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Research Article

SeraSeal, a Topical Primary Hemostatic Agent

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Abstract

SeraSeal is a topical primary hemostatic agent designed to arrest venous, arterial, and bone marrow hemorrhages and all four classes of hemorrhages, even in the presence of coagulopathies, within seconds. The active agents in SeraSeal: agar, bovine FIIa, FVIIa, FIXa, FXa, achieve hemostasis within seconds by catalyzing the normal coagulation cascade system that has been activated by the release of A major multicenter clinical study of SeraSeal vs cauterization as a primary [1,2] thromboplastin from the injured tissue. Bleeding is a major cause of morbidity and mortality in wounds. Hemorrhage is responsible for 30–40% of trauma mortality, and of those deaths, 33–56% occur during the prehospital period. Among those who reach hospital care, early mortality is caused by continued hemorrhage, coagulopathy, and incomplete resuscitation. Treatment of acute hemorrhage outside and inside the clinical setting with SeraSeal will reduce the trauma morbidity rate. hemostatic agent, was conducted on a wide range of tissues that significantly outperformed cauterization by achieving hemostasis more than 25% faster.

Keywords: Sera Seal; Primary; Hemostatic; Agent

Introduction

There are 5 common trauma challenges to control bleeding:

The first challenge, Hemorrhage

Better survival if the lapsed time between the traumatic injury and admission to the operating theater is minimized. This is particularly true for patients who are presented in an exsanguinated state or in severe hemorrhagic shock, due to penetrating vascular injuries. There is a significant decrease in mortality from shock, by having a 60-minute time limit for patients in a state of hemorrhagic shock [3].

Second challenge, five forms of shock

Hemorrhagic shock is the most important type encountered in resuscitation.

There are five classes of hemorrhagic shock [4,5].

- **Class 1:** 750 mL blood loss or up to 15% of total blood volume
- **Class 2:** 750 mL–1500 mL blood loss or 15–20% total blood volume
- **Class 3:** 1500 mL–2000 mL blood loss or 30–40% total blood volume
- **Class 4:** >2000 mL blood loss or over 40% total blood volume

Hypovolemic shock, a broader category is closely related to hemorrhagic shock [6,7].

Cardiogenic shock, aside from acute hemorrhage, cardiac output, is strictly the component by which the body cannot perfuse the rest of the body [8].

Neurogenic and septic shock deal with a decrease in systemic vascular resistance, which prevents the body from directing blood to vital organs due to the decreased pressure [9].

Adrenal insufficiency shock incorporates factors of cardiac output, systemic vascular resistance, and volume [10].

Third challenge, resuscitation

Balanced resuscitation minimizes the impact of trauma-induced coagulopathy, limits blood product waste, and reduces the complications that occur with aggressive crystalloid resuscitation. The lethal triad of trauma consists of hypothermia, acidosis, and coagulopathy [11]:

- Hypothermia contributes to worse metabolic acidosis, cardiac dysrhythmias, serious electrolyte disorders, and worse coagulopathy [12].
- Acidosis results from inadequate tissue perfusion, and subsequent production of lactic acidosis through anaerobic metabolism. Acidosis is during the administration of intravenous crystalloid or colloid fluids. Acute [14,15] often exacerbated by the overuse of normal saline for resuscitation [13].

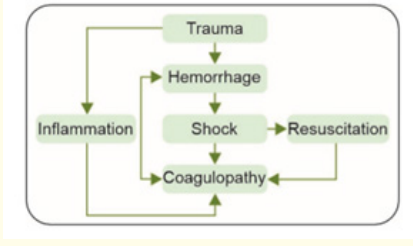
Fourth challenge, COAGULOPATHY

Coagulopathy is a combination of dilutional resuscitation-related coagulopathy and nondilutional acute traumatic coagulopathy. Dilutional coagulopathy occurs because of hemodilution traumatic coagulopathy occurs before the hemodilution of coagulation factors and is a result of direct activation of the protein-C pathway by tissue injury and hypoperfusion.

Firth challenge, inflammation

Massive injury leads to activation of the immune system. Infections, ischemia, or operations can further augment the systemic inflammation, which can lead to tissue destruction in organs not originally affected by the initial trauma, with subsequent development of multiorgan dysfunction. The Flowchart 1: Trauma hemorrhagic shock initial pro-inflammatory response after the fifth challenge and before is followed by an anti-inflammatory mechanism of SeraSeal response and can result in immune suppression with high risk of infection and sepsis [16].

