Available online at www.medicinescience.org

ORIGINAL RESEARCH

Medicine Science International Medical Journal

Medicine Science 2021;10(4):1469-73

Comparison of the algan hemostatic agent with celox in rat femoral artery bleeding model

Kenan Binnetoglu[1], Ali Kumandas[2], Husamettin Ekici[3], Abdullah Canberk Ozbaykus[4], Mehmet Tiryaki[5]

[1]Kafkas University, Faculty of Medicine, Depatment of General Surgery, Kars, Turkey
[2]Kirikkale University, Veterinary Faculty, Department of Surgery, Kirikkale, Turkey
[3]Kirikkale University, Veterinary Faculty, Department of Pharmacology and Toxicology, Kirikkale, Turkey
[4]Bahçeşehir University, Six grade Student, Department of Medicine Faculty, Istanbul, Turkey
[5]Dr. Lutfi Kirdar Kartal Education and Research Hospital, Department of Neurosurgery, Istanbul, Turkey

Received 24 May 2021; Accepted 06 July 2021
Available online 24.11.2021 with doi: 10.5455/medscience.2021.05.184

Abstract

The most important reasons of deaths after a trauma are major vascular injury. The effective and speedy control of the hemorrhage is crucial in reducing such deaths. Although many products are being used for this topic, most effective products have not yet been developed currently, and there is an urgent need for effective hemostatic. The aim of this study is to compare the efficacy of Algan hemostatic agent (AHA) with Celox in femoral artery incision model in rats. A total of 28 wistar albino rats divided into 4 equal groups. Experimental femoral artery injury was inflicted. In the control group, saline impregnated gauze was employed. AHA impregnated sponge, AHA powder, and Celox in powder form were utilized in the experimental groups. According to the results, there was no difference in bleeding control between AHA and C ($p>0.05$). When compared to the control group, AHA and Celox were found to be very effective in bleeding control ($p<0.001$). This study showed that AHA had a similar effect like Celox in controlling bleeding. Considering other characteristics such as AHA's naturalness, easy applicability and low cost, AHA has given hope as an effective hemostatic agent.

Keywords: Femoral artery, hemorrhage, bleeding, algan hemostatic agent, celox

Introduction

Bleeding is a problem that accounts for the vast majority of post-traumatic deaths. One of the main majority of preventable death is uncontrolled bleeding [1-3]. Hemorrhagic deaths after trauma occur within the first 6 hours. Blood circulation is stopped by direct pressure application to prevent bleeding in trauma patients [1]. Therefore, reducing deaths against bleeding after trauma should be controlled effectively and rapidly. In this way, the early diagnosis and control of bleeding is a crucial step in first aid and post-surgery because intraoperative blood loss increases the incidence of postoperative morbidity and mortality [4]. Thus, early detection and bleeding control is indispensable in emergencies and postoperative period since blood loss during the surgery increases the incidence of morbidity and mortality.

***Corresponding Author:** Kenan Binnetoglu, Kafkas University, Faculty of Medicine, Depatment of General Surgery, Kars, Turkey
E-mail: kenanbinnet@hotmail.com

During the past few years, tremendous advances have been made in the development of advanced hemostatic products that may be used in traumatic bleeding. These are fibrin-based, cellulose-based, gelatin-based and collagen-based hemostatic agents, sealants (tissue adhesives, such as cyanoacrylates, polyethylene glycol hydrogels, glutaraldehyde-albumina sealants), and combined products. Some of the locally available products are; microporous polysaccharide Hemospheres (TraumaDEX®), poly-N-acetylglucosamine (Chitin®), microporous hydrogel-forming polyacrylamide (BioHemostat®), chitosan linear polymer (Celox®), Ankaferd Blood Stopper®, Oxidized cellulose (Bloodcare®).

They are already available on the market and being used in prehospital settings, emergency departments, and operating rooms [5-20]. However, despite all the major improvements and many products produced for this purpose, an ideal product for bleeding control has not yet materialized. For further studies, development of most effective hemostatic products is being strongly demanded. Algan Hemostatic Agent is obtained from extracted six different plants via standardized blend. Also, the first and only patented product in the world. Each of the plants that make up the AHA has

a content that is active by itself or in combination with hemostasis [21-24] AHA acts by forming a mechanical barrier in front of bleeding. It also provides a rapid bleeding control as it activates intrinsic and extrinsic coagulation pathways. It has easily applied locally; prices are cheaper and does not require special storage conditions.

