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Investigation of the clinical efficacy and safety of herbal Algan Hemostatic Agent in coronary artery bypass graft surgery

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ABSTRACT

Background. Hemostatic agents have the potential to improve clinical outcomes by decreasing postoperative drainage and the need for transfusions. Algan Hemostatic Agent is a polysaccharide-based hemostatic agent obtained from a mixture of six different herbs. The aim of this study is to investigate the clinical efficacy and safety of Algan Hemostatic Agent as a local hemostatic agent in coronary artery bypass operations. *Methods*. 28 subjects who underwent isolated coronary artery bypass graft surgery and met the inclusion criteria were included in this clinical study. Traditional methods (cautery, ligation, etc.) were used in the control group, whereas Algan Hemostatic Agent was added in the study group. A sponge soaked in Algan Hemostatic Agent liquid was lightly compressed to the bleeding area for 120 seconds. *Results*. Both groups were comparable in terms of preoperative demographic data and perioperative laboratory values. Drainage on the postoperative first day (650 ml vs 896 ml; p=0.381) and total drainage (817 ml vs 1210 ml; p=0.031) were found higher in the control group. Another significant difference was observed between the groups in terms of erythrocyte suspension utilization rate (1.14 U in the treatment group and 2.06 U in the control group, p=0.004). Algan Hemostatic Agent did not cause any complications during administration. *Conclusion*. In conclusion, Algan Hemostatic Agent has been found effective and safe in controlling bleeding during coronary artery bypass operations.

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Introduction

Controlling bleeding in surgical operations or other emergencies is very important in terms of preventing the negative consequences of hypovolemia and/ or blood transfusions. Hemostatic agents are increasingly used for this purpose to stop minor and major bleeding after injuries, traumatic cuts, dental operations, and surgical interventions. Coronary artery bypass grafting (CABG) operations are among the operations with high bleeding risk [1-3]. Bleeding control can be challenging during coronary bypass operations, due to factors like preoperative medications and cardiopulmonary bypass effect on coagulation. Therefore, a fast and effective hemostatic agent is needed in CABG surgery.

Currently, many hemostatic products with various forms are developed for use in different bleeding indications [4-8]. Some of them are very expensive, inadequate, or harmful to tissues. They may cause some complications such as nerve damage, infection, and antibody development in the area where they are applied [9-14]. Others are ineffective and do not provide an optimum level of bleeding control. Therefore, it is important to develop a natural, effective, harmless, and economical anti-hemorrhage product that can be used safely.

Algan Hemostatic Agent (AHA) is a 100% herbal polysaccharide-based product derived from a standardized blend of six different plants. AHA has a certification number that is designed to help control bleeding during surgical procedures. The AHA does not contain animal or human components. AHA is a biocompatible, non-flammable, thin, dry, sterile, colorless liquid. AHA is water-soluble, so there is no need for post-coagulation clearance from application sites. AHA is used in surgical interventions (excluding pediatric, eye, and central nervous system interventions) as an auxiliary hemorrhage stopper when pressure, suture, or other routine surgical bleeding

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stopping procedures are ineffective in the control of capillary, venous and arterial bleeding. AHA turns into a polymeric network in the area where it is applied, accelerates the coagulation by trapping the blood in it, and creates a mechanical barrier in front of the bleeding vein [15-18].

The main purpose of this study is to investigate the clinical efficacy and safety of the hemostatic product called AHA in patients undergoing elective CABG operation.

Materials and Methods

Identity of the research product

AHA is a polysaccharide-rich product obtained from a standard blend of six different herbs without a single active ingredient (Table 1 and Figure 1). Plants where AHA is formed are: Mistletoe, Yarrow, grape leaf, blackberry leaf, walnut leaf, and wolf claw. As a result of the analysis, the rate of polysaccharide was found to be 57%. The content of phenolic substance was found as 3.015 mg GAE / g gallic acid equivalent in 50 mg AHA sample. There are various sizes of tampons with liquid hemostatic impregnation.

Table 1. Algan Hemostatic Agent 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 1. AHA application in coronary bypass operation in the operating room.

Ethical approval

Study was approved by the X Clinical Research Ethics Committee with the decision number 2019/8/101, dated 21.10.2019. The study was conducted in accordance with the ethical principles in the Declaration of Helsinki. Informed consent was obtained from the patients before the operation.