Trauma hemorrhagic shock after the fifth challenge and before mechanism of SeraSeal is shown in flowchart 1.



Flow chart 1

Mechanism of Seraseal

Agar, the complex sugar in SeraSeal, when added to a bleeding wound, will cross-link with the ions of platelet phospholipids, and cations from amine 39 groups in fibrinogen/fibrin monomers and tissue proteins, forming an α-1,6linked galactophospho and α-1,6-galactoamine forming a gelatin barrier over the wound. This barrier reduces blood from escaping through the opening of the wound, allowing the patient's cascade system to form a fibrin clot sooner. The Factors IIa, VIIa, IXa, and Xa, function in an ancillary way, by facilitating the agar to cross-link with the platelets and fibrinogen, lending strength to the gelatin barrier, and by biologically facilitating only the blood outside of the wound, to facilitate the formation of a fibrin clot. The clotting cascade is a biological activity system, and the clotting factors in the product participate in this biological activity as a catalyst to form a fibrin clot.

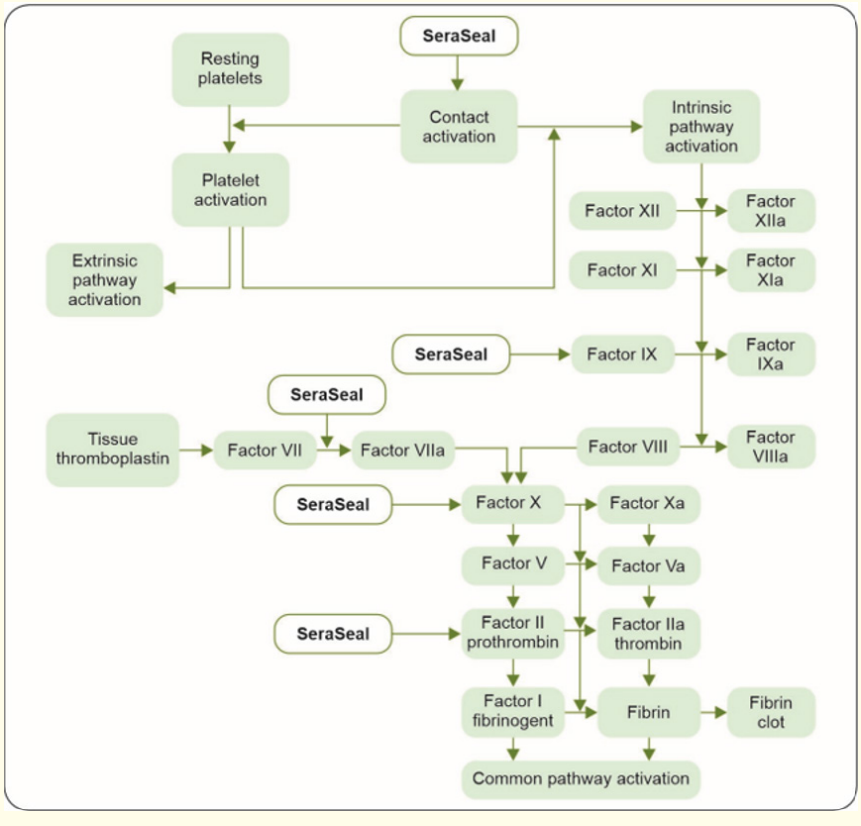
The activated platelets do an internal surface translocation, where more phospholipids are available to cross-link with agar, and where covalent lysine to glutamine linkages between gamma chains of adjacent fibrin molecules and between adjacent alpha chains, create clot stabilization.

The activation of the coagulation cascade system begins with the release activate Factor VII creates a link between the intrinsic and extrinsic pathways. of thromboplastin from the injured tissue. Thromboplastin will then bind to the serine protease Factor VII, activating the extrinsic coagulation pathway at the site of injury. Factor VIIa, in turn, will cleave Factor X to Factor Xa in the same

manner as Factor IXa of the intrinsic pathway. The activation of Factor VII occurs through the action of thrombin or Factor Xa. The ability of Factor Xa to An additional link between the two pathways exists through the ability of tissue factor and Factor VIIa to activate Factor IX.

