Global Journal of Clinical Medicine and Medical Research [GJCMMR]
ISSN: 2583-987X (Online)
Abbreviated key title: Glob.J.Clinic.Medici.Medica.Res.
Frequency: Monthly
Published By GSAR Publishers
Journal Homepage Link- https://gsarpublishers.com/journal-gjcmmr-home/

Investigation of the Clinical Efficacy and Safety of Algan Products, a Herbal Hemostatic Agent, in Open Heart Surgery.

BY

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Article History

Received: 10/07/2024
Accepted: 21/07/2024
Published: 23/07/2024

Vol – 2 Issue – 7

PP: -34-39

Abstract

Objective: *Stopping bleeding that occurs during surgical operations or other emergencies is very important to prevent negative consequences by reducing blood loss. The aim of this study is to investigate the hemostatic effectiveness and safety of the polysaccharide-based Algan hemostatic agent, a herbal product, in open heart surgery.*

Material and Methods: *140 patients who underwent coronary surgery were included in this study. The patients were randomly divided into 4 groups, each consisting of 35 patients. The 1st group was determined as the Algan Powder, the 2nd group as the Algan Sponge, the 3rd group as the Algan liquid, and the 4th group as the control group in which only traditional haemostatic methods were used. Algan hemostatic agent was used to control bleeding in coronary anastomoses and perivascular fatty tissue in the myocardium.*

Results: *On the first postoperative day, the average drainage was 363 ml in Algan powder, 442 ml in Algan sponge, 545 ml in Algan liquid, and 997 ml in the control group. These results were found to be statistically significant in favor of all three different versions of Algan ($p < 0.039$). Additionally, as an important difference, the treatment group was found to be statistically more significant than Algan's groups in terms of the rate of erythrocyte suspension use ($p < 0.004$).*

Conclusion: *It was observed that powder, sponge, and liquid forms of Algan hemostatic agent can be used safely and effectively as a hemostatic agent in open heart surgery.*

Keywords: *Algan hemostatic agent, Open heart surgery, Bleeding*

1. Introduction:

Controlling intraoperative and postoperative bleeding in trauma and major surgical operations is very important in terms of mortality and morbidity (1, 2). In order to eliminate the negative consequences of hypovolemia that develops as a result of bleeding, postoperative blood, and blood products need to be used more. Therefore, hemostatic agents are needed more and more every day to prevent this and keep the patient's hemodynamics stable. Open heart surgery is one of the major surgeries with high bleeding problems (3). Important problems such as deterioration of hemodynamic stability due to bleeding, hypotension, arrhythmia, renal failure, prolonged ventilation, and low cardiac output can be seen in open heart surgery and in the intensive care unit in the postoperative period.

Therefore, the use of a reliable hemostatic agent is an important aid in open heart surgery. Hemostatic agents support clinical recovery by reducing postoperative drainage and the need for transfusion. Powder, sponge, and liquid forms of the herbal Algan hemostatic agent we used in this study were used in both capillary, venous, and arterial bleeding. Algan hemostatic agent products create a polymeric network structure by using the proteins in the environment and formulation in the area where they are applied, trapping the blood in it, ensuring coagulation, and creating a mechanical barrier in front of the bleeding vessel (4-8). Our aim in this study is to investigate the clinical effectiveness and safety of this agent in open heart surgery operations.

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2. Material and Methods:

Algan Hemostatic Agent products ALGAN Group Health Services Import Export Industry and Trade Ltd. Ltd. provided by.

Algan Hemostatic Agent powder (AHA powder) (Figure 1) is a plant polysaccharide-based product and is an absorbable medical device consisting of powder-shaped particles designed to control bleeding during injuries and surgical procedures. These special particles; It quickly absorbs the fluid in the blood and when it comes into contact with blood, it quickly adheres to the bleeding tissue and creates a mechanical barrier. The gelled structure also helps stop bleeding quickly by accelerating blood clotting. Algan dust particles are rapidly absorbed and excreted in the body. AHA powder is available in 3, 5, 10, 15, 20-gram packages. 3-gram packages were used in this study.

Figure 1: AHA powder

Algan Hemostatic Agent sponge (AHA sponge) (Figure 2) is obtained by purifying naturally adhesive absorbable modified special polysaccharides. It can be cut and shaped by the surgeon according to the size of the bleeding and operation area. It is 100% herbal. It acts quickly by effectively controlling leakage and bleeding. It is left in the body after application and prevents the risk of post-operative bleeding. It adheres to the application area by providing natural adhesion with its polysaccharide component. It is non-pyrogenic, compatible with blood and tissue, and biocompatible. It does not contain active ingredients of human or animal origin. It is quickly absorbed in the body. It protects the sternum and all risky areas by creating a barrier. It has a shelf life of 4 years.