Study Design

A total of 28 consecutive volunteers (Study group, n=14; and Control group, n=14) who had CABG surgery and met the inclusion criteria were randomly included in this clinical study. AHA was used as an aid in routine hemostatic applications such as ligation, only the effect and reliability of AHA being monitored. The product was applied to patients only in case of bleeding during the operation. The primary endpoint of the study was bleeding as determined by postoperative drainage levels and safety of AHA use. Patients whose operation was planned for isolated coronary artery disease who met the inclusion criteria were invited to the study. Patients who accepted to participate in the study were randomly divided into two groups as study and control groups using the closed-envelope method before the operation. The working group has been informed in detail and has been insured by the sponsor company.

Standard on-pump CABG procedures were applied in both groups, and in both groups, cautery, clip etc. are used as a standard for bleeding control as well.

AHA was used as follows: For bleeding that occurs on the leg after the great saphenous vein harvesting. In the study group, sponge impregnated with Algan hemostatic agent was applied along the entire wound line with light pressure for 120 seconds. In the control group, compression was applied to the same area with flat sponge for the same period. Another graft used in the operation is the left internal mammary artery, which is freed from the thoracic wall. Arterial bleeding may occur following the release and separation of this artery, which has many branches, from the chest wall. In the study group, sponge impregnated with Algan hemostatic agent was applied under pressure for 120 seconds along the line of the chest wall where the internal mammary artery was removed. In the control group, it was applied to the same area with a plain sponge in the same period. During the bleeding control phase of the operation, bleeding arising from large vessels, anastomosis lines of by-pass grafts, soft tissue cut for exploration and cut bones, AHA was applied for 120 seconds in the study group. In the control group, a plain sponge was applied.

Demographic data

Preoperative demographic data in both groups, using ascorbic salicylic acid (ASA), clopidogrel use; perioperative data such as perfusion duration, aortic cross

clamp time; and postoperative data such as drainage, urea, creatinine, hemoglobin, hematocrit and platelet values, erythrocyte suspension, fresh frozen plasma, platelet suspension and whole blood usage amounts were compared.

Working population selection

The inclusion criteria of the volunteers for the study were determined as follows: patients, undergoing elective coronary artery bypass surgery, being between the ages of 50-75, signing the volunteer consent form for the research.

Exclusion criteria; the criteria for volunteers not to be included in the research are: patients, who need any other concomitant surgeries, who have blood disease like hemophilia A, B, etc., not signing the voluntary consent form, pregnant women or nursing mothers, with dialysis dependent chronic renal failure.

Dose selection in the study: each patient received as many AHAs as needed; there is no specific dose selection. Blinding; since the control product was not used, it was not performed for this study.

Statistical Methods

Power analysis was applied to determine the sample size. 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. In order for the study to be carried out under the conditions described above, at least 9 patients should be included in the groups. In this study, 14 patients were used in each group. One-way Wilcoxon Signed Ranks Test was used for comparisons between groups, and Mann-Whitney test was used for comparisons between pairs.

Results

Preoperative and operative data were presented in the Table 2. The number of preoperative ASA usage was 10 in the treatment group and 6 in the control group. The number of preoperative clopidogrel use was 8 in the treatment group and 4 in the control group. Preoperative perfusion time was 115 minutes in the treatment group and 131 minutes in the control group. The preoperative aortic cross clamp time was 62 minutes in the treatment group and 77 minutes in the control group.

There was no statistically significant difference between the treatment group and the control group in terms of age, gender, hypertension, diabetes, preoperative ASA and clopidogrel use, preoperative perfusion time and preoperative aortic cross clamp time. Results obtained in this study are presented in Table 2.