Materials and Methods

For this study, approval was obtained from Kirikkale University Animal Experiments Local Ethics Committee (Decision no. 2018/06). All animal studies conformed with the animal experiment guidelines of the Committee for Humane Care. All animals received care in compliance with the "Principles of Laboratory Animal Care" formulated by the National Society for Medical Research and the "Guide for the Care and Use of Laboratory Animals" prepared by the US National Academy of Sciences and published by the US National Institute of Health (NIH Publications, No:80-23). In the study, 28 rats, 180-210 grams, 5-7-week-old Albino Wistar were used. Rats were fed ad libitum and examined under standard laboratory conditions according to a 12-hour dark-light period. A total of 28 rats divided into 4 equal groups. The groups were control, AHA powder (Algan group health services, Turkey), AHA liquid (Algan group health services, Turkey) and Celox (MedTrade Product Ltd, Cheshire, UK).

All surgical procedures performed using ketamine hydrochloride (100 mg/kg) and xylazine hydrochloride (10 mg/kg) anesthesia. After completing the experimental study, rats were scarified by using 100 mg/kg IV sodium thiopental (Pental Sodium®, U.E. Ulagay).

Bleeding test

The right inguinal area of the rats was wiped then shaved with Povidine Iodine, then skin and subcutaneous tissues were incised to expose the femoral vein and artery. Bleeding time was measured comparing to previous studies [11]. The femoral artery was marred by a green injector tip while another person pressed this area with the sponge for 10 seconds, and then the sponge was lifted off. Celox, AHA spong, AHA powder, and the saline impregnated buffer was placed on this area and fixed on the tampon. Bleeding was checked 2 minutes after time started. If the bleeding stopped, it was recorded as "bleeding stopped". If the bleeding cannot stop immediately, the same amount of material was used for compression for another 2 minutes. After two minutes, bleeding was investigated and if there is no bleeding, it was named as 'bleeding under control' for the second application. The same procedure was applied for the third time and was implemented for 2 minutes. At the end of the additional 2 minutes, the bleeding was checked and recorded as "stopped bleeding at the 6. minute" if the bleeding under control and "failed" if the bleeding was still continuing after the fourth minute.

Statistical analysis

IBM-SPSS 22.0 (SPSS Inc., Chicago, IL) was used to analyze the data of this study. To evaluate weight, bleeding time and adherence scores, mean±sd values were used to compare among the four groups. ANOVA test and post hoc Duncan's multiple range test was used to improve differences between the groups. The results were assessed at a 95% confidence interval and a significance level of $p < 0.05$.

Results

AHA powder and Celox controlled the bleeding in all rats at the first application (in 2 minutes). Bleeding could not be controlled in the control group. AHA sponge controlled the bleeding in 6 rats at the first application (in 2 minutes) and 1 rat at the second application (in 4 minutes). That the AHA liquid, the AHA powder, and Celox controlled the bleeding in the first two minutes compared to the control group was found to be statistically significant ($p<0.001$). The results are given in the table.

