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Experimental Evaluation of Hemostatic Agents and Powdered Sorbent Effectiveness on the Dynamics of Blood Aggregate State Regulation using the Method of Thromboelastography

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Abstract

Background: This article presents the results of an experimental study on the effect of hemostatic agents (Hemostatic collagen sponge, Tachocomb, Surgitamp and granular sorbent Molselect G-50) on the system regulating the aggregate state of the blood (SRASB) using piezoelectric thromboelastography (TEG).

Methods and Results: The study involved 18 healthy men aged between 21 and 43 years with normal indicators of the SRASB. In the first series of experiments, TEG of the blood was recorded without the addition of the test material (the control stage). At the second stage of the experiment, the hemostatic properties of the Hemostatic collagen sponge, Tachocomb, hemostatic gauze Surgitamp and granular sorbent Molselect G-50 were studied.

In vitro experimental studies to assess the effect of hemostatic agents and granular sorbent on the SRASB using piezoelectric TEG have shown that the use of Hemostatic collagen sponge, Tachocomb, Surgitamp, and the granular sorbent Molselect G-50 convincingly affects all links of the thrombosis process. However, Surgitamp and the granular sorbent Molselect G-50 show the greatest influence on such important indicators as the time of blood clotting and maximum clot density, which gives reason to conclude they are effective in clinical use in surgical practice.(**International Journal of Biomedicine. 2022;12(2):289-292.**)

Key Words: thromboelastography • aggregate state of the blood • hemostatic agents • granular sorbents

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Abbreviations

MCD, maximum clot density; **SRASB**, system regulating the aggregate state of the blood; **TEG**, thromboelastography; **TCPC**, time of the contact phase of coagulation; **TRTC**, time to reach the thrombin constant; **TBC**, time of blood clotting; **TPC**, time of polymerization of the clot; **TFTC**, time of formation of fibrin-platelet clot; **TOF**, the time of the onset of fibrinolysis.

Introduction

Abdominal trauma remains one of the urgent problems of emergency surgery. Liver injury ranks second among other abdominal injuries. One of the technically difficult issues of hemostasis is the stopping of parenchymal bleeding.[1-3]

Many methods of hemostasis have been proposed to stop bleeding from liver wounds. The main surgical method is wound suturing. The disadvantage of all sutures applied in cases of liver injury is that necrosis zones appear between the sutures. For surface, large-area injuries, various methods of coagulation devices are used (diathermocoagulation, laser coagulation, argon-plasma coagulation). All these methods of coagulation give an unstable hemostatic result, often expanding the necrosis zone in the wound. In large surgical clinics, hepatic arteries are embolized. The main disadvantages

of this method are the high cost and the lack of the necessary equipment in city and district hospitals.[4-7]

In the conditions of conventional clinics for hemostasis in liver wounds, options for wound tamponing are increasingly used, for example, with an omentum and various hemostatic agents (sponges, powders, films). At the same time, there remain problems of bioinertness and the presence of local and systemic reactions.[8,9]

A promising method in the complex treatment of hemorrhagic complications is the use of polymer granular sorbents, which, when swelling, form soft hydrogels that have hemostatic, plastic, and other properties. However, the mechanism of action of granular sorbents in combination with a local hemostatic on the SRASB is not fully understood.[10-16]

The aim of this research was to study the comparative features of the effect of hemostatic agents (Hemostatic collagen sponge, Tachocomb, Surgitamp, and granular sorbent Molselect G–50) on the system regulating the aggregate state of the blood (SRASB) in vitro experiments using modern capabilities of piezoelectric TEG.

Materials and Methods

The present study involved 18 healthy men aged between 21 and 43 years [29.0 (25.0-32.5) years] with normal indicators of the SRASB.

The venous blood of healthy volunteers served as the material for research. In the conditions of the treatment room, the cubital vein was punctured and blood was taken into sterile vacuum tubes containing a 3.8% sodium citrate solution with a volume of 4.5ml, intended for coagulographic studies. The study of the SRASB processes was performed by piezoelectric thromboelastography using the piezoelectric thromboelastograph ARP-01M "Mednord."