Table 2. Demographic data of groups

Patient number	Age		Gender		DM		HT		Preop. ASA		Preop. Clopidogrel		Perfusion time (min)		Aortic cross clamp time (min)	
	CG	TG	CG	TG	CG	TG	CG	TG	CG	TG	CG	TG	CG	TG	CG	TG
1	63	49	M	M	1	1	1	1	1	1	1	0	98	99	46	60
2	48	57	M	M	0	1	1	1	0	1	1	1	78	73	46	40
3	60	64	M	M	0	1	1	1	0	0	1	0	110	165	70	82
4	67	62	F	M	1	1	1	1	0	1	0	1	224	112	96	62
5	53	68	M	M	1	0	1	1	1	1	0	0	110	118	67	64
6	64	48	F	M	1	0	1	1	0	1	0	1	120	123	85	63
7	54	64	M	M	1	0	1	1	0	1	0	1	115	128	68	70
8	57	52	M	F	1	1	1	1	1	1	0	0	112	120	60	50
9	66	66	M	F	1	0	1	1	0	0	0	1	98	93	55	47
10	59	48	M	M	1	1	1	1	0	0	0	1	225	71	173	40
11	55	55	F	M	1	0	1	0	1	0	0	0	233	126	143	75
12	33	59	M	M	1	0	1	1	0	1	0	0	123	150	55	100
13	74	70	M	M	0	1	1	1	1	1	0	1	73	135	32	67
14	43	64	M	M	0	0	0	1	1	1	1	1	122	110	84	52
Average	56.85 ± 10.56	59 ± 7.57	11M/ 3F	12M/ 2F	0.71 ± 0.46	0.5 ± 0.32	0.92 ± 0.26	0.92 ± 0.26	0.42 ± 0.51	0.71 ± 0.46	0.28 ± 0.46	0.57 ± 0.51	131.5 ± 52.66	115 ± 26.27	77.07 ± 37.76	62 ± 16.51
P	>0.05		>0.05		>0.05		>0.05		>0.05		>0.05		>0.05		>0.05	

In the treatment group - the number of preoperative, postoperative day 1 and discharged WBCs were 9, 13.20 and 11.78, respectively. In the control group - the number of preoperative, postoperative day 1 and discharged WBCs were 9.42, 11.63 and 10.71, respectively. In the treatment group - preoperative, postoperative 1st day and discharged urea were 32.50, 31.10 and 37.28, respectively. In the control group - the preoperative, postoperative 1st day and discharged urea were found as 41, 40.57 and 43.15, respectively. In the treatment group - the amount of creatinine in preoperative, postoperative 1st day and discharged was 0.86, 0.91 and 0.82, respectively. In the control group - preoperative, postoperative 1st day and the amount of discharged creatinine were 0.89, 1.26 and 0.92, respectively. There was no significant difference between the groups in terms of preoperative, postoperative 1st day and discharge WBC, urea and creatinine values. WBC, urea and creatinine values of the groups are given in Table 3.

Table 3. Biochemical findings of the groups

Case no.	Preop WBC		Postop 1 WBC		Discharged WBC		Preop Urea		Postop 1 Urea		Discharged Urea		Preop Creat.		Postop 1 Creat.		Discharged Creat.	
	CG	TG	CG	TG	CG	TG	CG	TG	CG	TG	CG	TG	CG	TG	CG	TG	CG	TG
1	11.00	12.90	9.2	20.9	11.6	19.4	56	32	63	33	59	62	1.3	0.72	1.6	0.93	1.39	0.94
2	9.60	11.40	8.5	18.2	7.5	15.6	41	27	29	33	46	49	0.9	0.89	0.81	1.04	0.76	0.94
3	9.30	4.50	13.2	8.7	12.1	6.1	39	38	37	44	63	41	1.1	0.92	1.39	0.92	1.14	0.66
4	5.20	7.90	10.1	12.5	10.1	13.1	41	40	48	31	71	42	0.7	0.89	0.97	0.7	1.03	0.88
5	10.60	6.30	9.8	4.1	8.8	6.5	57	37	39	33	24	35	0.86	0.88	1.1	0.76	0.84	0.7
6	5.30	8.30	10.5	23	6.5	9.9	39	31	31	37	44	36	0.74	0.97	0.78	1.19	0.81	0.82
7	9.5	9.60	12.1	14.5	10.8	11.1	32	32	28	34	33.2	24	0.9	0.81	0.93	0.82	0.78	0.62
8	5.00	10.40	11.4	14.2	10.1	11.4	50	17	35	18	34	16	0.9	0.56	1.1	0.61	0.91	0.53
9	11.00	7.60	13.7	9.2	20	9.3	50	28	43	29	56	44	1.09	0.88	1.47	1.04	1.15	0.87
10	12.50	8.20	12.6	8	12.2	8	21	37	91	23	32	28	0.6	1.2	3.5	1.02	0.6	1
11	12.30	11.60	12.4	17.2	10	14.3	39	38	30	34	44	41	0.8	0.93	1.06	1.02	0.8	0.86
12	13.80	10.50	15.6	11.6	8.4	14.5	43	34	30	26	36	34	1.03	0.69	0.8	0.65	0.87	0.56
13	7.1	5.80	12.9	10.9	10.2	9.8	41	34	35	35	42	30	0.9	0.85	1.12	1.06	1.05	1.02
14	9.70	11.00	10.9	11.8	11.7	16	25	30	29	25	20	40	0.77	0.98	1.08	1.04	0.76	1.15
Average	9.42 ± 2.81	9 ± 2.81	11.63 ± 2.45	13.2 ± 1.94	10.71 ± 5.22	11.78 ± 3.17	41 ± 3.86	32.5 ± 10.35	40.57 ± 5.95	31.1 ± 17.37	43.15 ± 6.49	37.2 ± 14.82	0.89 ± 11.22	0.86 ± 0.18	1.26 ± 0.15	0.91 ± 0.68	0.92 ± 0.20	0.82 ± 0.18
P	>0.05		>0.05		>0.05		>0.05		>0.05		>0.05		>0.05		>0.05		>0.05	