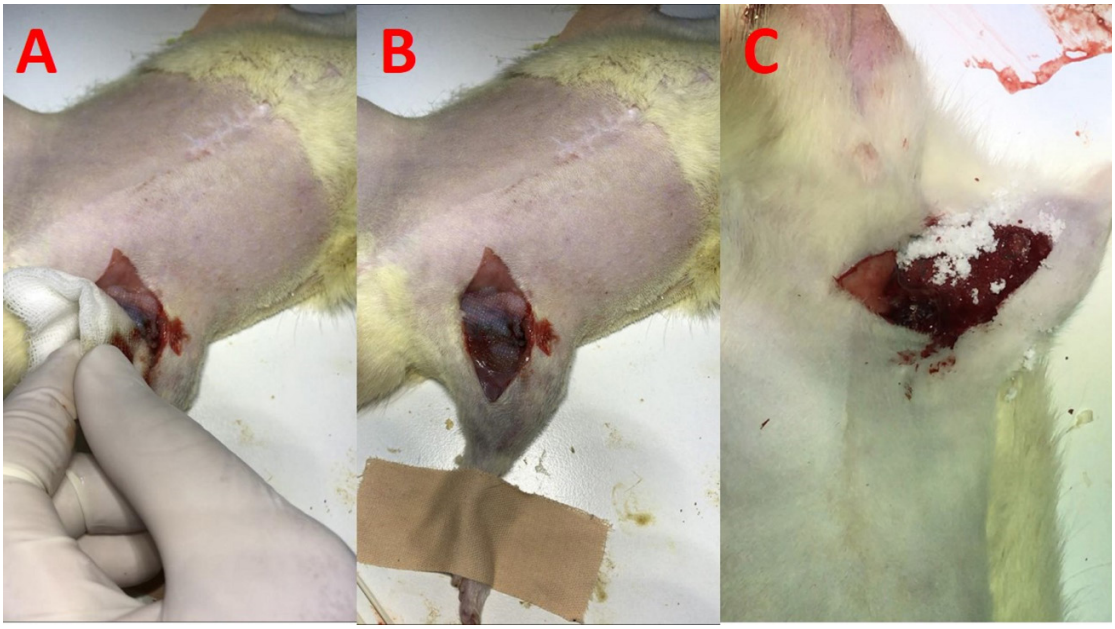

Figure 1. 1a: Removing the sponge after AHA liquid application, 1b: Creating a mechanical barrier of AHA liquid. 1a: AHA powder application.

