BioGecko

Vol 12 Issue 01 2023
ISSN NO: 2230-5807

Efficacy of Haemocoagulase as a Topical Haemostatic Agent after Minor Oral Surgical Procedures—A Prospective Study

Running Title: Minor Oral Surgical Procedure

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Abstract
Purpose: Haemocoagulase is a topical haemostatic agent which provides the adequate haemostasis after minor oral surgical procedures and it has also been proved to be beneficial in promotingwound healing.
Aim: The aim of this study was to check the efficacy of haemocoagulase in stopping thebleeding and its effect over wound healing after the minor oral surgical procedure.
Material&Method: This study is comprised of 150 surgical sites in 75 patients. The subjects were divided in-to 2 groups in which Group1consists of 50 surgical sites in 25 patients andGroupIIconsistsof100 surgical sites in 50 patients. Group I comprised of the group of simple extraction. In these patients one tooth socket was selected as haemocoagulase site and the other socket was the controlgroup in which no drug was used to control haemorrhage. Group II comprised of the group of patients with bilateral impactions. 50 sockets and surgical sites were sprinkled with Haemocoagulase, and 50 sockets and surgical sites were used as control side in which no drug was used to control haemorrhage.
Results: In Group I bleeding was stopped with the average time of 1.00 - 1.8 minutes, In Group IIbleeding was stopped with average time for haemostasis being 1.00-2.5 minutes, while at control sidethe bleeding was stopped in an average time of 1.80 - 3.00 minutes.
Conclusion: Haemocoagulase after minor oral surgery not only provides faster haemostas is butal so enhances healing.

Keywords: Local Haemostatic Agents, Haemocoagulase, Botox

INTRODUCTION

Persistent bleeding from an inaccessible portion of the oral cavity can cause the patient anxiety, misery, and discomfort, as well as distract the oral surgeon from the working field, resulting in frustration and time consumption. Haemostasis, or the physiological halt of haemorrhage at the site of arterial injury, is a marvellous evolutionary feat [1]. Bleeding control in the oral cavity is more important than in the extraoral operating site because access is already limited, and bleeding reduces visibility at the surgical site [2]. Bleeding can occur as a result of a number of local or systemic reasons. Predisposing variables include a failure to follow post-surgical recommendations, such as avoiding gargling or rinsing and spitting constantly. Pre-existin glocal infections such as pericoronitis, periapical granulomas and presence of nutritional deficiency such as anaemia may also besited as being significant to the development of excessive bleeding which may require additional haemostaticagents.

Local haemostatic agents are chemicals that are used to control surface bleeding and capillary leaking on a local level. A good agent should produce haemostasis in a short period of time, be biocompatible, not impede healing, and function well for a specific surgical technique [2]. Previously, several of these bleeding problems required the use of various haemostatic measures such as pressure packing and suturing the socket, as well as the use of an adrenaline pack or an acrylic splint; however, some bleeding is caused by capillaries and cannot be controlled mechanically, so a haemostatic drug would be especially useful in these procedures.

We've been using topical hemostatic agents including Microfibrillar collagen, gelatine sponge, topical thrombin, feracryllum, bone wax, and others since the beginning. These agents, on the other hand, tend to induce infection and impede wound healing. Haemocoagulase was the first pharmaceutical preparation used therapeutically, and it is based on the coagulative and anti-hemorrhagic activities of fractions extracted from the venom of "Bothrops jararaca" or "Bothropsatrox 2, 3." Haemocoagulase lowers bleeding duration and enhances wound healing by stimulating capillary development in the wound space [3]. We employed haemocoagulase as a topical haemostatic agent based on its therapeutic uses. With haemocoa-gulase adequate haemostasis is achieved after the minor oral surgical procedures and it is also proved to be beneficial in promoting wound healing.

