

EFFECT OF COLLAPLUG® ON THE HEALING OF EXTRACTION SOCKETS IN PATIENTS UNDER ORAL ANTICOAGULANT THERAPY (CLINICAL STUDY)

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Abstract:

Introduction: Dentists perform a variety of surgical procedures frequently requiring the need for a hemostatic agent, in cases where oral anticoagulants are used. Most cases of postoperative bleeding are easily treated with local measures such as packing with a haemostatic dressing, suturing and pressure.

Objectives: We aimed to evaluate the efficacy of Collaplug® in minimizing postoperative bleeding and pain following tooth extraction in patients under oral anticoagulant therapy.

Materials and methods: A prospective study was conducted on a total of 40 adult patients under oral anticoagulant therapy, who needed tooth extraction. Patients were divided equally into two groups, each group consisting of 20 patients. Group A (Study group): the extraction of the tooth was followed by the application of Collaplug® prior to suturing of the socket. Group B (Control group): the extraction of the tooth was followed by suturing only.

Results: A total of 40 patients 21 female (52%) and 19 (48%) male, aged between 30 and 60 years were included in the present study. All patients underwent simple tooth extraction. In the study group: there was a clinical significance in cessation of bleeding 2 hours and 6 hours after extraction than the control group. All patients of study and control groups had their international normalized ratio (INR) ≤ 3 within the therapeutic range.

Conclusion:

The study concluded that Collaplug® is an effective local hemostatic material following minor oral surgery in patients under oral anticoagulant therapy, also shows acceleration of soft tissue healing and reduce postoperative pain.

Key Words: Extraction, collagen sponge, local hemostasis, warfarin, anticoagulants.

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INTRODUCTION

Despite advances in surgical technique, bleeding remains one of the major complications associated with surgery and may lead to poor clinical outcomes. The risk of bleeding is increased in patients taking anticoagulants or antiplatelet agents, those with underlying intrinsic bleeding disorders, or those with specific problems, including diabetes mellitus, hypertension, and renal insufficiency (1,2). Further, primary complications of surgery, such as infection, can lead to the development of disseminated intravascular coagulation and widespread diffuse bleeding (1).

Many patients taking coumarin derivatives, such as warfarin, present to the oral and maxillofacial surgeon need to extract their teeth. The surgeon is faced with the choice of altering or stopping warfarin and risking thromboembolism or leaving the patient on the warfarin and risking uncontrolled bleeding (3).

Warfarin, which acts by antagonizing the effect of vitamin K, is one of the most commonly used oral anticoagulants. The drug can be absorbed completely and reaches its peak in 1 hour after ingestion (4). Albumin is bound to circulating warfarin, and the half-life of warfarin is approximately 36 hours (5). The liver metabolizes warfarin into inactive compounds, which are then excreted, mainly into the urine. Warfarin has been used to decrease the thromboembolism in millions of patients worldwide (4,5).

Its effect is measured by international normalized ratio (INR), which is a measure of patient's prothrombin time divided by the laboratory control value of prothrombin

time (6). The level of INR suitable for the patient depends on the condition of the patient. The recommended INR level according to the American College of Chest Physicians is between 2.0 and 3.0 for most conditions; however, patients using prosthetic heart valves may require higher level of INR (7).

Many reports stated that patients requiring a minor dental procedure and having an INR of up to 4.0 are able to continue warfarin without any dose adjustment (6,8,9). It has, however, been debated whether stopping warfarin can increase the risk of cerebrovascular accidents (CVA) (10).

Most bleeding tendencies resulting from the use of anticoagulants (11), usually prescribed to treat a number of cardiac or vascular disorders, including atrial fibrillation, ischemic cardiac disease, cardiac valvular disease, prosthetic cardiac valves, post-myocardial infarction, deep venous thrombosis, pulmonary embolism, cerebrovascular accident, and many others (12-14).

Assessing both risks and benefits is very important in patients receiving warfarin, and a very close communication and consultation with the patient's physician regarding the best management is critical (7).

Various local measures to control bleeding in patients on warfarin treatment are available, including local hemostatic agents, suturing, and tranexamic acid (9,10).