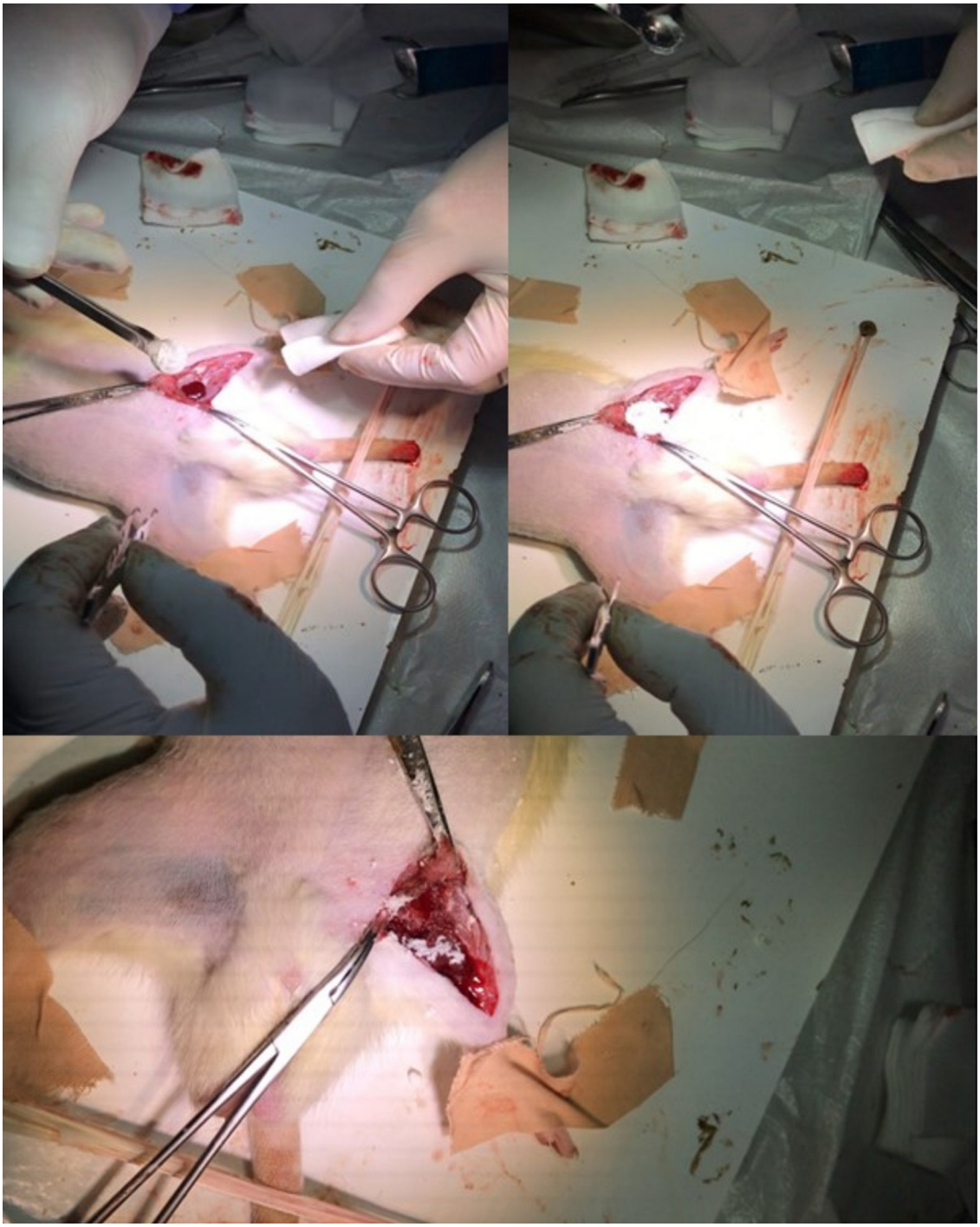

Figure 2. 2a and 2b: Celox application, 2c: View after Celox application.

Table 1. Control and homeostasis times of groups

	Bleeding controlled within 2 minutes	Bleeding controlled within 4 minutes	Bleeding controlled within 6 minutes	Unsuccessful	p
Control	0 (0%)	0 (0%)	0 (0%)	8 (100%)	P<0.01 Control- AHA powder, AHA liquid and Celox
AHA powder	7 (100%)	0 (0%)	0 (0%)	0 (0%)	P>0.05 AHA powder, AHA liquid and Celox
AHA liquid	6 (86%)	1 (14%)	0 (0%)	0 (0%)	
Celox	7 (100%)	0 (0%)	0 (0%)	0 (0%)	

Discussion

In this study, two different forms of AHA powder, and liquid (sponge) were compared to Celox. All were found to be very effective. Although the powder form, controlled bleeding more effectively, the fluid form of AHA was also effective and no statistically significant difference was observed between them in terms of bleeding control efficacy. However, relative to the control group, a statistically significant difference was found. Bleeding time was much longer in the control group than the experimental groups. The liquid form promised to be an effective hemostat in internal bleeds that were not conducive to compression.

In the literature, there are few studies comparing local hemostatic agents using similar processes [5-7,25]. No significant differences among the effective local hemostatic agents were reported. Similar test methods yielded different results in control groups [8, 9]. Due to the many factors such as the weights of the animals, the experience of the practitioner, technical differences, vessel variations, laboratory conditions, etc., this comparison needs to be compared to other products being tested under similar conditions to assess the bleeding effectiveness of other bleeding stoppers.

Recently, a variety of effective hemostatic agents have been emerged along with traditional hemostasis treatments like cauterization, direct pressure, and ligation [14-20, 26]. Nonetheless, these treatments may have some limitations like allergic reactions and infections [27].

In some studies, the efficacy of hemostatic agents (Floseal®, Celox) used as controls in our study was shown [7, 11-13, 15-20, 28, 29]. In the literature, there is a study comparing Floseal and Celox. In this study, control, Glubran 2, Celox, Floceal and Ankaferd were compared. Partial nephrectomy was applied to rats. In this study, the best results were obtained with Glubran 2, while Floseal and Celox showed similar positive results [25]. There are many studies in the literature showing the effectiveness of Celox in the femoral artery model [7, 12, 13]. Since the AHA powder form is easily absorbed, it is quickly cleaned from the area where it is applied. In this way, it provides a clean working area in surgical operations. No side effects have been encountered in preclinical and clinical studies related to AHA so far. There are some commercial products that act like AHA. Nevertheless, commercially available products may have an important disadvantage such as misfit for deep and narrow wounds and induce tissue damage because of the massive exothermic reaction [26]. Most bleeding-related deaths in the patients occur from non-compressible and heavy intra-cavitary bleeding that cannot be completely managed by emergency procedures [28, 30]. The ideal hemostatic agent should be inexpensive, safe, effective, simple to apply, and should not be easily affected by environmental conditions [27]. It must not allow the transmission of bacterial or viral infection, and it must be able to sustain hemostasis for at least several hours.