Figure 2: AHA sponge

Algan Hemostatic Agent (AHA) liquid formulation, which consists of a mixture of six different plants, is given in Table 1. AHA liquid is a water-soluble, 100% herbal product. During its application, AHA liquid sponge is absorbed by the physician, and bleeding is stopped by pressure. In addition, bleeding can be stopped by applying herbal liquid to the bleeding area and simultaneously applying pressure with a sponge. These usage methods are left to the physician's preference for ease of application during the operation.

Table 1. Algan Hemostatic Agent Liquid Formulation

Plant name	Amount (gr)	Water	Infusion time (hour)	Bath temp.	Overall mix percentage
Blackberry leaf	100 gr	1 lt	48-49	50-60 °C	%8
Walnut leaf	70 gr	1 lt	48-49	50-60 °C	%10
Mistletoe, whole plant	100 gr	1 lt	48-49	50-60 °C	%35
Yarrow, above-ground part	120 gr	1 lt	24-25	50-60 °C	%25
Wolf claw, above-ground part	150 gr	1 lt	24-25	50-60 °C	%7
Grape leaf	70 gr	1 lt	48-49	50-60 °C	%15

Figure 3: AHA liquid

Ethical approval

The study was conducted based on the ethics committee decision sample approved by the relevant committee of Clinical Research Ethics with the decision dated 2019/8/101. It was conducted between 2023/01 -2023/12 in accordance with the ethical principles in the Declaration of Helsinki. Informed consent was obtained from the patients before the procedure.

Study design

A total of 140 consecutive volunteers were randomly selected from those who met the inclusion criteria for the study. The patients were randomly divided into 4 groups, each consisting of 35 patients. The 1st group was determined as the Algan Powder, the 2nd group as the Algan Sponge, the 3rd group as the Algan liquid, and the 4th group as the control group in which only traditional hemostatic methods were used.

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The cases in the study were isolated coronary artery patients. The surgeries were performed as routine procedures with the aid of a heart-lung pump, and AHA was used as a haemostatic agent in cases of bleeding or a high probability of bleeding. AHA graft was applied into the anastomosis areas, the atrium incision, and the fat tissue adjacent to the damaged coronary artery in the myocardium. Both the powder form (35 patients), the AHA liquid-impregnated sponge form (35 patients), and the sponge form (35 patients) of the product were used. After the powder form was applied, a two-minute light pressure compression was applied on it with a clean sponge. When using AHA-impregnated sponge, a two-minute moderate compression was applied. After the sponge form was applied, 2 minutes of light compression was applied with a sponge.

The criteria for including volunteers in the study were determined as follows:

Patients who are undergoing elective treatment and who will undergo coronary artery bypass surgery, aged between 50-80, and who have signed the voluntary consent form.

Exclusion criteria are; non-voluntariness, patients who need other treatment, those who need simultaneous surgery, those with blood diseases such as hemophilia A, B, etc., patients with chronic kidney failure, pregnant or breastfeeding mothers, patients who need urgent surgery, new and effective blood thinners such as ticagrelor. They were defined as patients using medication.

Evaluated parameters

Preoperative demographic data of the groups; use of acetyl salicylic acid (ASA), clopidogrel; perioperative data such as perfusion time, aortic cross-over time; Postoperative data such as drainage, urea, creatinine, hemoglobin, hematocrit and platelet values, and the amount of erythrocyte suspension-fresh frozen plasma-platelet suspension and whole blood used were compared.

Statistical Methods

Power analysis was applied to determine the sample. The evaluation was made as follows. $\alpha = 0.05$, $\beta = 0.20$, Test power = 0.80, Control group success rate = 0.20, Experimental group success rate = 0.70. 35 patients in each group were used in this study. Wilcoxon Signed Rank test was used for one-way comparisons. Mann-Whitney test was used between groups.

3. Results:

In this study, age, gender, preoperative ASA use and clopidogrel, diabetes, hypertension, perfusion time, aortic cross-clamp time, WBC, urea, creatinine, hemoglobin, hematocrit and platelet values, fresh frozen plasma, platelet suspension and whole blood use were among the groups. There is no statistical difference between the groups in terms of (Table 2 and Table 3).