In the treatment group - preoperative, postoperative 1st day and the amount of hemoglobin during discharge were 13.24, 9.19 and 9.37 mg / dl, respectively. In the control group - the amount of hemoglobin preoperatively, postoperatively on the 1st day and discharged was 13.74, 9.23 and 9.17 mg / dl, respectively. In the treatment group - the amount of hematocrit preoperatively, postoperatively on the 1st day and discharged were found as 39.93, 27.72 and 28.70%, respectively. In the control group - preoperative, postoperative 1st day and the amount of hematocrit discharged were found as 41.33, 27.75 and 28.02%, respectively. In the treatment group - the average amount of platelets preoperatively, postoperatively on the first day and discharged was 285, 188 and 372 thousand/ ml, respectively. In the control group - the mean amount of platelets in preoperative, postoperative 1st day and discharged was found to be 280, 183 and 366 thousand/ ml, respectively. There was no significant difference between the groups in terms of preoperative, postoperative 1st day and discharge hemoglobin, hematocrit and platelet. Hemoglobin, hematocrit and platelet amounts of the groups are given in Table 4.

Table 4. Blood values of the groups

Case no.	Preop Hgb.		Postop1 Hgb.		Discharge Hgb.		Preop Htc.		Postop1 Htc.		Discharge Htc.		Preop Plt.		Postop1 Plt.		Discharge Plt.	
	CG	TG	CG	TG	CG	TG	CG	TG	CG	TG	CG	TG	CG	TG	CG	TG	CG	TG
1	11,5	12.9	9.7	9.2	10	9,5	35,3	38.9	29.1	27,8	30.8	29,8	277	334	166	353	404	845
2	13,3	14.3	8.6	11.1	7.2	8,1	39,8	42.9	25.7	34,7	21.7	24,9	226	260	226	342	175	267
3	14,1	13.4	7.3	8.1	7.7	8,6	43,6	39.6	21.5	25,2	23.1	26,4	263	135	190	143	182	235
4	12,2	11.3	9.9	9.3	7.7	8,1	38,2	32.8	29.8	28,3	22.6	25,3	158	284	100	192	84	171
5	13,7	13.1	10	9.3	9.2	9,9	43,1	41	30.2	28,1	28.3	29,8	581	280	186	130	252	233
6	14,1	13.3	11.3	10.1	10.2	9,7	44,6	39.6	32.5	30,7	30.9	29,4	288	248	238	311	531	457
7	13,9	10.9	11.4	9.6	9.3	8,3	41,4	33	34.1	28,7	27.3	25	206	287	179	264	236	251
8	11	11.2	10.2	9.3	11.4	8,1	34,5	36.1	30.8	28,2	34.8	24,9	182	325	141	287	534	399
9	12,7	18	7.8	8.7	9.6	9	39	52.3	23.8	27,1	29	27,5	243	277	139	165	219	278
10	14,4	12.4	8.7	10.6	10	7,7	41,8	37.6	27	30,2	33.1	23,9	403	245	242	179	662	269
11	14,1	12.9	7.6	7.9	9.4	9	42,9	37.2	23	24,5	29.2	27,9	296	202	131	190	630	203
12	15,2	14	9.1	9.6	10.9	8,6	46,3	43.9	27.9	29,2	32.9	25,9	342	271	270	157	655	178
13	13,7	13.3	11	11.8	8.8	11,2	40,8	40.9	33	34,6	27	30	232	145	229	119	383	148
14	16,5	14.4	6.7	9.1	7.1	9,8	50,4	43.3	20.1	28,5	21.6	30,6	231	225	131	191	189	350
Average	13.6 ± 1.42	13.24 ± 1.75	9.23 ± 1.51	9.55 ± 1.07	9.17 ± 1.33	8.97 ± 0.95	41.55 ± 4.19	39.93 ± 4.95	27.75 ± 4.40	28.98 ± 2.91	28.02 ± 4.38	27.23 ± 2.32	280 ± 107	251 ± 58	183 ± 51	215 ± 79	366 ± 202	306 ± 177
P	>0.05		>0.05		>0.05		>0.05		>0.05		>0.05		>0.05		>0.05		>0.05	