AHA meet all these needs. In the application of the liquid form, no compression was required in the area where it was applied after femoral artery injury, and hemostasis was achieved in 6 (86%) rats in the first two minutes of application. In animals with higher femoral artery pressure and in humans on the battlefield, AHA is not expected to provide hemostasis without compressing the area where it is applied in such external injuries. However, AHA is very promising in internal bleeding where it is not possible to apply compresses.

Although it is a standard processing, the difference in the amount of bleeding among rats is one of the limitations of this study. Intercalarily, there is a difference in form between the products used as liquid and powder. Consequently, AHA showed 100% achievement in controlling bleeding within the first two minutes like Celox. AHA Liquid form achieved 86% success in bleeding control in the first two minutes. These results show that AHA is a strong hemostatic candidate.

Conclusion

According to the results of this study, although AHA is an extremely effective hemostatic agent used for this purpose in the world in the femoral arterial hemorrhage model in the literature, the actual difference can be demonstrated by more comparative studies. This status will be clearer with new research. The efficacy of AHA in femoral artery bleeding model was compared to two different products, which are widely used in the clinic and whose hemostatic efficiencies are well known, and the powder form was successful in controlling bleeding in all rats in two minutes. Since similar results were observed in the Celox, studies with larger series or using different methods are required for superiority assessment. Although this study shows that AHA is a effective hemostatic agent, it needs to be demonstrated by more detailed studies.

Conflict of interests
The authors declare that they have no competing interests.

Financial Disclosure
All authors declare no financial support.

Ethical approval
For this study, approval was obtained from Kirikkale University Animal Experiments Local Ethics Committee (Decision no. 2018/06)

References

1. Sauaia A, Moore FA, Moore EE, et al. Epidemiology of trauma deaths: a reassessment. J Trauma Acute Care Surg. 1995;38:185-193.
2. Champion HR, Bellamy RF, Roberts CP, et al. A profile of combat injury. J Trauma Acute Care Surg. 2003;54:13-19.
3. Carson J, Spence R, Poses R, et al. Severity of anaemia and operative mortality and morbidity. Lancet. 1988;331:727-9.
4. Wu WC, Trivedi A, Friedmann PD, et al. Association between hospital intraoperative blood transfusion practices for surgical blood loss and hospital surgical mortality rates. Ann surg. 2012;255:708-14.
5. Huri E, Akgül KT, Yücel MÖ, Aet al. The second step in vitro trial of Ankaferd® Bloodstopper®: comparison with other hemostatic agents. Turk J Med Sci. 2011;41:7-15.
6. Hanks JB, Kjaergard HK, Hollingsbee DA. A comparison of the haemostatic effect of Vivostat® patient-derived fibrin sealant with oxidised cellulose (Surgicel®) in multiple surgical procedures. Eur Surg Res. 2003;35:439-444
7. Aydinoglu A, Ersoy G, Dogan A, et al. Hemostatic effect of microporous polysaccharide hemosphere in a heparinized rat model with femoral artery bleeding. Eur J Emerg Med. 2008;15:286–306.
8. Akarsu C, Kalaycı MU, Yavuz E,et el. Comparison of the hemostatic efficiency of Ankaferd Blood Stopper and fibrin glue on a liver laceration model in rats. Ulus Travma Acil Cerrahi Derg. 2011;17:308-12.
9. Jackson MR. New and potential uses of fibrin sealants as an adjunct to surgical hemostasis. Am j surg 2001;182:36-9.

10. Abacıoğlu S, Aydın K, Büyükcam F, et al. Comparison of the efficiencies of buffers containing Ankaferd and Chitosan on hemostasis in an experimental rat model with femoral artery bleeding. Turk J Hematol. 2016;33: 48.-52.