The common point in both pathways is the activation of Factor X to Factor Xa. Factor Xa activates prothrombin (FII) to thrombin (FIIa). Thrombin, in turn, converts fibrinogen (Factor I) to fibrin. The activation of thrombin occurs on the surface of activated platelets and requires formation of a prothrombinase complex. This complex is composed of the platelet phospholipids, phosphatidylinositol and phosphatidylserine, calcium, Factors Va and Xa, and prothrombin. Factor V is a cofactor in the formation of the prothrombinase complex, like the role of Factor VIII in the intrinsic tenase complex formation. Like Factor VIII activation, Factor V is activated to FVa by means of minute amounts of thrombin and inactivated by increased levels of thrombin. Factor Va binds to the GP1b receptor site of the activated platelets and forms a complex with prothrombin and Factor Xa, as shown in Flowchart 2.

The active agents in SeraSeal: agar, Factors IIa, VIIa, IXa, and Xa, are effective to overcome a wide range of coagulopathies, due to platelet inhibitors, anticoagulant medications, and factor deficiencies. Platelet inhibitors, such as clopidogrel, ticagrelor, prasugrel, and aspirin, bind to a specific receptor site on the platelet, while agar binds to platelet phospholipids, bypassing the inhibitor effects of treated platelets. When SeraSeal is applied to a bleeding wound in a patient on heparin or warfarin therapy, untreated Factor IXa and Factor VIIa in the hemostatic agent. bridges the inhibited intrinsic and extrinsic coagulation pathways, respectively. Likewise, when there is a factor deficiency anywhere in the coagulation cascade system, the serine proteases in SeraSeal will bridge the deficiency in the extrinsic pathway at Factor VII, in the intrinsic pathway at Factor IX, and in the common pathway at Factor X and Factor II sites.



Flow chart 2: The mechanism behind SeraSeal hemostatic matrix.

SeraSeal provides a proprietary combination of two independent hemostatic agents

- Agar binds to ions of platelet phospholipids and cations from amnio groups fibrinogen/fibrin and tissue proteins, forming an a-1, 6-glactophospho and a-1, 6-glactoamine forming a gelatin-platelet barrier over the bleeding wound
- High concentrations of serine proteases Factors IIa, VIIa, IXa, and Xa are ancillary effects on all three normal coagulation pathways: the extrinsic, intrinsic, and common pathways to form a fibrin clot barrier over the bleeding wound.

Clinical study of seraseal vs cauterization as a primary hemostatic agent

The primary efficacy measurement defined by the protocol stated that at specified bleeding sites, known for moderate to severe blood loss, SeraSeal would achieve a total collective time to hemostasis of the individual bleeds at the target site 25% faster than cauterization in 90% of the total surgical cases [17].

This was a multicenter, single blinded, randomized surgical study of 238 patients. It included patients of all ages, 20 months–90 years, both genders, and patients on heparin therapy. The surgical procedures included tissue of the heart, vascular, liver, spleen, brain, vertebra, head and neck, bone, intestinal, uterus, lip tongue, dental, skin. Cauterization was used as control (Table 1).

The total time to hemostasis ranged from 0.03 to 10 minutes, with a mean of 1.59 minutes for SeraSeal, compared to a 2–90-minute range for cauterization, with a mean of 31.22 minutes, statistical significance ($P < 0.0001$) and nearly 20 times faster for clot formation over the control (Table 2 and Figure 1). Children treated by cauterization ($P < 0.0001$) (Tables 2 to 5 and Figure 1 to 3). treated with SeraSeal significantly achieved hemostasis sooner than children in the control group, with a mean 1.77-minute clotting time compared to a mean 51.69 minutes ($P < 0.0001$). Significant time to hemostasis was also observed in SeraSeal treated heparinized patients with a mean 0.72-minute (± 0.29) clotting time compared to a mean 10.00 minutes (± 8.10) in heparinized patients Twenty-six patients (24.4%) were on heparin, with 14 men having a mean dosage of 302.86 U/kg and 248.91 U for 11 women. There was no significant difference between the two groups (P=0.2320). The mean heparin dosage was 279.12 U/kg (± 110.21). Comparing normal treated patients to heparin treated patients, the mean SeraSeal dosage was 4,039 IU and 5,076 IU, respectively, statistically significant between the two groups ($P = 0.0156$) (Table 4 and Figure 2).

In every SeraSeal surgical case, hemostasis occurred after only one application of the hemostatic agent for each individual hemorrhage.