The average erythrocyte suspension usage rate was 1.14 in the treatment group and 2.06 in the control group. The average usage of fresh frozen plasma was 0.14 in the treatment group and 0.86 in the control group. The mean platelet suspension usage rate was 0.14 in the treatment group and 0.33 in the control group. The mean whole blood usage rate was 0.07 in the treatment group and 0.13 in the control group. In the treatment group, postoperative 0 drainage and total drainage were found 650 ml and 817 ml respectively. In the control group, postoperative 0 drainage and total drainage were found 896 ml and 1210 ml respectively. A significant difference was observed between the groups in terms of the rate of erythrocyte suspension use and postoperative drainage values. The amounts of erythrocyte suspension, fresh frozen plasma, platelet suspension and whole blood use of groups are presented in Table 5.

Table 5. Blood products used in groups

Case no.	Total ES		Total plasma		Total PLT susp.		Whole blood		Postop. 0 drainage (ml)		Total drainage (ml)	
	CG	TG	CG	TG	CG	TG	CG	TG	CG	TG	CG	TG
1	2	0	0	0	1	0	0	0	750	300	750	400
2	2	0	0	0	0	0	0	0	1350	750	1550	1000
3	1	2	0	0	2	0	1	0	650	300	850	600
4	2	1	0	0	0	0	0	0	800	1000	1100	1250
5	5	2	2	2	0	0	0	1	600	850	650	1000
6	0	0	1	0	0	0	0	0	650	1000	900	1200
7	1	4	0	0	0	1	0	0	950	700	1000	800
8	0	1	0	0	0	0	0	0	700	350	1000	450
9	2	1	0	0	0	0	0	0	1000	600	1900	650
10	3	0	2	0	0	0	0	0	450	700	750	800
11	2	2	2	0	0	0	0	0	950	500	1050	500
12	3	1	0	0	0	0	0	0	400	750	700	950
13	0	0	0	0	0	0	0	0	2000	400	2950	500
14	4	2	3	0	1	1	0	0	1300	900	1800	1350
Average	2.06	1.14	0.86	0.14	0.33	0.14	0.13	0.07	896	650	1210	817
P	< 0.004		>0.05		>0.05		>0.05		>0.05		<0.031	

Statistical results

In this study, age, gender, preoperative use of ASA 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 analyzed. There was no statistical difference between the groups in terms of parameters. The use of erythrocyte suspension was higher in the control group and was statistically significant. There was also a significant difference in postoperative drainage values. Statistics results are given in Table 6.

There was no difference in wound healing sites in the AHA group. There was no situation that would require the patients to be excluded from the evaluation. All treatment group patients were evaluated. Planned follow-up observations were made in these patients.

Treatment compliance was evaluated by the surgeon who conducted the study. There was no adherence to treatment in any of the participants. The use of AHAs did not cause serious side effects such as death or disability. In addition, AHA did not cause undesirable side effects such as local tissue damage, temperature increase, vascular occlusion causing normal circulation deterioration. The primary endpoint of this study was determined as demonstrating efficacy and safety in 14 patients who were administered the application, and this aim was achieved at the end of the study. AHA has been found to be effective and safe as a result of this clinical trial. The study has no secondary endpoints. There is a statistically significant difference in the use of erythrocyte suspension and total drainage parameters when comparing control-treatment groups.