11. Ersoy G, Kaynak, MF, Yilmaz O, et al. Hemostatic effects of microporous polysaccharide hemosphere® in a rat model with severe femoral artery bleeding. Adv ther. 2007;24:485-92.

12. Aktop S, Emekli-Alturfan E, Ozer C, et al. Effects of Ankaferd Blood Stopper and Celox on the tissue factor activities of warfarin-treated rats. Clin Appl Thromb Hemost. 2014;20:16-21.

13. Ozgur D, Gurkan E, Osman Y, et al. The effect of application of local oxidised cellulose powder on hemostasis time in a rat model with femoral artery bleeding. Acta Med Mediterr. 2015;31:179–82.

14. Sabatini L, Trecci A, Imariso D, et al. Fibrin tissue adhesive reduces postoperative blood loss in total knee arthroplasty. J Orthop Trauma. 2012; 13:145-51.

15. Echave M, Oyagüez I, Casado MA. Use of Floseal®, a human gelatine-thrombin matrix sealant, in surgery: a systematic review. BMC surg. 2014; 14:111.

16. Richter F, Schnorr D, Deger S, et al. Improvement of hemostasis in open and laparoscopically performed partial nephrectomy using a gelatin matrix-thrombin tissue sealant (FloSeal). Urology. 2003;61:73–7.

17. Helito CP, Bonadio, MB, et al. Comparison of floseal® and tranexamic acid for bleeding control after total knee arthroplasty: a prospective randomized study. Clinics. 2019;74:1186.

18. Beyea JA, Rotenberg BW. Comparison of purified plant polysaccharide (HemoStase) versus gelatin-thrombin matrix (FloSeal) in controlling bleeding during sinus surgery: a randomized controlled trial. Ann Otol Rhinol Laryngol. 2011;120:495–8.

19. Testini M, Marzaioli R, Lissidini G, et al. The effectiveness of FloSeal matrix hemostatic agent in thyroid surgery: a prospective, randomized, control study. Langenbecks Arch Surg. 2009;394:837-42.

20. Angioli R, Muzii L, Montera R, et al. Feasibility of the use of novel matrix hemostatic sealant (FloSeal) to achieve hemostasis during laparoscopic excision of endometrioma. J Minim Invasive Gynecol. 2009;16:153–6.

21. Midi, A, Kumandas A, Ekici H,et al. Investigation of the efficacy of algan hemostatic agent in liver laceration model in Rats. EJMO. 2019;3:37-42.

22. Midi A, Ozyurek HE, Karahan S, Eet al. Investigation of efficacy of the plant based algan hemostatic agent in hepatectomy bleeding model in rats. EJMI. 2018;2:195-201.

23. Midi A, Ekici H, Kumandas A, et al. Investigation of the effectiveness of algan hemostatic agent in bleeding control using an experimental partial splenectomy model in rats. Marmara Med J. 2019;32:27-32

24. Midi A, Kumandas A, Ekici H, et al. Investigation of the effectiveness of algan hemostatic agent in renal venous bleeding model in rats. EJMI. 2018;2:129-32.

25. Huri E, Akgül T, Ayyıldız A,et al. Hemostatic role of a folkloric medicinal plant extract in a rat partial nephrectomy model: controlled experimental trial. J urol. 2009;181:2349-54.

26. Song H, Zhang L, Zhao X. Hemostatic efficacy of biological self-assembling peptide nanofibers in a rat kidney model. Macromol Biosci. 2010;10:33-9.

27. Yasunaga H. Risk of authoritarianism: fibrinogen-transmitted hepatitis C in Japan. Lancet. 2007;370:2063-7.

28. Rhee P, Brown C, Martin M, et al. QuikClot use in trauma for hemorrhage control: case series of 103 documented uses. J Trauma Acute Care Surg. 2008;64:1093-9.

29. Schwab PE, Thienpont E. Use of a haemostatic matrix (FloSeal®) does not reduce blood loss in minimally invasive total knee arthroplasty performed under continued aspirin. Blood Transf. 2016;14:134.

30. Kauvar DS, Lefering R, Wade CE. Impact of hemorrhage on trauma outcome: an overview of epidemiology, clinical presentations, and therapeutic considerations. J Trauma Acute Care Surg. 2006;60:3-11.