In the first series of experiments, TEG of the blood was recorded without the addition of the test material (the control stage). At the second stage of the experiment, the hemostatic properties of the Hemostatic collagen sponge, Tachocomb, hemostatic gauze Surgitamp and granular sorbent Molselect G-50 were studied. To study the SRASB processes, 0.3 ml of citrate blood was injected into the thromboelastograph cuvette installed in the thermostat chamber. Then a fixed amount (1.0mg) of the studied drug was added to the cell of the device. The contents of the cuvette were mixed evenly, an activator solution (0.025 M calcium chloride solution) was added and the study was started.

The results of the studies were analyzed by evaluating the following parameters (time in minutes): the time of the contact phase of coagulation (TCPC), the time to reach the thrombin constant (TRTC), the time of blood clotting (TBC), the time of polymerization of the clot (TPC), the time of formation of a fibrin-platelet clot (TFTC), the time of the onset of fibrinolysis (TOF), and maximum clot density (MCD).

Statistical processing of the results of the study was carried out using STATISTICA Base (License dated 17.12.2010). For descriptive analysis, results are presented as median (Me), lower quartile (Q1) and upper quartile (Q3). A non-parametric Kruskal-Wallis test was used for comparisons of median values among three groups, followed by post-hoc testing using un-paired Mann-Whitney U tests. A probability value of $P<0.05$ was considered statistically significant.

The study was conducted in accordance with ethical principles of the WMA Declaration of Helsinki (1964, ed. 2013) and approved by the Ethics Committee of Voronezh State Medical University named after N. N. Burdenko. Written informed consent was obtained from all participants.

Results and Discussion

The results of the study are presented in Table 1. When analyzing the TCPC indicator reflecting the adhesive-aggregation activity of platelets and the suspension activity of shaped blood elements, it was found that in the control stage, TCPC was 1.0(1.0-1.05) min. No significant changes in TCPC were observed when using Tachocomb, Surgitamp or Molselect G-50, and for all these drugs this indicator was 1.0(1.0-1.0) min. With the addition of a Hemostatic collagen sponge to the cell of the device, TCPC became elongated (1.0(1.0-2.25) min); however, no statistical significance was observed, compared to the control (P=0.5137). Thus, Hemostatic collagen sponge, Tachocomb, Surgitamp and Molselect G–50 do not have a significant effect on the initial process of blood clotting–adhesion and platelet aggregation.

When studying the TRTC, it was found that in the control stage this indicator was 6.5(4.8-7.6) min. For Tachocomb, TRTC occurred at an earlier time and amounted to 5.4(4.5-5.9) min; however, compared with the control, the differences were statistically insignificant (P=0.0780). Applications of Hemostatic collagen sponge reduced TRTC to 2.9(2.2-4.2) min (P=0.0001), Surgitamp to 2.9(2.2-3.4) min (P=0.0000). The best result of achieving the thrombin constant was shown by the granular sorbent Molselect G-50 – 2.6(2.2-3.3) min (P=0.0000). Thus, the Hemostatic collagen sponge, Surgitamp and Molselect G-50 begin to show their hemostatic activity precisely at the stage of achieving the thrombin constant, possibly potentiating the activity of prothrombinase.

Analyzing TBC, the key SRASB indicator, reflecting the transition of liquid blood states to gel-like, it was found that in the control stage, TBC occurred at 12.9(12.1-13.9) min. The use of all the agents we studied led to a statistically significant reduction in TBC: for Hemostatic collagen sponge – 9.5(8.9-10.1) min (P=0.0000), for Tachocomb – 6.4(6.1-6.9) min (P=0.0000), for Molselect G-50 – 4.3(3.9-5.1) min (P=0.0000). Thus, the use of all the drugs we studied significantly reduce the time of blood transition from a liquid to a gel-like state, which reflects their hemostatic potential and determines the effectiveness of their clinical use.

In the study of TPC, an indicator characterizing the process of frontal and lateral assembly of fibrin monomers and the formation of protofibrils with their subsequent polymerization and cross-linking, it was found that in the control stage, TPC was 23.5(22.1-24.4) min. The use of Hemostatic collagen sponge reduced TPC to 19.8(18.6-24.6) min, but the difference compared to the control was statistically insignificant (P=0.0887). For Tachocomb, TPC was 16.5(15.7-17.1) min (P=0.0000). The best indicators of TPC were observed with the use of Surgistamp – 14.7(13.8-15.5) min (P=0.0000) and for Molselect G-50 – 14.7(14.0-15.7) min (P=0.0000).

