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Efficacy of T-HEMOVINE as Topical Hemostatic Agent: A Clinical Study

Andi Asadul Islam[1], Juliani Ibrahim[2]*, Venansius R. Kurniawan[1]

[1]*Department of Surgery, Faculty of Medicine, Hasanuddin University, South Sulawesi, Indonesia;* [2]*Department of Public Health, Faculty of Medicine and Health Science, Universitas Muhammadiyah Makassar, South Sulawesi, Indonesia*

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***Correspondence:** Juliani Ibrahim, Department of Public Health, Faculty of Medicine and Health Science, Universitas Muhammadiyah Makassar, South Sulawesi, Indonesia. E-mail: juliani@med.unismuh.ac.id
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ABSTRACT

AIM: Clinical trials using hemostatic T-Hemovine derived from bovine gelatin, to stop bleeding during surgery was performed.

METHODS: Twenty (20) patients (aged 8 months–70 years) who underwent neurosurgery at Dr. Wahidin Sudirohusodo Hospital and Hasanuddin University Teaching Hospital, from September 16, to December 13, 2019, are willing to receive T-Hemovine to control bleeding.

RESULTS: This approach was successfully used in twenty patients. Four patients stopped bleeding at the 3rd min (20%), nineteen patients stopped bleeding at the 5th min or less (95%) and twenty patients stopped bleeding before the 10th min (100%). There were no post-operative bleeding events, no infection, and no other post-operative complications.

CONCLUSION: Therefore, there is no effect, and the safety of using T-Hemovine hemostatic is the same as the effect and safety of using surgeon hemostatic and other hemostatic.

Introduction

Bleeding during the surgical procedure can interfere with the course of the surgical procedure so that the surgical time becomes longer. In the context of surgical wounds, the large volume of blood discharged or lost can indeed cause concern. This condition will result in the reduced flow of food and oxygen to tissues or organs. Furthermore, due to their anatomical position or a higher risk of infection, some surgical wounds, such as external wounds, are more challenging to cure [1]. In addition, the blood that appears on the wound area during surgery will block the operator's view of the surgical wound area.

There are several ways to stop bleeding [2]. For example, the traditional figure to stop bleeding at the time of the differentiation procedure, namely, by emphasizing the location of the bleeding, binding or clamping the blood vessels, also by means of cauterization, administration of epinephrine, Vitamin K, protamine, and vasopressor. However, sometimes these various methods cannot be done because of bleeding that is massive or difficult to reach. Recently, the effect of hemostatic agents has mainly been measured by the success rate in terms of the time necessary to obtain adequate hemostasis and the volume of intra- or post-operative blood loss [3]. Therefore, certain situations, such as severe bleeding resulting from penetrating trauma, do not depend exclusively on the control of the surgical team and require the support of new solutions that decrease or control bleeding [4].

For more than 60 years, there have been widely used various *agents* that can inhibit or stop bleeding during surgical procedures [5]. The agent is *Topical Hemostatic Agents*. One type of topical hemostatic agent is derived from gelatin (cow), in the form of spoons [6], with various trade names that have long been circulating and used in the world since 1940 [7].

The hemostatic is sometimes expensive and unaffordable, the availability is uncertain in the market, and the quality of the product including packaging selection can affect the effectiveness and safety of use. The selection of raw materials is also a major obstacle, especially in a country with a Muslim majority.

Concern about raw materials and to increasing the choice, as well as overcome the various shortcomings that exist in hemostatic products that have been circulating in Indonesia, this hemostatic from the basic raw material *Bovine Gelatin* (cow) is a possible choice for hemostasis in cases where there is a relatively large amount of bleeding.

Hence, with this a product exposure is compiled which aims to obtain approval for registration of a distribution permit from the Ministry of Health of the Republic of Indonesia for T-Hemovine products.