Local measures such as Bone wax which is a sterile mixture of beeswax, paraffin, and isopropyl palmitate (15). Mild inflammatory reactions have been reported in tissues adjacent to the site of Bone Wax implantation (15).

Gelfoam® is one of the more commonly employed agents for the control of minor bleeding. It is a porous, pliable sponge made from dried and sterilized porcine skin gelatin. It is believed to be related to formation of a mechanical matrix that facilitates clot formation (16).

Collagen-based agents were introduced in 1970 (17). The hemostatic collagen products in general are: soft, pliable, non-friable, coherent and sponge-like structures. They are fabricated from bovine collagen (15).

Collaplug® derived from bovine deep flexor tendons due to its rod-shape form, was found to be used in the extraction sites, 4-wall sockets and biopsy sites (18,19). It is an absorbable wound dressing, because of the coherent sponge structure, application of the dressings to the wound is easily controlled (18).

In this study, we aimed to evaluate the efficacy of Collaplug® in minimizing postoperative bleeding and pain following tooth extraction in patients under oral anticoagulant therapy.

MATERIALS AND METHODS

All patients included in this study were undergoing warfarin treatment and were referred to the Department of Oral and Maxillofacial Surgery (OMF) for simple dental extraction, with age ranging from 30 to 60 years old, each patient was informed about the aim of the study and gave informed consent, medical and surgical history was taken from the patients, all patients were purely under oral anticoagulant treatment, their $INR \leq 3$ as shown in table (1).

Exclusion criteria: any patient beyond the age range, patients with $INR > 3$, patients with uncontrolled arterial blood pressure, and any patient who refused to sign the consent or otherwise refused to participate in the study.

Table (1): INR (International normalized ratio).

INR	Control group	Study group	χ^2	MCp
0-0.9	0	1	3.963	0.110
1-1.9	14	8		
2-3	6	11		

χ^2 : Value for Chi square

MC: Monte Carlo test

The study was conducted on a total number of 40 adult patients treated with oral anticoagulant therapy, who were indicated for tooth extraction, in order to evaluate the efficacy of Collaplug® in minimizing postoperative bleeding and pain following tooth extraction in patients under oral anticoagulant therapy, patients were divided equally into two groups, each consisting of 20 patients.

Group (1) study group

Physicians did not stop any of the anticoagulant therapies of the patients. In addition, their INR within the therapeutic range ≤ 3 .

Non surgical extraction was done then application of local hemostatic material Collaplug® in the extracted socket and wound suturing.

Group (2) Control group

Physicians did not stop any of the anticoagulant therapies of the patients. In addition, their INR within the therapeutic range ≤ 3 .

Non surgical extraction was done, then suturing using atraumatic round needle.

Materials:

Collaplug® is fabricated from bovine collagen (Collaplug® produced by zimmer dental 1900 Aston Avenue Carlsbad, CA 92008-7308.USA), it is highly porous, highly absorbent.

- It controls bleeding and stabilizes blood clot.
- It induces clot formation in half the time taken by the cotton gauze, allows hemostasis from 2 to 2.5 minutes, it is absorbed within 10 to 14 days.
- It protects wound bed, provides matrix for tissue ingrowth.
- Collaplug® dressing holds up to 60 times its own weight in fluids.
- Contains more than 90% open pores of its volume.
- Absorbable collagen wound dressings soft, white, pliable, non friable sponges used in dental surgery. Because of the coherent sponge structure, application of the dressings to the wound was easily controlled. The dressings supplied in sterile individual bubble packs. Available in 1 cm x 2 cm wrapped dressings.

Methods

1. Preoperative phase

- All the patients were subjected to complete history taking including name, age, gender, occupation, medical and dental history.
- All the patients were subjected to intraoral examination to determine the condition of the tooth before extraction as shown in (Fig.1)
- The following laboratory investigations were done 24 hours before dental extraction:
 - Complete blood count.
 - Coagulation profile.
 - International normalized ratio. ($INR \leq 3$ within the therapeutic range as all patients are under oral anticoagulant therapy).
 - Aseptic surgical technique and infection control precautions were used during the whole procedures, including the use of sterilized instruments



Fig. (1): Preoperative intraoral view of upper left central incisor.