A secondary efficacy measurement was blood loss. The mean blood loss for SeraSeal treated patients was 184.30 mL, with a range of 1–2,000 mL, compared to a mean of 583.19 mL and a 100–3,000 mL range n the cauterization treatment group with a statistical significance of ($P < 0.001$). The mean blood loss in SeraSeal treated children was 42.92 mL (± 70.60) significantly less compared to a mean 329.17 mL (± 219.98) children treated in the control group ($P = 0.0003$). There was significantly less blood loss in SeraSeal treated heparinized patients, with a mean 347.20 mL (± 141.38) to a mean 720.00 mL (± 272.34) in heparinized subjects treated by cauterization (Table 5 and Figure 4).

There were no therapeutic breaks of SeraSeal to cauterization, achieving 100% success in obtaining hemostasis greater than 25% faster than the employment of cauterization.

Safety evaluation

All the patients were exposed to the hemostatic agent in under 12 minutes with each application, throughout the surgical procedure. Once hemostasis had occurred, the investigational product was removed through irrigation and suction. During the 30-day evaluation period, there were no reported adverse events.

To date, SeraSeal has been applied to more than 1 million patients and to every tissue of the human body without one reported adverse event.

Benefits and drawbacks of the hemostatic agents

All current hemostatic agents on the market today are classified as an adjunct to control bleeding, except SeraSeal, a primary hemostatic agent. Fibrin glues are the most effective of the adjunct hemostatic agents. Table 6, comparison of SeraSeal to fibrin glue hemostatic agents, is a stark contrast of the effectiveness of SeraSeal over the leading adjunct hemostatic agents.

Treatment group				
Baseline characteristics	Adult (N=107)		Pediatric (N=12)	
	M 56 (52.3%)	F 51 (46.8%)	M 6 (50%)	F 6 (50%)
Preoperative mean (SD)				
HBG (g/dL)	13.90 ± 1.56	12.43 ± 1.02	15.02 ± 1.83	14.62 ± 0.46
HCT (%)	41.58 ± 4.71	36.56 ± 5.66	46.37 ± 2.71	43.72 ± 1.16
PT (sec)	11.58 ± 0.22	11.68 ± 0.26	11.68 ± 0.19	11.42 ± 0.17
PTT (sec)	34.56 ± 12.91	32.36 ± 12.54	32.26 ± 12.54	23.67 ± 0.82
Anticoagulant therapy (Heparin) number	16 (13.4%)	12 (10.1%)	0 (0.0%)	0 (0.0%)
Dose (U/kg) Mean (SD)	303.1 ± 112.1	248.9 ± 110.8	0.00	0.0
Associated illness				
Arterial hypertension	16 (13.4%)	12 (10.1%)	0 (0.0%)	0 (0.0%)
Diabetes mellitus	3 (2.5%)	2 (1.7%)	0 (0.0%)	0 (0.0%)
Depression	3 (2.5%)	8 (6.7%)	0 (0.0%)	0 (0.0%)
Targeted organ				
Heart	15 (5.9%)		0 (0.0%)	
Arteries	22 (8.9%)		0 (0.0%)	
Brain	4 (1.6%)		0 (0.0%)	
Vertebra	8 (3.1%)		0 (0.0%)	
Thyroid	2 (0.8%)		0 (0.0%)	
Oral	3 (1.2%)		0 (0.0%)	
Parotid	1 (0.4%)		0 (0.0%)	
Sinuses	2 (0.8%)		0 (0.0%)	
Radical neck	5 (2.0%)		3 (1.2%)	
Leg amputation	1 (0.4%)		1 (0.4%)	
Hip	2 (0.8%)		0 (0.0%)	
Femur	2 (0.8%)		0 (0.0%)	
Liver	16 (6.3%)		1 (0.4%)	
Spleen	6 (2.4%)		0 (0.0%)	
Gastro	22 (8.7%)		3 (1.2%)	
Pancreas	3 (1.2%)		0 (0.0%)	
Gallbladder	8 (3.1%)		0 (0.0%)	
Breast	1 (0.4%)		0 (0.0%)	
Ovary	1 (0.4%)		0 (0.0%)	
Skin-muscle	85 (33.5%)		0 (0.0%)	
Lung	1 (0.4%)		0 (0.0%)	
Tongue	1 (0.4%)		0 (0.0%)	
Bone	31 (12.2%)		4 (1.6%)	

Table 1: Baseline characteristics.