Purpose of providing products

The objectives of PT Triton Manufactures preparing the production of T-Hemovine are as follows: Availability *of topical* products *hemostatic agents* based on cow gelatin that is easier to obtain and more guaranteed availability in all corners of the country; availability of domestic *topical hemostatic agent* products made by the nation's children with the best quality; the availability *of topical hemostatic agent* products at affordable prices in accordance with the government program of the National Health Insurance; availability *of topical hemostatic agent* products that will get halal certification from the Indonesian Ulama Council. Because the first T-Hemovine product was tested in Indonesia and predicted to get a lot of users who generally adhere to Islam, it is necessary to get recognition from MUI, which has endorsed that the product is suitable for medical purposes and declared the product halal. Furthermore, we consider that using T-Hemovine in the surgical procedure will give more benefits as truly grade gelatin and more advantages such as T-Hemovine is a product that can stop bleeding effectively and safely <10 min, can be absorbed by the body within 3–4 weeks, no side effect, can absorb blood up to 40–50 times the product weight and non-allergenic (Appendix 1 for supporting data).

Methods

This study was carried out based on concern the regulation of the Minister of Health No. 63 of 2017 concerning How to Test Good Medical Devices, Appendix 2 Part A p. 41: *General Principles of The Need for Clinical Trials* [8].

Sample

In this clinical trial, 20 patients (aged 8 months–70 years) underwent neurosurgery surgery at Dr. Wahidin Sudirohusodo Hospital Makassar and Hasanuddin University Teaching Hospital. From September 16, to December 13, 2019 who are available to receive T-Hemovine control bleeding. Intra-operative and post-operative findings were evaluated. Hemostasis is achieved when no bleeding is seen from the resection wound. This approach was successfully used in twenty patients. Four patients stopped bleeding at the 3rd min (20%), nineteen patients stopped bleeding at the 5th min or before (95%), and twenty patients stopped bleeding at the 10th min and before (100%). There were no post-operative bleeding events, no infection, and no other post-operative complications.

Case presentation

T-Hemovine is used under sterile operating conditions after adequate preparation of location which will be operated on sliced T-Hemovine is applied gently to dry directly on the surface to be cured. The duration of application varies depending on the bleeding stopped in general, 2–6 min is sufficient. T-Hemovine can be cut to the required size for the application. Because T-Hemovine is resorbable, it can be left *in situ* after achieving hemostatic. However, it is recommended that excess material be removed.

Results

Hemostatic drugs that are secure, simple to use, and have substantial hemostatic effects are required to address the aforementioned issues. The effectiveness and safety of T-Hemovine in the use of hemostatic in surgery were not found to be different from the effectiveness and safety of using another gelatin-based hemostatic (according to the library) in surgery. (Appendix 2 for supporting data).

Discussion

Hemostatic agent

T-Hemovine is produced from a very pure first-order gelatin material (lyophilized hydrolyzed collagen) foam that has uniform pores and reacts neutrally, T-Hemovine is a sterile gelatin foam, soft, insoluble in water, absorbable, held to stop bleeding by attaching it to a bloody surface. When implanted *in vivo* and used in the right quantities, it is fully absorbed within 3–4 weeks, without residue and encapsulation. When attached to the area of the bloody mucosa, it melts within 2–5 days. It is sterilized with gamma rays and does not require special storage. Non-toxic, non-allergenic, and non-immunogenic on-pyrogenic can be used in conjunction with antibiotics, thrombin, and chemotherapy without reducing its use hemostatic effect. As for T-Hemovine characteristics are as follows; can absorb blood/fluid 40–50× from its volume so that it can reduce/avoid bleeding meaningfully; it can be easily cut to adjust the size to the need at the site of bleeding; while T-Hemovine is applied *in vivo* with the amount of use as needed, T-Hemovine will be absorbed by the

body within 3–4 weeks; Then, T-Hemovine products do not affect wound/tissue healing in the application area. Therefore, this study would compare the efficacy and safety of the T-Hemovine during surgeries.