Table 2. *Demographic data of the patients*

Groups	*Average Age*	*Gendeer*	*D.M.*	*H.T.*	*Preop ASA*	*Preop Clopidogrel*	*Average Pump time*	*Average Kross clamp time*
Algan powder group (n=35)	*65,45*	*25 M, 10 F*	*12*	*16*	*12*	*4*	*89 min.*	*57 min.*
Algan sponge group (n=35)	*64,33*	*26 M, 9 F*	*11*	*17*	*11*	*3*	*94 min.*	*59 min.*
Algan liquid group (n=35)	*66,27*	*23 M, 12 F*	*10*	*14*	*13*	*4*	*99 min.*	*62 min.*
Control group (n=35)	*65,32*	*26 M, 9 F*	*8*	*14*	*12*	*4*	*105 min.*	*64 min.*
P value	*> 0.05*	*> 0.05*	*> 0.05*	*> 0.05*	*> 0.05*	*> 0.05*	*> 0.05*	*> 0.05*

The number of ASA usages before surgery were 12, 11, 13, and 12 in the Algan powder, sponge, liquid, and control groups, respectively. The preoperative clopidogrel usage rate was 4, 3, 4, and 4 in the Algan powder, sponge, liquid, and control groups, respectively. Pump time was 89, 94, 99, 105 minutes in Algan powder, sponge, liquid, and control groups, respectively. Cross clamp time was 57, 59, 62, 64 minutes in the Algan powder, sponge, liquid, and control groups, respectively.

Preoperative and postoperative hemoglobin, hematocrit, and platelet levels were lower in both groups compared to preoperative values, but there was no significant difference between the groups (Table 3). There was no significant difference between the groups in terms of plasma suspension use (> 0.05).

The use of erythrocyte suspension was higher in the control group and was statistically significant ($p < 0.004$), and there was also a significant difference in postoperative drainage ($p < 0.039$).

Table 3. Laboratory and follow-up data of the patients

Groups	Averag e Preop	Average Postop	Average Preop	Average Postop	Average Preop	Average Postop	Averag e	Average Plasma	Average Erythroc

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	Hb	Hb	Htc	Htc	Plt	Plt	Drainage	susp	yte susp
Algan powder group (n=35)	14.6	11.9	44,6	38.8	255000	212000	363	0.78	0.64
Algan sponge group (n=35)	14.2	11.2	43,1	37.9	252000	211000	454	1.23	1.20
Algan liquid group (n=35)	13.9	10.2	43,1	36.7	242000	205000	543	1.33	1.62
Control group (n=35)	14.1	10.8	42.0	35.9	264000	215000	995	1.38	1.95
P value	> 0.05	> 0.05	> 0.05	> 0.05	> 0.05	> 0.05	**< 0.039**	> 0.05	**< 0.004**

4. Discussion:

In this study, the rate of erythrocyte suspension use and amount of drainage in the Algan-applied groups were found to be lower than the control group. Additionally, no complications occurred during the operation in the Algan-applied groups.

In a study in the literature where the effectiveness and safety of Algan hemostatic Agent in coronary artery bypass grafting (CABG) surgery was used, the results showed that the liquid form of Algan was effective in controlling bleeding and did not cause serious side effects (9). In this study, the average erythrocyte suspension use was found to be 1.14 in the treatment group and 2.06 in the control group. The results of the current study are similar to this study, and the average erythrocyte suspension usage was found to be 0.94, 1.20, 1.62 in the AHA powder, AHA sponge, and AHA liquid groups, respectively. In our study, the average use of erythrocyte suspension in the control group was 1.95 and was similar.

In the current study, total drainage was found to be 363, 454, 543, 995 mL in the AHA powder, AHA sponge, and AHA liquid groups, respectively. In this study conducted with AHA in the literature, total drainage was found to be 817 mL in the AHA liquid group and 1210 ml in the control group. These results are higher than our current study (9).

In another study, the liquid form was applied in lumbar disc operations and a significant difference was found in terms of hemoglobin and hematocrit values between the control and AHA-treated groups of 14 patients each (10). In this study, it was shown that the use of AHA significantly reduced the use of cautery. Similarly, a similar clinical study conducted on another hemostatic agent stated to be herbal-based showed that local use of Ankaferd Blood Clotter significantly reduced bleeding (11).

Preventing bleeding occurring in an organ or tissue is the process of clot formation and stopping bleeding as a result of the relationship between platelets and clotting factors, which is defined as hemostasis. In this study, it was shown that Algan Hemostatic Agent was effective in hemostasis in reducing blood loss in open heart surgery (9).