Primary efficacy	SeraSeal				Cauterization			
Total time to hemostasis (min)								
n	119				119			
Mean	1.59				31.22			
SD(±)	2.32				19.72			
Range	0.03–10				2–90			
Blood loss (mL)								
Mean	199.66				595.63			
SD(±)					527.64			
Range	2,000							
Time to hemostasis of adult and pediatric and by gender (min)	SeraSeal				Cauterization			
	Adult		Pediatric		Adult		Pediatric	
	M	F	M	F	M	F	M	F
n	56	51	6	7	56	51	6	6
Mean	1.69	1.44	1.33	2.14	28.66	28.82	48.33	54.57
SD(±)	2.64	2.21	0.82	1.34	17.48	17.96	20.41	28.98
Range	0.03–10	0.03–10	1–3	1–5	2–60	5–60	10–60	20–90

Total time to hemostasis of heparin patients (min)	SeraSeal		Cauterization	
n	24		24	
Mean	0.73		10.42	
SD(±)	0.29		8.13	
Range			2–35	
Time to hemostasis of heparin patients by gender (min)	SeraSeal		Cauterization	
	M	F	M	F
n	14	10	14	10
Mean	0.75	0.70	10.36	10.50
SD(±)	0.32	0.26	10.00	4.97
Range	0.03–1	0.5–1	2–35	5–20

Secondary efficacy total blood loss (mL)	SeraSeal				Cauterization			
n	119				119			
Mean	184.30				583.19			
SD(±)	243.04				541.63			
Range	2,000				100–3,000			
Blood loss of normal patients by gender (mL)					Cauterization			
	Adult		Pediatric		Adult		Pediatric	
	M	F	M	F	M	F	M	F
	56	51	6	6	56	51	6	6
	216.23	184.96	75.00	70.83	653.57	546.60	375.00	283.33
	299.61	183.85	92.03	4.92	635.24	472.30	311.05	68.31
	2,000	1–500	10–250	5–50	3,000	2,000	250–400	200–400

Table 2: Efficacy of SeraSeal vs. cauterization .

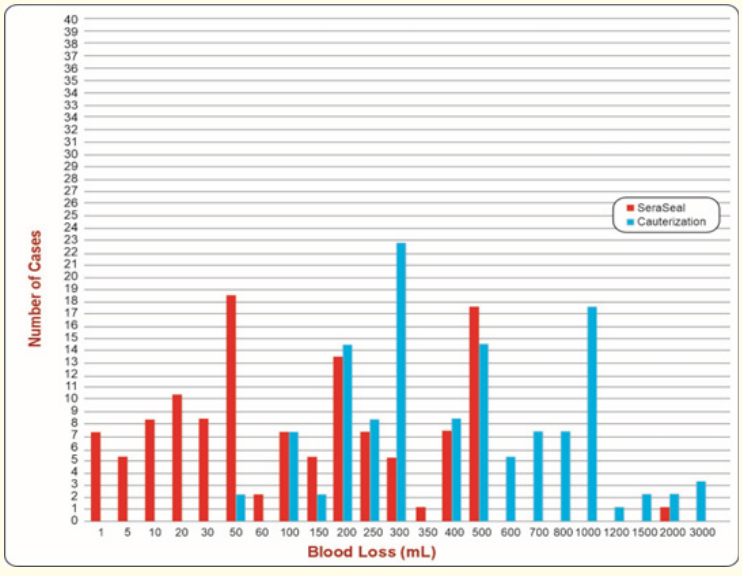


Figure 1: Efficacy: Blood loss SeraSeal vs. cauterization.