Table 6. Statistics results

	Control group		Treatment Group		p
	Average	SD	Average	SD	
Perfusion time	131,50	52,66	115,93	26,28	0,505
ACC	77,07	37,76	62,29	16,52	0,129
Preop. WBC	9,42	3,04	9,00	2,46	0,982
Preop. Hgb	13,74	1,76	13,60	1,43	0,300
Preop. Htc	41,33	4,95	41,55	4,20	0,241
Preop. Plt	280,57	106,79	251,29	58,55	0,535
Preop. Ure	41,00	10,38	32,50	5,96	0,006
Preop. Cr	0,89	0,20	0,87	0,15	0,535
Postop. 1 WBC	11,63	2,07	13,20	5,23	0,323
Postop. 1 Hgb	9,23	1,28	9,55	1,07	0,395
Postop. 1 Htc	27,75	3,62	28,99	2,91	0,346
Postop. 1 Plt	183,42	61,09	215,93	79,65	0,358
Postop. 1 Urea	40,57	17,72	31,07	6,50	0,112
Postop. 1 Cr.	1,26	0,70	0,91	0,18	0,066
Discharge WBC	10,71	3,45	11,79	3,87	0,280
Discharge Hgb.	9,17	1,26	8,97	0,96	0,279
Discharge Htc.	28,02	4,25	27,24	2,33	0,270
Discharge Plt.	366,85	202,38	306,00	177,84	0,462
Discharge Urea	43,15	16,96	37,29	11,22	0,135
Discharge Cr.	0,92	0,22	0,83	0,19	0,301
Postop_0 drainage	896,42	243	650	247	0,381
Total drainage	1210,71	339	817	314	**0,031**
Erythrocyte suspension	2,07	1,089	1,14	1,167	**0,004**

Discussion

Algan Hemostatic Agent has been shown to be effective in controlling bleeding and reducing blood loss in coronary bypass operations. AHA significantly reduces erythrocyte suspension transfusion and postoperative drainage. It was also considered reliable because no complications occurred.

In cases where compression, ligation or cauterization is not applied on the vessel, bleeding control cannot be easy with existing hemostatic agents. Therefore, regardless of the hemostatic agent used, it is used as an aid to traditional methods. AHA is one such product, with many advantages such as being ready to use, easy to use and inexpensive. In practice, hemostatic agents have many benefits, such as

reducing the duration of hospital stay, protection from adverse events related to bleeding complications, and economic advantages [19-21]. Most importantly, they facilitate the operating process and thus are life-saving.

Despite the fact that hemostatic agents are so important and there are many products on the market, there are not enough research articles on the subject. There are very few areas in medicine with such a small number of studies, depending on their importance. There could be many reasons for this. The products used in this field consist of a wide variety of products with their mechanism of action and content. It is difficult to classify hemostatic agents because it is a mixture of different products as well as stand-alone products. Some are in liquid form, some in powder form and some in the form of bandages. Although it was stated in a study that collagen-based hemostatic agents are more effective in multiple surgical indications, which product will be used in which indication creates a separate problem in this variety [22]. Even if there are a limited number of publications, there are some suggestions about which product should be used in which case [23, 24]. Studies have also been conducted in the field of cardiothoracic surgery and algorithms have been proposed [25]. In another study, mechanical hemostatic agents were reported to be more effective in cardiothoracic surgery [26]. Hemostatic agents have been used for a long time in cardiac surgery [27,28]; today, many different hemostatic agents are used in cardiac surgery [29-34]. Some products have many side effects such as foreign body reaction, fever, immunological reaction, antibody production, and nerve damage [35]. The products mostly used in the field of cardiovascular surgery are products containing fibrinogen and thrombin (fibrin sealants). Studies show that fibrin sealants are well tolerated and effective in cardiac and aortic surgery in providing hemostasis. Fibrin sealants are used topically and form a clot by affecting the coagulation cascade at the final stage [36]. On the other hand, AHA also creates a mechanical barrier in front of bleeding by rapidly imprisoning the blood in the tissues due to its rich polymeric network, in addition to activating the coagulation pathways by using coagulation factors to intercept and induce bleeding arrest.

Gelatin-based matrix and thrombin, oxidized regenerated cellulose, purified porcine skin gelatin were compared in a study conducted in the field of cardiac surgery. In this study, the product consisting of gelatin-based matrix and thrombin was shown to be more effective in providing hemostasis [37].

