimoto et al. 2008</td>
<td>Prospective, Case series</td>
<td>Test group 1</td>
<td>134/278</td>
<td>1.5-4.0</td>
<td>59.0</td>
<td>Surgicel</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>7 (4.4%)</td>
<td>n/a</td>
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<td>Morimoto et al. 2008</td>
<td>Prospective, Case series</td>
<td>Test group 2</td>
<td>49/91</td>
<td>1.5-3.0</td>
<td>62.9</td>
<td>Surgicel</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>2 (3.9%)</td>
<td>n/a</td>
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<tr>
<td>Morimoto et al. 2008</td>
<td>Prospective, Case series</td>
<td>Test group 3</td>
<td>87/144</td>
<td>n/a</td>
<td>61.4</td>
<td>Surgicel</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>2 (2.2%)</td>
<td>n/a</td>
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</table>
patients are in their therapeutic range and require a tooth removal (2,7,12,17,21,22).

The recommended therapeutic INR range in Sweden is 2.0-3.0 for all medical diagnosis. The literature, confirms that the rate of postoperative bleeding after tooth removal in patients on warfarin is low when the INR is ≤3.5 and local hemostatic management are instituted, Table 4. In addition, a number of articles confirm that even a higher INR than 3.5 is possible when a tooth removal is required, Table 4. Blinder et al. (3) did not find a statistical significant correlation between preoperative INR value and incidence of postoperative bleeding. Malden et al. (13) found a significant difference in INR before and after surgery when multiple extractions and surgical removals were compared with single extractions. The INR is known to fluctuate e.g. in relation to diet habits and medicine intake (14,19).

Regarding the use of local hemostatic procedures, the literature is not homogenous. The majority of published studies use one or several local hemostatics to compensate for the anticoagulant effect of warfarin, and thereby prevent a postoperative bleeding.

The majority of studies on the incidence of postoperative bleeding have used a local hemostatic agent that is placed in the alveolus and all these studies have had a very low incidence of postoperative bleeding, Table 3. However, Ferrieri et al. (7) did not use a local hemostatic agent placed in the alveolus and showed a low incidence of postoperative bleeding.

Sutures are mostly used after a surgical extraction but also to hold a local hemostatic agent in place in the alveolus. Al-Mubarak et al. (1) investigated postoperative bleeding in 214 patients in relation to INR value and the role of suturing. Only non-surgical extractions were performed. Suturing resulted in a higher incidence of postoperative bleeding compared to when not suturing.

Tranexamic acid has an antifibrinolytic effect and several studies have investigated its clinical effect on postoperative bleeding after tooth extraction in patients on anticoagulant treatment. Carter et al. (5) noted that there was no statistical difference in the risk of postoperative bleeding, when patients rinsed with tranexamic acid for 2 days versus 5 days. The drug is used for rinsing or as a solution to soak gauze used for compression postoperative. The use of gauze soaked in a tranexamic acid solution for compression is an alternative for preventing a postoperative bleeding.

Ferrieri et al. (7) only used sutures and compression, with or without tranexamic acid, as local hemostatic procedures with a low incidence of postoperative bleedings.

In the present study, all patients with postoperative bleeding received a surgical extraction in the premolar/molar region of the maxilla. This is in accordance with a review by Rodriguez-Cabrera et al. (17). They concluded that there was a tendency for a higher incidence of postoperative bleeding from the maxilla versus the mandible. Four of the 5 patients with a postoperative bleeding had their teeth removed because of caries/apical periodontitis and one because of marginal periodontitis. Blinder et al. (4) concluded that there was a higher tendency of a postoperative bleeding when a tooth diagnosed with periodontitis was extracted. A higher incidence of postoperative bleeding in the presence of an acute inflammation in the surgical region has been verified (14).

Three patients out of 5 had multiple extractions performed but postoperative bleeding only occurred from one site. This is in accordance with Blinder et al. (4).

The objective of the peroperative procedure in this study was to achieve complete soft tissue closure of the extraction socket by suturing. When needed a Rehrmann plasty was performed. When primary closure was performed after tooth removal the incidence of postoperative bleeding in this study was 4%. This is in accordance with Sacco et al. (18) who at primary closure noted that 9.2% returned with postoperative bleeding. Other articles have shown that the incidence of postoperative bleeding is 0.9%-2.2% when the patient is not using warfarin (2,15,22).

Conclusion

According to the protocol of this study the risk of postoperative bleeding after tooth removal in patients on continued warfarin medication is low. Gentle handling of the soft and hard tissues has to be the standard when performing tooth removals in patients on warfarin. But the minimum measures that have to be taken for sufficient homeostasis has not yet been established. There is a need for prospective randomised controlled trials, where each step has to be evaluated.

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References


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