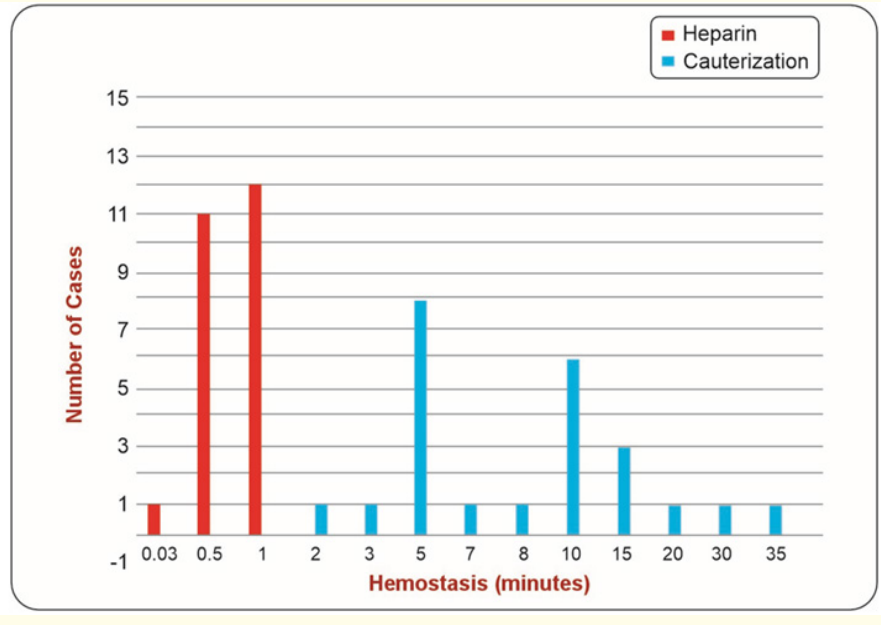


Figure 2: Heparin patients treated by SeraSeal vs cauterization.

Hemostasis (min)	Treatment group			
	Normal (n = 95)		Heparin (n = 24)	
	n	%	n	%
0.03	3	3.16	1	4.17
0.33	2	2.10	0	0.00
0.5	3	3.16	11	45.83
0.67	5	5.26	0	0.00
0.83	2	2.10	0	0.00
1	64	67.37	12	50.00
2	7	7.37	0	0.00
3	1	1.05	0	0.00
10	8	8.42	0	0.00

Table 3: SeraSeal treated normal patients vs. SeraSeal treated heparinized patients.

Hemostasis (min)	Treatment group			
	SeraSeal		Cauterization	
	n	%	n	%
0.03	1	4.17	0	0.00
0.5	11	45.83	0	0.00
1	12	50.00	0	0.00
2	0	0.00	1	4.17
3	0	0.00	1	4.17
5	0	0.00	8	33.33
7	0	0.00	1	4.17
8	0	0.00	1	4.17
10	0	0.00	6	25.00
15	0	0.00	3	12.5
20	0	0.00	1	4.17
30	0	0.00	1	4.17
35	0	0.00	1	4.17

Table 4: Heparin patients treated by SeraSeal vs. cauterization.

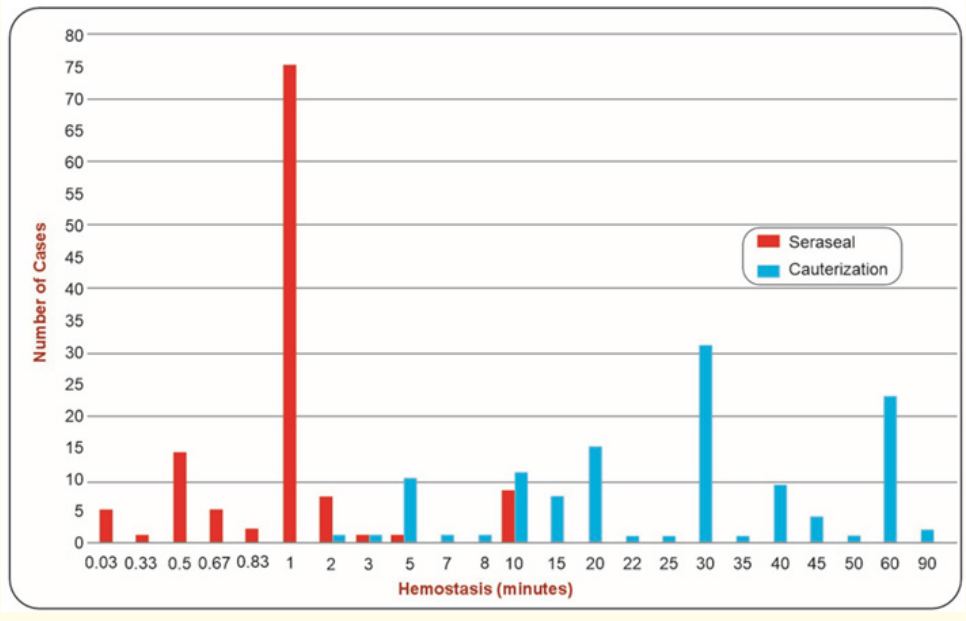


Figure 3: Efficacy: Time to Hemostasis-SeraSeal vs. cauterization.

