Safety and Efficacy of Ankaferd Blood Stopper in Dental Surgery

Sevil ERCETIN[1], Ibrahim C. HAZNEDAROGLU[2], Mevlut KURT[3], Ibrahim K. ONAL[3], Alper AKTAS[4], Ozlem K. KURT[5], Hakan GOKER[2], Oktay OZDEMIR[6], Serafettin KIRAZLI[1], Huseyin C. FIRAT[1]

[1] Ankaferd Health Products Ltd, Istanbul

[2] Hacettepe University Facultyof Medicine, Department of Hematology, Ankara

[3] Turkiye Yuksek Ihtisas Education and Research Hospital, Department of Gastroenterology, Ankara

[4] Hacettepe University, Faculty of Dentistry, Department of Oral Surgery, Ankara

[5] Ataturk Chest Disease and Chest Surgery Education and Research Hospital, Department of Chest Diseases, Ankara

[6] Yorum Consultancy Limited Company, Istanbul, TURKEY

ABSTRACT

The aim of this study was to assess retrospectively the hemostatic efficacy and safety of the topical use of Ankaferd Blood Stopper (ABS) in the setting of dental surgery. Following the approval from of the Local Research Ethics Committee ABS as a hemostatic agent in Dentistry, ABS was topically applied by homogeneously spraying to the 25 patients during dental interventions. Based on this retrospective evaluation; Tissue healing was evaluated at the 48th hour. The patients received 1 to 5 mL of ABS; the median dose was 2 mL. Bleeding stopped in median 1.8 seconds (1 to 3 seconds) in the first ABS application in 20 patients. Five patients needed a second dose of ABS; four of them were given 5 mL ABS totally. No patient had wound infection and the healing process appeared to be normal. ABS is useful for the local hemostasis and wound healing in periodontal surgeries.

Keywords: Ankaferd Blood Stopper, Dentistry, Bleeding, Wound healing

ÖZET

Ankaferd Blood Stopper'ın Diş Cerrahisinde Etkinliği ve Güvenilirliği

Çalışmanın amacı diş cerrahisinde Ankaferd Blood Stopper'ın (ABS) topikal uygulanışının hemostatik etkinliğini ve güvenilirliğini güvenilirliğine ilişkin verileri retrospektif olarak değerlendirmektir. Lokal Etik Komitesinden onay alındıktanABS ülkemizde dental tedavide topikal hemostatik ajan olarak ruhsat aldıktan sonra sonra, 25 hastaya dişlerle ilgili müdahaleler sırasında, ABS homojen bir şekilde püskürtülerek uygulandı. Bu retrospektif değerlendirmenin verilerine göre; Doku iyileşmesi 48. saatte değerlendirildi. Hastalara ortanca 2 mL (1-5 mL arası) ABS uygulandı. Yirmi hastada ilk uygulama sonrası kanama durdu, bu grupta kanamanın durması için ortanca süre 1.8 sn (1-3 sn arası) idi. Beş hastada, 2. doz ABS sprey uygulaması gerekti, bunlardan dördüne toplam 5 ml ABS verildi. Hiçbirinde yara enfeksiyonu görülmedi ve yara iyileşme süreci normal göründü. ABS'nin periodontal cerrahilerde lokal hemostaz ve yara iyileşmesi için yararlı olabileceği düşünüldü.

Anahtar Kelimeler: Ankaferd Blood Stopper, Diş hekimliği, Kanama, Yara iyileşmesi

INTRODUCTION

Ankaferd Blood Stopper (ABS) (Ankaferd Health Products Ltd., Istanbul, Turkey) as a medicinal product has been approved in the management of external haemorrhage and dental surgery bleedings in Turkey based on the safety and efficacy reports indicating its sterility and non-toxicity. ABS comprises a standardized mixture of the plants Thymus vulgaris, Glycyrrhiza glabra, Vitis vinifera, Alpinia officinarum and Urtica dioica.[1] The basic mechanism of action for ABS is the formation of an encapsulated protein network that provides focal points for vital erythrocyte aggregation. ABS-induced protein network formation with blood cells particularly erythrocytes covers the primary and secondary haemostatic system without disturbing individual coagulation factor.[1] Exaggerated bleeding, particularly in patients with hereditary or acquired hemorrhagic diathesis, is a challenging problem for the dental profession on a daily basis.[2] Antithrombotic, procoagulant, and antifibrinolytic medications are frequently used for the management of bleeding in dentistry. ABS-induced formation of the protein network covers the entire physiological haemostatic process without unequally affecting any individual clotting factor. ABS may, therefore, be effective both in individuals with normal haemostatic parameters and in patients with deficient primary hemostasis and/or secondary haemostasis.[1] After the approval of ABS for the management of dental bleeding by Turkish Ministry of Health, ABS has been added to the protocols of prevention and treatment of exaggerated hemorrhage due to dental procedures in Turkey. Topical hemostatic efficacy of ABS has been previously tested in animals with normal and defective hemostasis.[3-5] Physiological cell-based coagulation could be clinically managed via topical ABS application to prevent and treat bleeding in many distinct clinicopathological states.[6-11] Neither local nor systemic adverse effect and/or toxicity have not been observed in association with the use of ABS in the experimental and anecdotal topical applications. The aim of this study is to report post-marketing safety and efficacy of local ABS application to manage bleeding following dental procedures in a group of patients with normal and handicapped hemostasis.