2. Operative phase

Group (1): Collaplug® dental dressing was applied into the socket.

Steps:

- Local Anesthesia without vasoconstrictor, Mepivacaine HCL3%, (Mepecaine® 1.8ml carpule, produced by: Alexandria Co. for pharmaceuticals-Egypt).
- Non surgical tooth extraction and immediate bleeding is recorded. (Fig.2).
- The socket was examined for any tooth or bone fragments.
- Insertion of Collaplug® (Fig.3).
- Collaplug® inserted in the socket and cessation of bleeding. (Fig.4).
- Visual inspection of the dressing before suturing of the socket ,using atraumatic round needle. (Fig.5).

Group (2):

Same steps as group (1) without application of Collaplug®

Steps:

- Suturing using atraumatic round needle.
- A sterile cotton dressing was placed over the socket and the patient was asked to apply a gentle biting pressure.



Fig (2): Immediate bleeding after extraction.



Fig (3): During application of collaplug® and cessation of bleeding



Fig (4): After Collaplug® inserted.



Fig (5): Suturing of the socket

3. Postoperative phase

Patients were given the usual postoperative instructions. Postoperative antibiotics 1gm Amoxicillin and Clavulanic acid (Augmentin® manufactured by GalaxoSmithKline - United Kingdom). One tablet every 12 hours was given for cardiac patients with prosthetic valve replacement , analgesics Paracetamol 500 mg (Abimol® manufactured by GalaxoSmithKline -United Kingdom) was prescribed if required.

a. Immediate postoperative phase

The patients were assessed :Immediately, 2 hours, 6 hours , 24 hours, 48hours and 7th day postoperatively. The results regarding postoperative bleeding were recorded. The post extraction instructions were explained thoroughly to the patients as: keep biting on the gauze pack, no mouth rinsing for the rest of the day and no hot food or hot drink for 24 hours.

All the patients were asked to be in contact, in case of excessive bleeding occurred at the operative or postoperative days.

b. Intermediate postoperative phase

Evaluation of the postoperative findings including; bleeding

for the first 2 hours,6 hours,24 hours,48 hours and 7th.day after extraction, pain was assessed for the first 24 hours.

c. Delayed postoperative phase

Sutures were removed at the seventh postoperative day.

The postoperative evaluation was done clinically as follows:

Postoperative bleeding

Bleeding was assessed and recorded postoperatively from the extraction site by WHO bleeding scale (20).

- **Grade 0:** Very low (almost no bleeding).
- **Grade 1:** Low (slight oozing of blood from the socket which usually stopped by its self or after pressure was applied).
- **Grade 2:** Normal. (Clinically significant)
- **Grade 3:** High. (Bleeding occurred after clot significantly formed).
- **Grade 4:** Very high (excessive bleeding that could not be controlled by local hemostatic agents or stitches).

Postoperative pain

Pain was assessed after 24 hours from extraction according to the numerical rating pain scale (21).

Postoperative wound healing

Healing was evaluated clinically at the seventh day postoperatively after sutures removal regarding the presence or absence of infection, inflammation or dry socket as shown in (Fig.6).



Fig (6): Suture removal.

Statistical analysis

The data were collected and entered into the personal computer. Statistical analysis was done:

- Number and percentage of each group (study group and control group).
- Chi square test and monte carlo test used to compare between laboratory investigations of both groups.
- Wilcoxon signed ranks test for comparing between Immediate and each other period.

RESULTS

This study was conducted on 40 patients of both genders 21 females (52%) and 19 males (48%). Their ages ranged between 30-60 years old, they were selected from the in-patients Department Faculty of Medicine, Alexandria University and from the out-patient Clinic of Oral and Maxillofacial Surgery Department, Faculty of Dentistry, Alexandria University. All patients were under oral anticoagulants therapy, patients were divided equally into two groups, each consisting of 20 patients as study and control group.

All 40 patients were under oral anticoagulant therapy due to the following conditions: twenty six patients with valvular heart diseases (65%), ten patients with ischemic heart diseases (25%), two patients with cardiomyopathies (5%), and two patients with stroke (5%).