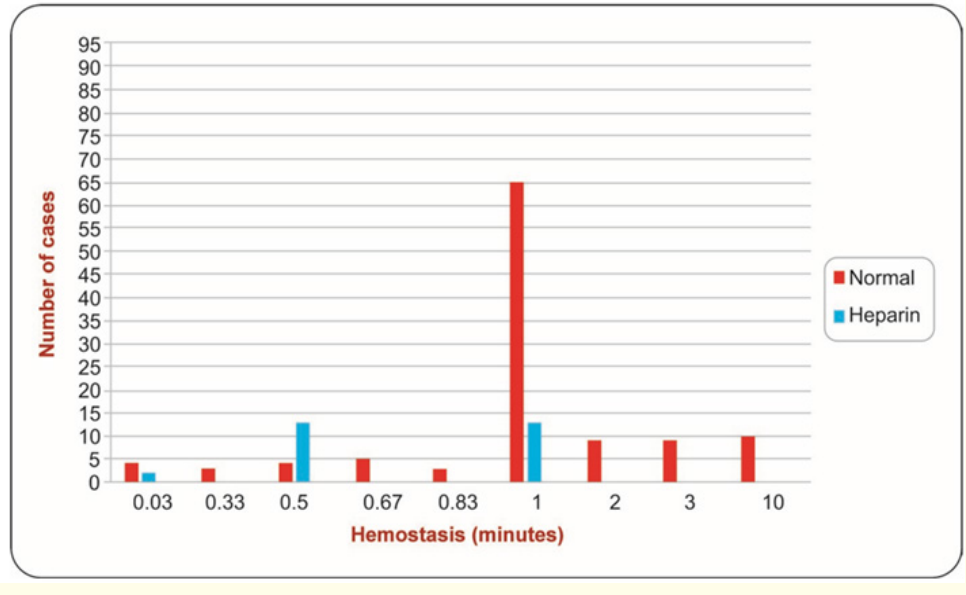


Figure 4: SeraSeal treated Normal Patients vs SeraSeal Heparinized Patients.

Total blood loss of heparin patients (mL)	SeraSeal		Cauterization	
n	24		24	
Mean	370.00		766.67	
SD (±)	133.97		251.37	
Range	30–500		250–1,200	
Blood loss of heparin patients by gender (mL)	SeraSeal		Cauterization	
	M	F	M	F
n	14	10	14	10
Mean	378.57	358.00	771.43	760.00
SD (±)	110.44	167.25	249.39	267.50
Range	200–500	30–500	500–1,200	300–1,000
Number bleeds treated/seraseal application	Adult		Pediatric	
	M	F	M	F
	(n = 56)	(n = 51)	(n = 6)	(n = 6)
1	2 (3.6%)	- (0.0%)	- (0.0%)	- (0.0%)
2	10 (17.9%)		2 (33.3%)	2 (33.3%)
3	22 (39.3%)	24 (47.0%)	2 (33.3%)	1 (16.7%)
4	9 (16.1%)	7 (13.7%)	2 (33.3%)	- (0.0%)
5	7 (12.5%)	6 (11.8%)	- (0.0%)	1 (16.7%)
6	2 (3.6%)	1 (2.0%)	- (0.0%)	2 (33.3%)
7	3 (5.4%)	- (0.0%)	- (0.0%)	- (0.0%)
8	- (0.0%)	- (0.0%)	- (0.0%)	- (0.0%)
9	- (0.0%)	- (0.0%)	- (0.0%)	- (0.0%)
10	1 (1.8%)	- (0.0%)	- (0.0%)	- (0.0%)
Treated bleeds	1 (n = 56)	1 (n = 51)	1 (n = 6)	1 (n = 6)

Table 5: Total blood loss of heparin patients.

	SeraSeal	Fibrin glues
Type of hemostatic agent	Primary	Adjunct
Time to hemostasis: Venous	1–2 seconds	1–3 minutes
Small artery	5–10 seconds	5–10 minutes
Medium artery	15–30 seconds	Ineffective
Large artery	< 60 seconds	Ineffective
Effective in all forms of coagulopathy	Yes	No
Can be used in emergency trauma cases	Yes	No
Can be applied to all tissues, including bone marrow	Yes	No
Reduce blood loss	by 90% in most cases	< 10%
Reduce surgical time	Yes	No
Loss of tissue or adhesions	No	Yes
Multiple delivery systems	Yes	No
Can it be used outside clinical settings	Yes	No

Table 6: Comparison of SeraSeal to fibrin glue hemostatic agents.

