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Investigation of Hemostatic Effects of Ankaferd Blood Stopper During Periodontal Surgery on Antithrombotic Condititoned Rats

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Abstract: This research evaluated the intraoperative hemostatic effects of a novel hemostatic agent (Ankaferd Blood Stopper (ABS)) during periodontal surgery on antithrombotic condition, without interruption or diminution of the medication. In total, 20 rats which are on antithrombotic condition were randomized into 2 groups, each consisted of 10 rats. In group I (control group), local hemostasis was achieved with direct packing with gauze. In group II, local hemostasis was achieved by the local application of ABS on the site. The bleeding time was compared between 2 groups following the periodontal surgery. The bleeding time in the operation site applied with ABS was statistically lower compared to the control group. It is concluded that the periodontal surgical operations could be performed appropriately with ABS without interruption of the medication in rats on antithrombotic condition.

Key words: Bleeding, hemostasis, anticoagulants, antiplatelet drugs, ABS, group

INTRODUCTION

The Prothrombin Time (PT) and its derived measures of Prothrombin Ratio (PR) and International Normalized Ratio (INR) are measures of the extrinsic pathway of coagulation. They determine the clotting tendency of blood, in the measure of warfarin dosa, liver damage and vitamin K status. PT measures factors I (fibrinogen), II (prothrombin), V, VII and X. It is used in conjunction with the activated Partial Thromboplastin Time (aPTT) which measures the intrinsic pathway.

The reference range for prothrombin time is usually around 12-13 sec and the INR in absence of anticoagulation therapy is 0.8-1.2. The target range for INR in anticoagulant use (e.g., Warfarin) is 2-3. In some cases, if more intense anticoagulation is thought to be required, the target range may be as high as 2.5-3.5 depending on the indication for anticoagulation.

The prothrombin time is the time it takes plasma to clot after addition of tissue factor (obtained from animals such as rabbits or recombinant tissue factor or from brains of autopsy patients). This measures the quality of the extrinsic pathway (as well as the common pathway) of coagulation. The speed of the extrinsic pathway is greatly affected by levels of functional factor VII in the body. Factor VII has a short half-life and the carboxylation of its glutamate residues requires vitamin K. The prothrombin time can be prolonged as a result of deficiencies in vitamin K, warfarin therapy, malabsorption or lack of intestinal colonization by bacteria (such as in newborns). In addition, poor factor VII synthesis (due to liver disease) or increased consumption (in disseminated intravascular coagulation) may prolong the PT.

Ankaferd Blood Stopper (ABS) is a unique medicinal plant extract which has historically been used in Turkish traditional medicine as a hemostatic agent. The ABS has been approved in the management of external hemorrhage and dental surgery bleedings in Turkey, based on the safety and efficacy reports indicating its sterility and nontoxicity. The ABS comprises a standardized mixture of the plants which are *Thymus vulgaris*, *Glycyrrhiza glabra*, *Vitis vinifera*, *Alpinia officinarum* and *Urtica dioica*. The basic mechanism of the action for ABS is the formation of an encapsulated protein network that provides focal points for vital erythrocyte aggregation (Ercetin *et al*., 2010; Isler *et al*., 2010).

This study was designed to evaluate ABS an alternative hemostatic agent and its effects on bleeding time following periodontal surgeries.

MATERIALS AND METHODS

In total, 10 of, 20 rats who were on antithrombotic medication, had an International Normalized Ratio (INR) ≤4.0 and were included for the present study.

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Table 1: Comparison of control and study groups regarding the levels of INR

Groups	INR								
Study group	2.09	2.30	2.25	2.38	1.90	2.01	2.00	3.01	2.57
Control group	1.03	1.10	1.05	1.03	1.13	1.15	1.07	1.09	1.05

INR = International Normalized Ratio

Table 2: Comparison of control and study groups regarding the levels of bleeding time

Groups	Bleeding time with ankaferd (sec)								
Study group	90	80	85	97	82	95	78	84	115
Control group	60	57	46	62	55	50	48	54	55

A group of 20 rats (10 control and 10 study), underwent periodontal surgeries without any modification of their antithrombotic therapy and bleeding time is evaluated both in control and study groups. The study group of rats were medicated by dicoumarol for a month and INR is measured by the end of the month in both groups (Table 1 and 2).

RESULTS

Ten antithrombotic-medicated ten unmedicated rats were enrolled in the study. In control group, the bleeding time is measured between normal values, otherwise in study group bleeding time is measured longer because of the increasement of protrombin time. There was a significant clinical difference between the groups were associated with the use of ABS. A protein network formation (clot) was observed immediately after the application of the agent, in all periodontal surgical areas treated with ABS.

The criteria used to compare the treatment groups were local hemostasis and late bleeding. In this point, complete hemostasis was immediately obtained from 2 groups except 2 rats from the study group. In the study group, the rats were administered 1-2 mL of ABS. About 1 mL of ABS was enough for most of the rats to control bleeding. Two rats from the study group which were on anticoagulant therapy with an INR level of 2.38 and 2.57, experienced immediate postoperative bleeding. A secondary dose of ABS was applied on the surgical area. The bleeding time was between 90 and 120 sec for this rats.

DISCUSSION

Traditionally, stopping antithrombotic therapy for 2-6 days before oral surgeries was suggested as severe hemorrhage may occur postoperatively (Ziffer *et al*., 1957). Now a days, it has been suggested to carry out the surgical operations without any interruption or diminution of the antithrombotic therapy but with an emphasis on the efficiency of the local hemostasis (Sacco *et al*., 2007).

Various agents (oxidized cellulose, gelatin sponge, fibrin glue, bone wax, fibrin glue and tranexamic acid) have been used in order to maintain local hemostasis (Rodriguez-Cabrera *et al*., 2011). A retrospective study showed that there is no marked difference in local hemostasis among oxidized cellulose, gelatin sponge and fibrin glue, for tooth extraction in patients on oral antithrombotic therapy (Morimoto *et al*., 2009).

Within the limit of this study, it is thought that ABS is effective, safe, quick and easy to use compare to the control. Another advantage is associated with the mechanism of action. Blood stopping process is driven by protein agglutination. The ABS stimulates the formation of an encapsulated protein network that provides spaces for erythrocyte aggregation in the injured vascular area. Furthermore, ABS also interacts with fibrinogen as well as other blood proteins. The ABS-induced formation of the protein network affected the entire physiological hemostatic process without affecting any individual clotting factor. The levels of coagulation factors II, V, VII, VIII, IX, X, XI and XIII were not affected by ABS. Therefore, it might be used in patients with deficient primary hemostasis and/or secondary hemostasis including the patients with disseminated intravascular coagulation (Ercetin *et al*., 2010).

Baykul *et al*. (2010) investigated the efficacy of the topical application of ABS in 4 patients on hemorrhagic diathesis, following dental procedures under different conditions. The ABS was found to be effective within 10-20 min in controlling bleeding in most of the patients after dental surgery (Baykul *et al*., 2010).

It is important to emphasize that there are currently no reported side effects after ABS application in the literature, possibly due to its natural ingredients except the metallic taste in the mouth lasting to approximately 5 min as reported in the present study (Ercetin *et al*., 2010).

CONCLUSION

This study suggests that the ABS significantly shortens bleeding time and appears to be sufficient as a hemostatic agent for the management of patients on antithrombotic therapy and who have an INR 4.0 without interruption or diminution of the medication.

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