After performing the extraction and placement of Collaplug®, suturing for the study group and suturing only for the control group, hemostasis condition was assessed 2 hours, 6 hours, 24 hours, 48hours and 7th day postoperatively, results of post operative bleeding after extraction were recorded in table (2).

Table (2): Bleeding grades according to WHO scale

	Immediate		After application of Collaplug® (in study group only)		2 hrs		6 hrs		24 hrs		48 hrs		7 th day	
	C	S	C	S	C	S	C	S	C	S	C	S	C	S
G0	0	0	0	18	4	16	14	20	17	20	13	17	16	18
G1	0	0	0	2	11	4	4	0	2	0	5	3	4	2
G2	20	20	20	0	5	0	2	0	1	0	2	0	0	0
G3	0	0	0	0	0	0	0	0	0	0	0	0	0	0
G4	0	0	0	0	0	0	0	0	0	0	0	0	0	0
χ ²	-		47.505*		15.362*		6.371*		2.801		2.658		0.784	
P	-		NSP<0.001*		NSP<0.001*		NSP=0.019*		NSP=0.231		NSP=0.331		FP=0.661	

Results of the immediate postoperative phase

Study group: all 20 cases showed mild bleeding grade 2 (G2) according to WHO scale, after application of Collaplug® 2 cases only showed bleeding grade 1 (G1) and the rest of cases showed grade 0 G (0) no bleeding.

Control group: all 20 cases showed mild bleeding grade 2(G2) according to WHO scale.

Results of the intermediate postoperative phase

Six hours postoperatively after extraction;

Study group: all patients showed no bleeding grade 0(G0) according to the WHO scale.

Control group: 14 patients showed no bleeding grade 0 (G0), 4 patients showed bleeding grade 1(G1) and 2patients showed bleeding grade2 (G2).

After 48 hours postoperatively;

Study group: 17 cases showed no bleeding grade 0(G0) and 3 cases were grade 1(G1).

Control group: 13 cases showed no bleeding grade0 (G0),

5 cases showed bleeding grade 1 (G1) and 2 cases showed bleeding grade 2(G2) cases according to the WHO scale.

Results of delayed postoperative phase

Study group: 18 cases showed no bleeding grade 0(G0) and 2 cases showed grade 1 (G1) in all the 20 cases.

Control group: 16 cases showed no bleeding grade 0(G0) and 4 cases showed grade 1 (G1) according to WHO scale.

Classification of teeth according to the site of extracted teeth is shown in table (3).

Study group: There were bleeding grade 1 G(1) in 3 cases, the 3 cases (100%) were maxillary teeth, after 48 hours.

Control group: There were bleeding varying between grade 2(G2) and grade 1(G1) after first 48 hours in 7 cases (35%), 4 cases (57%) of them were maxillary teeth.

Table (3): Classification of teeth according to site of extracted teeth.

Control group.		Study group.	
Maxillary Teeth.	Mandibular Teeth.	Maxillary Teeth.	Mandibular Teeth.
12	8	11	9

Pain

Study group: Showed one case (5%) only needed paracetamol 500 mg, only one tablet in the day of the extraction.

Control group: 8 cases showed pain (40%), prescribed for them paracetamol 500mg only one tablet in the day of the extraction, and there was no need for analgesics for rest of patients.

DISCUSSION

In this study we were facing difficult conditions not only due to the medical conditions of the patients but also for the consultation with their physicians, a patient undergoing anticoagulant treatment should be carefully evaluated prior to such a dental procedure.

Simple tooth extraction involves gentle forceps manipulation of the tooth with minimal trauma to the tissue. A patient undergoing warfarin treatment should be carefully evaluated prior to such a dental procedure (7).

In this study, we tried to compare between the study group which included the application of a local haemostatic material, that was effective to be locally applied in the extracted socket, sutures were taken over the material to keep it in place, without interruption of the anticoagulant treatment of those patients, and the control group underwent only suturing of the sockets, without interruption of their anticoagulant treatment, and without application of any local hemostatic materials, in order to evaluate the efficacy of Collaplug® in minimizing postoperative bleeding and

pain following tooth extraction in patients under oral anticoagulant therapy.