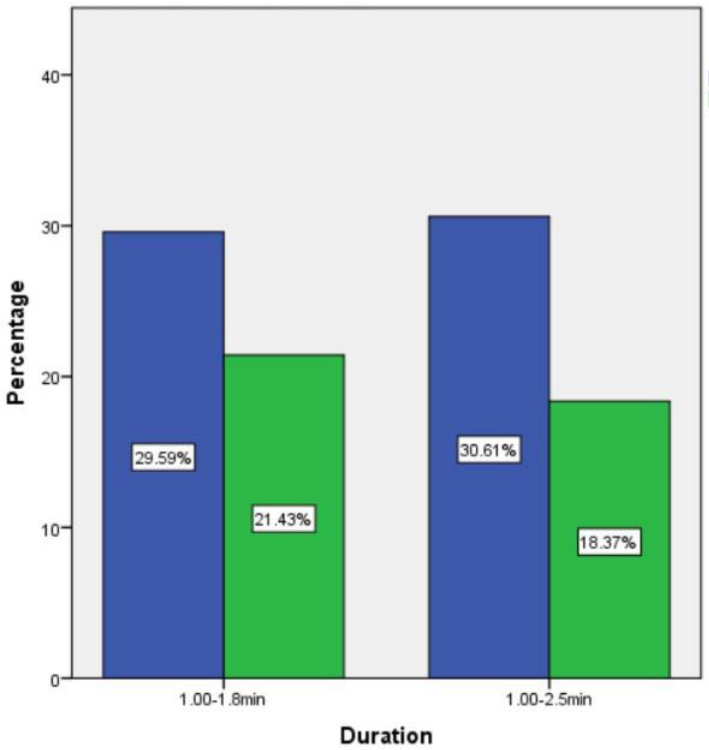
MaterialsandMethods

The current study includes subjects for a simple blind trial consisting of 150 surgical sites in 75 patients indicated for minor oral surgical procedures (impactions, simple extractions, transalveolar extractions), selected serially from the OPD of the department of Oral and Maxillofacial Surgery with the approval of the ethical committee.

Criteria for inclusion and exclusion:

1) There was no gender bias, and the patients ranged in age from 20 to 50 years.
2) No local pathology, such as cysts, tumours, widespread jaw bone, or systemic disorders, interfering with or influencing haemorrhage, clotting, or wound healing.
3) Patients with normal haemograms, bleeding times, and clotting times with no bleeding or clotting disorders.
4) Patients in generally good condition (ASA I & II) with no contraindications to minor surgery and/or local anesthesia.
5) Pregnant patients are excluded from the study.

The individuals were separated into two groups: Group I, which included 25 patients with 50 surgical sites, and Group II, which included 50 patients with 100 surgical sites. Group I consists of patients who have had many extractions, such as whole mouth extraction for dentures and orthodontic extraction. In these patients, one tooth socket was designated as the haemocoagulase site, where haemocoagulase was applied topically via local irrigation to prevent haemorrhage, and the other socket was designated as the control group, where no medicine



was used to control haemorrhage. When the bleeding stops, a pressure pack is applied to both areas. Group II—50 patients with bilateral impactions who had 50 sockets and surgical sites sprinkled with haemocoagulase to stop bleeding.

The criteria for evaluation were:

1) Time taken for bleeding to cease—the time was measured from application of solution into the socket orsurgical site up to the complete stoppage of bleeding by using a stopwatch. Bleeding time checked on study and control side by using no other haemostaticmeasures.
2) Post operative pain and swelling.
3) Nature of wound healing.
4) Complication and side effect.

Post operatively one information chart in the form of a visual analogue scale was given to each patient forevaluating the post operative bleeding, pain, & swelling and patient has informed how to evaluate these parame-ters. No patient suffered from uncontrolled bleeding in our study.

Composition—EachmlofBotroclot[1]contains:

- Aqueoussolutionofhaemocoagulase0.2cu.
- Chlorhexidinegluconatesolution0.1%V/Vaddedaspreservativeandantiseptic.
- Water for injection quantum sufficient (q.s.).Mechanismofaction:

Results

In this study the surgical sites in 75 patients are divided into two groups. The student t-test for equality of means was used to draw the results. In Group I bleeding was stopped at haemocoagulase side in a range of 1.00 - 1.8 minutes in all the patients with average time to achieve haemostasis being 1.35 minutes.

Graph 1 : Comparison of Bleeding with time Duration.

From graph 1 we can see that, in group 1 (1.00-1.8minutes) 29.59% were group 1 and in (1.00-2.5minutes) 30,61% were group 1. For group 2 it was 21.34% and 18.37% respectively.

While at control side bleeding was stopped inrange of 1.75 - 2.75 minutes with average time to achieve haemostasis was 2.25 minutes. Hence faster haemos-tas is achieved at haemocoagulase side(P =2.08)statistically significant.

At haemocoagulase side 18 patients (36%) had pain after 2 hours increasing up to 20 pa-tients (40%) by 3 hours while by 6 hours number of patients reduced to 8 (16%). While on a control side 8 pa-tients(16%)hadpain after3 hours increaseup to 25patients (50%) by 6hours andreducedto12patients (24%) by9hours(P= 0.703). Also, haemocoagulaseside13patients(26%)hadswellingafter1hourandreducedto7patients(14%)by2hours.Atthecontrolside20patients(40%)hadswellingafter1hourandreducedto16 patients(29.9%)by3hours(P=0.273). In Group II bleeding was stopped in a time range of 1.00 - 2.5 minutes in all the patients on haemocoagulaseside with average time for haemostasis (18.37%) being 1.00-2.5 minutes. While at control side the bleeding was stopped in atime range of 1.80 - 3.00 minutes with an average time for haemostasis being 2.47 minutes. Hence faster hae-most as is was achieved athaemocoagulases ide(P=2.65). Statistically significant. Further, 13 patients (26%) had swelling after 9 hours increasing to 23 patients (46%) by 2nd dayand reduced to 3 patient (6%) by third day in the haemocoagulase side patients, while 10 patients (20%) hadswelling after 9 hours increasing to 19 patients (38%) by 2nd day and reduced to 13 patients (26%) by 3rd day incontrolpatients (P=0.850).