PATIENTS AND METHODS

Patients

Study population evaluated during this retrospective investigation included 25 patients (19 women, 6 men; aged 38±8 years) who had applied to dental clinic for the treatment of their dental problems. The patients, whose dental and/or medical conditions were considered to be problematic, were offered to volunteer to this survey. Written informed consents were obtained from all patients. The most frequent dental problems that urged the patient to apply to the clinic, were chronic marginal gingivitis (n= 7), periodontitis (n= 6) and remaining tooth root (n= 5). Dental intervention was tooth extraction in 9 of 25 patients. The second most common intervention was curettage (n= 8). Dental problems and dental interventions are summarized in Table 1. Forty-four percent of the patients (11 of 25) had one or more systemic disease that might interfere with the outcome of the dental intervention. Associated systemic diseases of the patients are listed in Table 2.

Study Procedures

The patients were routinely evaluated by departments of Internal Medicine and Hematology before and 48 hours after the topical application of ABS and dental procedure. ABS has been topically applied by homogeneously spraying with a high pressure to the cavity. If there was any further oozing, extra doses of ABS was topically given with not frequent than 45 seconds.

Ultracaine-DS® ampoule (40 mg of Articain HCL, 0.006 mg /mL of Epinephrine HCL) was used for local anesthesia, whereas Citanest® flacon (2% prilocaine) was preferred for patients with type II diabetes and hypertension.

At 48th hour, a thorough review of all gastrointestinal system was performed by asking all possible side effects form a symptom list that was developed by the investigators. Three patients did not come to the control visit at 48th hour; therefore post-treatment clinical evaluation could be done in 22 of 25 patients.

Laboratory tests including complete blood count, basic renal function tests, hepatic enzymes, serum beta-2 microglobulin, cystatin-C and urinalysis were assayed before and 48 hours after ABS administ-

Table 1. Dental problems and interventions of the patients.

Dental problems	n
Chronic marginal gingivitis	7
Periodontitis	6
Remaining tooth root	5
Chronic apical periodontitis	1
Acute ulcerative periodontitis	1
Pericoronitis	1
Gangrenous tooth	1
Gingivitis	1
Deep dentine caries	1
Prosthetic reasons	1
Dental interventions	
Tooth extraction	9*
Lower third molar	6
Root extraction	4
Lower second molar	2
Lower anterior incisive	2
Lower first molar	1
Upper first molar	1
Curetage	8
Dental scaling	4
Gingivectomy	2
Dental bridge	2

* Most patients had exposed to more than one extraction, the total number of the extractions exceeds the total number of patients (n= 9).

Table 2. Distribution of the associated systemic diseases

Systemic diseases	n*
Hypertension	4
Diabetes mellitus	3
Depression	2
Acromegaly	1
Arrythmia	1
Chronic venous ulceration	1
Dyslipidemia	1
Gastritis	1
Heroin and cocaine abuse	1
Hyperthyroidism	1
Hypothyroidism	1
Iron deficiency anemia	1
Valvular heart disease	1
Prostate cancer	1
Systemic lupus erythematosus	1
Vertigo	1
Total	11*

* Some patients had more than one concomitant disease, the total number of the diseases exceeds the total number of patients (n= 11).

ration. Both before and 48 hours after laboratory tests were present in 17 patients.

Tissue healing was evaluated at 48th hour by the dentist on a 5-point scale; ranging form excellent, better than expected, as expected, poorer than expected and very poor. This evaluation could be done in 22 patients.

Statistical Analyses

Study parameters were summarized by descriptive statistics, i.e. mean and median, standard deviation, 95% confidence interval and range for numeric variables and counts and percentages for categorical variables. Pre- and post-ABS values were both compared as mean and median values and also categorical variables as dichotomies as normal and abnormal (elevated of lowered). Pre and post-ABS values of laboratory tests were compared by Wilcoxon signed-rank test. Dichotomies were compared by McNemar test. Statistical analyses were performed by SPSS (Statistical Package for Social Sciences) v.9.0. Statistical significance was assigned to p values less than 0.05.