Table 1.

Effects of hemostatic agents (Hemostatic collagen sponge, Tachocomb, Surgitamp, and granular sorbent Molselect G–50) on the SRASB in vitro experiments

TEG indicators	Control stage	Hemostatic collagen sponge	Tachocomb	Surgitamp	Molselect G-50	*P*-value
TCPC, min	1.0(1.0-1.05)	1.0(1.0-2.25)	1.0(1.0-1.0)	1.0(1.0-1.0)	1.0(1.0-1.0)	0.0196
P-value		0.513723	0.887386	0.197808	0.127688	
TRTC, min	6.5(4.8-7.6)	2.9(2.2-4.2)	5.4(4.5-5.9)	2.9(2.2-3.4)	2.6(2.2-3.3)	0.0000
P-value		0.0001	0.0780	0.0000	0.0000	
TBC, min	12.9(12.1-13.9)	9.5(8.9-10.1)	6.4(6.1-6.9)	4.7(4.1-5.1)	4.3(3.9-5.1)	0.0000
P-value		0.0000	0.0000	0.0000	0.0000	
TPC, min	23.5(22.1-24.4)	19.8(18.6-24.6)	16.5(15.7-17.1)	14.7(13.8-15.5)	14.7(14.0-15.7)	0.0000
P-value		0.0887	0.0000	0.0000	0.0000	
TFTC, min	31.3(39.9-35.7)	28.7(28.1-29.0)	29.2(28.9-29.5)	29.1(28.6-29.5)	28.3(27.9-28.7)	0.0000
P-value		0.0000	0.0000	0.0000	0.0000	
TOF, min	29.5(28.7-29.6)	-	-	-	-	
MCD, U	399.5(339.5-427.0)	430.5(418.0-488.0)	533.5(516.0-577.0)	452.0(423.5-500.5)	556.5(535.0-573.5)	0.0000
P-value		0.0145	0.0001	0.0023	0.0001	

Analyzing the final stage of the thrombosis process (the formation of a fibrin-platelet clot), we found that TFTC in the control was 31.3(39.9-35.7) min. The use of all studied substances led to a reduction in TFTC index: for Tachocomb – 29.2(28.9-29.5) min (*P*=0.0000), for Surgistamp – 29.1(28.6-29.5) min (*P*=0.0001). The best results for TFTC showed Hemostatic collagen sponge – 28.7(28.1-29.0) min (*P*=0.0000) and Molselect G-50– 28.3(27.9-28.7) min (*P*=0.0000).

The stability of the formed fibrin-platelet clot was assessed by the time of the beginning of fibrinolysis. In the control stage, in 4 observations, the beginning of clot lysis was observed on 29.5(28.7-29.6) min. Analyzing the effect of Hemostatic collagen sponge, Tachocomb, Surgitamp and Molselect G-50, no clot lysis was observed in any observation, which indicates the pronounced antifibrinolytic activity of the substances we studied.

A qualitative indicator of the clot formation process is the maximum clot density (MCD), reflecting the stability of the fibrin-platelet thrombus to external influences. In the control stage, MCD was 399.5(339.5-427.0)U. The use of Hemostatic collagen sponge increased MCD up to 430.5(418.0-488.0)U (*P*=0.0145), Surgitamp – 452.0(423.5-500.5)U (*P*=0.0023), Tachocomb – 533.5(516.0-577.0)U (*P*=0.0001). The best result of MCD was shown by the granular sorbent Molselect G-50 – 556.5(535.0-573.5)U (*P*=0.0001).

Conclusion

In vitro experimental studies to assess the effect of hemostatic agents and granular sorbent on the SRASB using piezoelectric TEG allowed us to state that the use of Hemostatic collagen sponge, Tachocomb, Surgitamp, and the granular sorbent Molselect G-50 convincingly affects all links of the thrombosis process. However, Surgitamp and the granular sorbent Molselect G-50 show the greatest influence on such important indicators as TBC and MCD, which gives reason to conclude they are effective in clinical use in surgical practice.

Competing Interests

The authors declare that they have no competing interests.

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