Discussion

Bleeding at the surgery site is extremely upsetting for both the patient and the surgeon. There are various traditional haemostatic strategies for reducing blood loss. Manual pressure, ligature, and the use of a tourniquet are all examples of mechanical means. However, these approaches might be labour intensive and prolong the surgical procedure [4]. Thermal treatments such as electro cauterization or laser cauterization can also be used to seal bleeding vessels, although this results in areas of char and necrotic tissue, increasing the risk of infection and injuring wound edges. This may result in slowed healing [5]. Conventional treatments are also less effective in controlling bleeding from complex injuries and in areas where access to the bleeding site is difficult. Topical hemostatic drugs may be particularly useful. They have an impact in a variety of ways. Some help with primary hemostasis, whereas others increase fibrin production or inhibit fibrinolysis [6]. Some are a combination of a procoagulant chemical and a carrier, such as collagen matrix. Others employ a matrix as a template for the endogenous coagulation cascade in order to establish hemostasis. The type of procedure, cost, degree of bleeding, and the surgeons' personal expertise and preferences all influence the selection of an effective topical haemostat.

Rakoz proposed TranexamicAcid mouth wash, fibrin glue, cyanoacrylate, thrombin, microfibrillar collagen, and oxidised cellulose as newer local haemostatic agents in the extraction site [3]. However, mouthwash may have an effect on superficial clots but not on bleeding from the depth of the socket, which mouthwash cannot reach. Resorbable hemostatic agents, such as gel foam, absorbable collagen, microfibrillar collagen, and others, are susceptible to adhesion and infection, particularly if some component remains unabsorbable by tissue [13] [14]. Biological substances such as thrombin and fibrin glue are technically challenging to control, particularly in damp environments. All of these agents are highly expensive. Haemocoagulase is an enzyme complex that is primarily based on the coagulant and anti-hemorrhagic capabilities of fractions extracted from the toxin Bothrops jararaca. Its primary function is to convert fibrinogen to fibrin in the absence of clotting factors.

This thrombin like action is present even in the presence of antithrombinandisnotabsorbed infibrin clothencethe actionof haemocoagulaseisprolonged. It is completely free of neurotoxins and other toxic substances. It is pale yellow crystalline powder which issparingly soluble in water but readily soluble in phenolated saline. It is active over a wide pH range of 4 to 8. Aclotting enzyme of the venom *Bothrops jararaca* denoted FC-Bj was purified by gel chromatography on Sepha-dex G-100. The clotting factor coagulates fibrinogen to fibrin. The protein was of serine type. The amidolyticactivity of this enzyme was resistant to inhibitors such as heparin, aprotinin, EDTA. The importance of the dis-ulfide bridges for the structural integrity of the purified enzyme was indicated by the loss of amidolytic activityin thepresenceofbeta-mercaptoethanol[15]. A platelet aggregating enzyme PA-Bj was also isolated from the venom of snake *Bothrops jararaca* [16,17].

Haemocoagulase has two different enzymatic activities, which promote blood coagulation. One of these accele-rates the conversion of prothrombin to thrombin (thromboplastin like enzyme), while the other one causes a di-rect transformation of fibrinogen to fibrin monomer, which can be converted by thrombin into fibrin

clot(thrombin like enzyme). In vitro the thrombin like enzyme coagulates fibrinogen by gradually splitting off fi-brinopeptide A and B. This gives rise to des-A-fibrin monomer, which polymerize end to end to form fibrin clot.In the circulating blood the des-A-fibrin monomer produced by haemocoagulase remains in solution because
itformsacomplexwithnativefibrinogen.Thesecomplexesofhighmolecularweightacceleratetheplateletaggregation.

Conclusion

In the present study haemocoagulase is applied topically on the extracted tooth socket which has been acted asthe test side and compared with the extraction socket where no additional haemostatic measure has been appliedwhich has been acted as the control side. It is concluded from this study that the use of haemocoagulase after theminor oral surgery not only provides faster haemostasis but also enhances healing by rapid formation of healthytissue and less chances of infection. Based on our results further studies are required where we can prove the use of haemocoagulase in haemophilic patients andothersurgical patients.

Source of Funding: Nil
Acknowledgement: Nil
Conflict of Interest: Nil

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