Although there are effective hemostatic agents available on the market, many of them have some disadvantages such as difficulty in use, requiring special storage conditions, and being expensive (12). AHA is an advantageous product with its features such as being ready to use, easy to use, and cheap. In previous studies, shortening the duration of hospital stay, preventing adverse events related to bleeding complications, and economic advantages were achieved (9, 10). Although hemostatic agents are so important and there are a wide variety of products on the market, the search for an ideal product continues. There are various publications about which product should be used in which situation (13).

Today, many different hemostatic agents are used in cardiac surgery (3). The most commonly used hemostatic agents are hemostatic agents obtained from oxidized cellulose (14). Due to their ability to induce local hemostasis, these types of hemostatic agents are designed primarily for use as buffering. It does not contain any internal coagulation elements. It is designed to induce clot formation and provide a suitable three-dimensional framework for clot organization. For the functionality of these agents, the presence of a functioning coagulation system is required (15). Microfibrillar collagens are a water-insoluble acidic salt of bovine collagen and adhere topically to the bleeding site, producing a hemostatic effect. It initiates platelet activation and aggregation and activates the formed fibrin clot (16). Gelatin, a hydrocolloid made from the partial acid hydrolysis of porcine collagen that is converted into foam and then dried, and fibrinogen-containing filling agents such as Tisseel, Beriplast, Hemaseel, Crosseal/Quixil, Vivostat can be used as anastomotic adhesives (17). BioGlue (CryoLife Inc, Atlanta, GA), bovine albumin, and synthetic tissue adhesives derived from glutaraldehyde are other hemostatic agents that can be used. Additionally, chitin polymers exist as a crystalline microfibril synthesized by many living organisms and form structural components in the exoskeleton of arthropods and the cell walls of fungi and yeast (18). Zeolite, a naturally occurring mineral, functions by absorbing water from the damage area through an exothermic reaction. This induces clot formation by increasing the density of clotting factors and platelets (19).

Some products have many side effects such as foreign body reaction, fever, immunological reaction, antibody production, and nerve damage (20). The products used in cardiovascular surgery are mostly adhesives containing fibrinogen and thrombin. Fibrin sealants are used topically and act on tissue

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to form clots, but are well tolerated. AHA also creates a mechanical barrier against bleeding and traps blood in the tissue and uses clotting factors to stop clotting pathways and stop bleeding. It is used in surgical procedures as a bleeding stopper when routine bleeding controls cannot be controlled. In addition, AHA products have advantageous features. It had a long shelf life of 4 years. It does not require any additional precautions or special storage to transport the packages. Its use does not require special training. It is not affected by harsh storage conditions; It can be stored in hot, cold, and humid environments. It gives results in patients using blood thinners and hemophilia patients. It results in hypothermic injuries. There is no placement problem. It does not produce heat and does not cause pain when used. It does not cause additional irritation or damage in the wound area. It increases the rate of tissue healing (21). It is easy to clean after use in the trauma area. The packages are impact-resistant and can be opened easily. It can be easily applied by a single person, to someone else, or to oneself. If necessary, it can be easily cleaned from where it is applied to provide a clean working area during surgery. It does not cause side effects and does not cause allergic reactions. It does not pose a risk of absorption by the body.

In the current study, the rate of erythrocyte suspension usage and amount of drainage in the Algan-applied groups were found to be lower than the control group, and also the fact that no complications occurred during the operation in the Algan-applied groups were important in demonstrating the reliability of these products. There was a significant difference in the study group in terms of postoperative drainage and erythrocyte suspension administered, both in less drainage and in the use of blood products.

As a result, the use of AHA reduces blood loss by reducing postoperative drainage. It causes less blood usage in the postoperative period in open heart surgery operations. AHA, a topical hemostatic agent, was found to be more effective in controlling bleeding than traditional methods. Since it is a herbal product, no side effects were observed. In some studies, the hemostatic potential of microporous polysaccharide-based tissue adhesives has been found to be effective. Although Algan emphasizes that the hemostatic agent is an effective haemostatic agent, there is a need for comparative studies among haemostatic agents, which are an important auxiliary argument in open heart surgery, in terms of their effectiveness.

Funding

This study was supported by The Algan Group Health Services (Algan Group Health Services Import and Export Industry and Trade Limited Company, Istanbul, Turkey).

Acknowledgment:

The authors are grateful for the financial support provided by Algan Group Health Services Import and Export Industry and Trade Limited Company, Istanbul, Turkiye. The company had been responsible for the study materials provided for scientists but had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Conflict of Interest:

The authors declare that there is no conflict of interest.

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