RESULTS

The patients received 1 to 5 mL of ABS; the median dose was 2 mL. For most patients, 1 to 2 mL ABS was enough for adequate control for bleeding. No further bleeding was noted after the first dose of ABS was used and the bleeding stopped in 1.8 seconds (range, 1 to 3 seconds) in 20 patients. Five patients needed second dose of ABS; four of them were given 5 mL ABS totally. Local anesthesia was

used in 12 patients; median duration of anesthesia was 5 hours (2-7 hours).

Three patients did not come to 48th hour visit; therefore 22 patients could be evaluated with regards to tissue healing. It is reported that tissue healing was better than expected in 45% of the patients. It was considered excellent in 7 patients (31.8 %), better than expected in 3 patients (13.6 %) and as expected in 12 patients (54.6 %).

Eighteen patients reported a metallic taste in the mouth lasting 3 to 5 minutes. One patient had oral numbness and the feeling of the mouth being stretched that recovered within 10 minutes. One patient had a passage of watery feces once 24 hours after the ABS administration; her feeling of oral metallic taste and burning sensation in the throat continued for 24 hours.

There was no statistically and clinically significant difference between the pre- and post treatment values of the serum levels of blood urea nitrogen, creatinine, alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, total and direct bilirubin, total protein, albumin, uric acid, creatinine kinase, cystatin C, sodium and potassium ($p>0.05$). The increase in the serum β-2 microglobulin level from a median value of 1752 to 1952 was statistically significant ($p= 0.014$). In the 14 patients whose urinalysis could be performed, ABS had no effect on the urinary parameters including the color, appearance, pH, microscopy, density, glucose, protein, ketone, nitrite, bilirubin and urobilinogen ($p>0.05$).

The international normalized ratio (INR) and activated partial thromboplastin time (aPTT) values were normal for all the patients before the dental procedure except for one patient using warfarin. There was no difference between the pre- and post treatment values of INR, aPTT, prothrombin time, fibrinogen in the 17 patients evaluated ($p>0.05$). The treatment had no effect on the blood cell counts and other parameters of hematological analysis ($p>0.05$).

DISCUSSION

Hemostatic failure is one of the most serious problems encountered by the dental professionals. Because it may cause excessive postoperative bleeding, delay in wound healing and increase risk of infection.[2] Local hemostatic methods (nonresorbable sutures, fibrin glues), antifibrinolytic agents (tranexamic acid in mouthwash form), replacement therapy (recombinant or plasma derived clotting factors, platelet-rich plasma) and desmopressin are the usual management.[12-17] But some of them carry risk of transmitting viral infection and formation of factor inhibitors.[16] N-butyl-2-cyanoacrylate was used in warfarin-treated patients during dental intervention.[18]

ABS is a unique medicinal plant extract induces very rapid formation of a protein network in the plasma and serum samples.[1] Blood cells, particularly erythrocytes aggregate rapidly (< 1 s) in the presence of ABS and they are involved in the network formation.[1] Individual coagulation factors are not affected during this antihemorrhagic process.[1] ABS acts independently of the classic coagulation cascade and contribute to the wound healing process. The anti-infectivity action of ABS had been demonstrated in vitro and ABS also had been used topically for the management of hemorrhages uncontrolled by standard measures in a wide variety of difficult clinical conditions.[6-11,19,20]

In our series hemostasis was achieved in all of the twenty two patients. In one patient using warfarin and two patients using ASA, ABS effectively stopped bleeding. This observation also supported the idea that the effect of ABS is not dependent on coagulation factors and platelet function. We observed that the response was within one or three seconds and this may be important in the context of dental surgery. No patient had wound infection and the healing process appeared to be normal.

It is not necessary to reduce oral anticoagulant therapy in patients undergoing routine dental extractions with using local hemostasis.[16,21,22] During the local administration of ABS a local macroscopic dirty-white discoloration is observed. But, we later saw that it disappeared. No serious adverse systemic effect was detected after the administration of the medicinal product.

In conclusion, ABS as a new therapeutic agent was observed in a prospective manner to successfully control bleeding related to dental interventions. ABS can give the dental profession more time and confidence during the surgical intervention. It is useful not only for the local hemostasis in peri-

odontal surgeries and dental extractions, but also for wound healing and to prevent infections. In addition, future study is needed to clarify the role of this unique medicinal product in the setting of the dental surgery with hereditary bleeding disorders.

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Correspondence

Dr. Mevlut KURT

Türkiye Yüksek İhtisas Hastanesi

Gastroenteroloji Bölümü

Kızılay Sk. No: 2

06100 Sıhhiye, Ankara, TURKEY

Tel: (+90.505) 276 28 12

Fax: (+90.312) 312 41 20

E-mail: dr.mevlutkurt@gmail.com