Hemostasis is a physiological process that stops bleeding at the site of injury while maintaining normal blood flow in its circulation in other forgings. Bleeding is stopped through the formation of hemostatic clots. If the blood vessels are damaged, the components of the subendothelial components will be exposed to the blood. Some of these components, which mainly consist of platelets and fibrin activate the two main processes of hemostasis to initiate the formation of blood clots. This process is so strictly regulated that it is active within a few seconds after the bleeding but its location remains around the bleeding site.

There are two main components of hemostasis;

Primary hemostasis is the aggregation of platelets and [9] the formation of platelet clots. Platelets are activated in a multifaceted process, where these thrombolites attach at the site of bleeding, thereby affecting the bleeding [9].

Secondary hemostasis, which is an insoluble deposition of fibrin, produced by a cascade of proteolytic coagulations. This insoluble fibrin forms a mesh around platelet blockages. This mesh serves to strengthen and stabilize blood clots [10].

Supporting research

Considering that T-Hemovine is a *topical hemostatic agent* product that uses technology that has been used by similar products that have been on the market for a long time since 1940, both in Indonesia and in other countries, without any technological changes, T-Hemovine products have similar effectiveness and safety in surgical wounds.

Conclusions

Since, T-Hemovine is a product based on bovine gelatin (bovine), T-Hemovine is a product that can stop bleeding effectively and safely in certain surgical procedures, this study indicated T-Hemovine is a potentially safe procedure to prevent serious bleeding, which further prevents the possibility of organ failure. Moreover, T-Hemovine is produced using the same basic raw materials as hemostatibovine gelatin (cow) material with technology that has been used for about 80 years since 1940, T-Hemovine is a product that we propose to be included in the category of Class III D products that do not require pre-marketing clinical trials.

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Appendix

Appendix 1: Type of T-Hemovine

S. No.	Usability	Length	Width	Thick
1.	Anal	80 mm	30 mm	0 mm
2.	Dental	10 mm	10 mm	10 mm
3.	General	80 mm	50 mm	10 mm

Appendix 2: Characteristics of patient and post-surgery status

Patient No	Sex	Age	Type of surgery	3rd min	5th min	10th min	Status
No. 1	M	8 months	Fronto temporo parietal dextra			√	No complication No infection
No. 2	M	20 years	Craniectomy evacuasi hematom subdural			√	No complication No infection
No. 3	M	9 years	Craniectomy segmen fracture deprese			√	No complication
No. 4	F	29 years	Craniectomy hematom subdural+dekomprese			√	No infection
No. 5	M	24 years	Craniectomy evacuasi hematom epidural			√	No complication
No. 6	M	67 years	Craniectomy evacuasi hematom intracerebral subdural			√	No infection
No. 7	M	54 years	Craniectomy evacuasi hematom epidural			√	No complication
No. 8	M	43 years	Craniectomy segment fracture depress			√	No infection
No. 9	M	4 years	Craniectomy segment fracture depress			√	No complication
No. 10	M	11 years	Fronto segmen fracture depress+duroplasty			√	No infection
No. 11	M	65 years	Craniectomy hematom intracerebral			√	No complication
No. 12	F	10 years	Craniectomy hematom epidural			√	No infection
No. 13	M	12 years	Craniectomy removal corpus alienum			√	No complication
No. 14	M	49 years	Craniectomy hematom subdural			√	No infection
No. 15	M	58 years	Craniectomy hematom intracerebral			√	No complication
No. 16	M	70 years	Craniectomy hematom subdural+dekompresi			√	No infection
No. 17	M	12 years	Craniectomy segment Fracture			√	No complication
No. 18	M	47 years	Temporo basal dextra			√	No infection
No. 19	M	40 years	Craniectomy segment fracture depress+debrid			√	No complication
No. 20	M	4 years	Craniectomy evacuasi hematom intracerebral			√	No infection