In this study, there were nearly no postoperative complications from the use of the local haemostatic material (Collaplug®) but in contrast it enhanced wound healing, reduced bleeding and pain, so local hemostatic material helps in reducing the risk of bleeding and pain in these patients, this agrees with a study done in the Department of Oral and Maxillofacial Surgery, University of Washington (3).

The present study included forty patients of both genders 21 females (52%) and 19 males (48%). Their ages ranged between 30-60 years, INR of both study and control groups ≤ 3 , another study was done in the Oral and Maxillofacial Department, College of Dentistry, King Saud University, patients indicated for dental extractions, it was conducted on total of 35 patients (16 women and 19 men) aged between 38 and 57 years (mean =48.7) (7), both studies are nearly compatible with each other they showed that simple tooth extraction in patients on warfarin treatment can be performed safely without high risk of bleeding, providing that the INR is equal or less than 3.5 on the day of extraction.

In this study we noticed that the laboratory investigations revealed no much increase in the bleeding time as expected due to the anticoagulant therapy to all the patients even those who were under combination of anticoagulants drugs this was accepted by many authors (22).

So screening for preoperative bleeding time is not a reliable test for assessing the risk of clinically significant perioperative bleeding and should not be used for this purpose (23).

There have been studies showing that no statistical correlation between the preoperative bleeding time and the amount of blood loss (24,25).

The INR is used to monitor the level of anticoagulation (26), in this study it was found that it is safe to perform extraction for anticoagulated patients their INR ≤ 3 with application of local hemostatic material, which nearly agrees with the literature which confirms that the rate of postoperative bleeding after tooth removal in patients on warfarin is low when the INR is ≤ 3.5 with the use of local hemostatic material (27).

In addition, a number of articles confirm that even a higher INR than 3.5 is possible when a tooth removal is required, blinder et al. did not find a statistical significant correlation between preoperative INR value and incidence of postoperative bleeding (28).

In this study most of cases which showed either intermediate or delayed postoperative bleeding after extraction of their teeth in both study and control groups

were posterior maxillary teeth.

In this study the study group: there were signs of infection in only one case, socket closure showed improvement in the study group with no signs of inflammations or infection in most cases.

Although as with most hemostatic agents, collagens are not to be used in infected or contaminated wounds. The agents may serve as a nidus for abscess formation and may potentiate bacterial growth. Such results are similar to what has been reported for other hemostatic agents (15,16,18).

Like other local hemostatics agents may have side effects such as delayed wound healing as an example: at a hospital in Dammam, Saudi Arabia, it was noticed that many patients had developed dry socket after surgical removal of wisdom teeth and application of surgicel®.⁽³⁰⁾In periodontal surgery it was found to enhance healing (29).While in bone surgery it was reported to slightly retard healing (30,31).

The major conclusions of this study were: Collaplug® has been proven as an effective local haemostatic material following minor oral surgery in patients who are under oral anticoagulant therapy

In the absence of history of a bleeding disorder, the bleeding time is not a useful predictor of the risk of hemorrhage associated with surgical procedures, normal bleeding time does not exclude the possibility of excessive hemorrhage associated with invasive procedures. The bleeding time cannot be used to reliably identify patients who may have recently ingested aspirin or non-steroidal anti-inflammatory agents, or those who have a platelet defect attributable to these drugs. The best preoperative screen to predict bleeding is to take a clinical history carefully that includes family history, previous dental, surgical, traumatic injury, and drug histories (32).

The use of Collagen products as biocompatible material had been studied by many researchers with different points of views assured us about its safety especially when it is used to medically sensitive patients.

CONCLUSIONS

There is no need to stop the oral anticoagulants therapy ,extraction is done safely within INR(International normalized ratio) ≤ 3 with suturing of the socket but better to use a local hemostatic material as Collaplug® prior to suturing, this will control postoperative bleeding specially in posterior maxillary teeth extracted sockets, also it enhances wound healing and reduces post operative pain, Collaplug® has been proved as an effective local haemostatic material following minor oral surgery in patients under oral anticoagulant therapy which affects their coagulation mechanism and make them liable to prolonged post

operative bleeding, also shows acceleration of soft tissue healing and postoperative pain reduction in patients who are under oral anticoagulant therapy and are liable to suffer from delayed wound healing and postoperative pain.

CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

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