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Conclusion

In severely injured trauma patients, controlling blood loss from a Class 3 or Class 4 hemorrhage with an adjunct hemostatic agent is ineffective. However, SeraSeal is effective in a Class 4 hemorrhage to minimize hemorrhagic shock and prevent the very high early mortality rate in the first few hours following injury.

Another advantage SeraSeal offers over all other hemostatic agents is its effectiveness to overcome either dilutional-related coagulopathy or nondilutional acute traumatic coagulopathy. The active agents in SeraSeal will bridge the deficient factors in the normal coagulation cascade system to form both a fibrin and platelet seal over the bleeding wound site.

Finally, there are significant cost savings of SeraSeal when treating acute trauma cases. By arresting all hemorrhages, fewer units of whole blood, PRBC, plasma, platelets are required. By controlling bleeding throughout the surgical procedure, the operation will be shorter, with savings from the cost of the surgical theater time, and less anesthesia medication.

Key Points

- SeraSeal plays a vital role to arrest a Level IV type hemorrhage.
- The active serine proteases Factors IIa, VIIa, IXa, and Xa, are effective to achieve hemostasis in all forms of coagulopathies' in seconds.
- The collective time of hemostasis of the individual bleeds, SeraSeal outperformes cauterization by reducing blood loss by 50%.
- Unlike cauterization, there is no loss of tissue with SeraSeal. Therefore, wounds treated with SeraSeal heal faster.

Bibliography

1. Kauvar DS., *et al*. "Impact of hemorrhage on trauma outcome: an overview of epidemiology, clinical presentations, and therapeutic considerations". *Journal of Trauma* 60.6 (2006): S3-11.

2. Shackelford S and Eastridge B. "Epidemiology of prehospital and hospital traumatic deaths from life-threatening hemorrhage (2012).

3. Schaefer R. "Every Minute Matters in Hemorrhagic Shock. White Paper (2012).

4. Hooper N and Armstrong TJ. "Hemorrhagic shock (2012).

5. Karn A. "Hemorrhagic shock" (2012).

6. Nora Eccles Harrison Cardiovascular Research and Training Institute.

7. Dries DJ. "Hypovolemic and traumatic shock: nonsurgical management. In: and severe hemorrhage: role of hepatic 11β-hydroxysteroid dehydrogenase. Parillo JE, Dellinger RP. "Critical Care Medicine: Principles of Diagnosis and Management in the Adult. 5th edition. Philadelphia, PA: Elsevier (2019).

8. Quintana EN., *et al*. "Acute cardiogenic shock secondary to blunt traumatic aortic valve injury". *Trauma Case Reports* 51 (2024): 100995.

9. Seymour CW., *et al*. "Time to treatment and mortality during mandated emergency care for sepsis". *The New England Journal of Medicine* (2024).

10. Wang P., *et al*. "Mechanism of adrenal insufficiency following trauma". *Archives of Surgery* 134.4 (1999): 394-401.

11. Bougle A., *et al*. "Resuscitative strategies in traumatic hemorrhagic shock". *Annals of Intensive Care* 3.1 (2013): 1.

12. Subeg Y., *et al*. "Hypothermia caused by slow and limited-volume fluid resuscitation decreases organ damage by hemorrhagic shock". *Cytokine* 60.4 (2012): 68-75.

13. Balmaceda A., *et al*. "Resuscitation from a pH of 6.5: A case report and review of pathophysiological and management of extreme acidosis from hypovolemic shock after trauma". *Journal of Trauma and Injury* 32.4 (2019): 238-242.

14. Dodson GP. "Trauma of major surgery: A global problem that is not going away". *International Journal of Surgery* 81 (2020): 47-54.

15. Dodson GP., *et al*. "Traumatic induced coagulopathy as a systems failure: A new window into hemostasis". *Seminars in Thrombosis and Hemostasis* 46.2 (2020): 199-214.

16. Neylan T and O'Donovan A. "Inflammation and PTSD". *PTSD Research Quarterly* (2019).

17. Wortham L. "A Multi-Center, Single Blinded, Parallel, Randomized, Hemostatic Agent Clinical Study. Wortham Laboratories, Inc., WLI Document Number: WLI1196-PER (2004).