Some products such as Microporous polysaccharide hemospheres and Flowable hemostatic matrix, which are known as common and effective products in the market, are far from practical. They are not ready-to-use products and must be prepared during the operation. Products that do not need to be prepared and used are thrown away. Because they are expensive products, they create difficulties for patients.

In operations such as coronary bypass, it is not practical to use expensive hemostatic agents, namely in operations where the use of hemostatic agents in the patient cannot be predicted. Therefore, there is a need for easy-to-apply, ready-to-use inexpensive products. AHA is a ready-to-use product and can be used as needed. Unused products can be stored for use in other operations. Hemostasis is easily achieved by lightly compressing the AHA soaked snappy bleeding area. Spreading of the liquid over a wide area in the application area provides convenience in application.

Microfibrillar collagen hemostat (Colgel) and oxidized cellulose (Surgicel) were compared in a study conducted on patients with high-risk bleeding groups [38]. In this study, in the first 24 hours, the Chest tube drainage was found to be 373 ± 143 mL in the Colgel group and 571 ± 144 mL in the Surgicel group (P = .01). Total postoperative chest tube drainage was found to be 423 ± 154 mL (range, 280-1100 mL) in the Colgel group and 677 ± 128 mL (range, 285-1350 mL) in the Surgicel group (P = .01).

In our study, postoperative 0 drainage mean 650 ml and total drainage 817 ml in the treatment group, while 0 postoperative drainage mean 896 ml and total drainage 1210 ml in the control group. It is inevitable to touch or cut the vessels during the operation and bleeding is difficult to control. The hemostasis method commonly used in these operations is electrocoagulation. Electrocoagulation causes tissue damage by generating local heat, and there is a risk of damage to the peripheral nerve. In addition, the use of electrocoagulation is limited in cardiovascular surgery.

Some of the hemostatic products are in the form of absorbable fillers [39]. AHA is an easily absorbed product in liquid form that provides local hemostasis, which is not used as a filler. While it provides hemostasis in the area where it is applied, it does not create a mass effect by accumulating and does not need to be cleaned from the area. It contributes to hemostasis by easily spreading all over the area where it is applied.

Limitations of the study

Hemostasis is affected by many factors, such as the condition of the patient, the diameter and number of damaged vessels, the amount of bleeding that varies greatly from one patient to another. This means that it is not possible to get a standard result. In addition, the number of patients in the study may be the lowest number allowed for the statistical study, for ethical reasons. As this study is an efficacy and safety study, no comparison has been made with another product. Randomization was not performed in this study because no comparison product was used and there was no superiority study.

For all of the above reasons, comparative clinical trials are needed to investigate efficacy compared to other products used in the market.

As a result, the use of AHA reduces blood loss in coronary bypass operations, resulting in less blood use. In addition, AHA significantly decreases the amount of postoperative drainage.

Conclusions

AHA, a topical hemostatic agent, was found to be more effective in bleeding control than traditional methods in this study, where smaller blood transfusions were needed with no local complications. This study was conducted on a very limited number of people. Therefore, it is necessary to conduct comparative studies with other products known to be effective in this field and in extensive studies.

In this study, demographic data of treatment and control groups (age, gender, ASA use, clopidogrel use, diabetes, hypertension) perfusion time, aortic cross clamp time, WBC, urea, creatinine, hemoglobin, hematocrit and platelet values, erythrocyte suspension, fresh frozen plasma, platelet suspension and whole blood usage amounts were compared.

Among these parameters, the most important parameter showing the effectiveness of AHA is the average amount of blood products consumed per operation in 14 patients in each group. This study showed that AHA significantly reduced the use of erythrocyte suspension in coronary bypass operations. No difference was observed in hemoglobin, hematocrit and platelet parameters, since blood loss was urgently replaced with erythrocyte suspension.

This is an efficacy and safety study and has not been compared with another product. However, it would be appropriate to demonstrate the real effectiveness of AHA by performing superiority studies with more participants with other different products available in the market.

Acronyms and abbreviations

AHA: Algan Hemostatic Agent
ASA: ascorbic salicylic acid
CABG: coronary artery bypass grafting

Conflict of interest disclosure

There are no known conflicts of interest in the publication of this article. The manuscript was read and approved by all authors.

Compliance with ethical standards

Any aspect of the work covered in this manuscript has been conducted with the ethical approval of all relevant bodies and that such approvals are acknowledged within the manuscript.

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