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ORIGINAL RESEARCH

Effect of hemocoagulase on the coagulation parameters, blood transfusion volume and bleeding volume of patients with severe traumatic fractures

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Abstract

To investigate the effect of hemocoagulase on coagulation parameters, blood transfusion volume and bleeding volume in patients with severe traumatic fractures. A total of 116 patients with severe traumatic fractures admitted to our hospital. These patients were randomly divided into the study group (hemocoagulase injection) and control group (normal saline injection), with 58 patients in each group. The bleeding time, coagulation time, perioperative bleeding volume, blood transfusion volume, hematology and coagulation parameters of the two groups were observed and compared. At 24 h post-surgery, the bleeding time and coagulation time were significantly shorter in the study group than in the control group ($p < 0.05$). The intraoperative bleeding volume, 24 h postoperative drainage volume, and blood transfusion volume were significantly lower in the study group than in the control group ($p < 0.05$). In addition, the 24 h postoperative levels of hematology parameters were significantly higher in the study group than in the control group ($p < 0.05$). However, coagulation parameters were similar in both groups before and at 24 h after surgery. Hemocoagulase has a better hemostatic effect and can effectively reduce perioperative bleeding without affecting the coagulation functions of patients with severe traumatic fractures. Therefore, hemocoagulase is a reliable treatment regimen in clinical practice.

Keywords

Hemocoagulase; Severe traumatic fracture; Coagulation function; Blood transfusion volume; Bleeding volume

1. Introduction

There are clinical evidences [1, 2] indicating that patients often suffer bone, tendon and other deep tissue injuries during severe trauma to the limbs, and bone fractures are the most common outcome of these traumatic events. In some serious cases, severe trauma can lead to massive hemorrhage and pose a direct threat to the life and health of the patients. Emergency repair surgery is currently the mainstay of treatment for severe traumatic fracture, as this approach can quickly improve the patient's conditions and promote early functional recovery of the patient's limbs. Clinical studies [3, 4] have demonstrated that uncontrolled massive bleeding following a severe traumatic fracture can cause hemorrhagic shock in patients. In addition, patients with severe traumatic fractures have been reported to have clinically abnormal coagulation functions such as hypercoagulability and hyperfibrinolysis, leading to adverse reactions including venous thrombosis and gastrointestinal bleeding [5, 6]. These conditions not only affect the surgical treatment of patients, but also are extremely detrimental to their postoperative recovery [7, 8]. Therefore, how to effectively control the postoperative bleeding volume and improve coagulation functions in patients with severe traumatic fractures is an important issue that needs to be addressed in the clinical treatment and postoperative recovery of these patients. Hemocoagulase, an enzyme preparation isolated from snake venom, has demonstrated significant efficacy in treating bleeding disorders and improving bleeding in patients [9, 10]. In this comparative study, the effect of hemocoagulase on the coagulation parameters, blood transfusion volume, and bleeding volume were examined in patients with severe traumatic fractures admitted to hospital.

2. Subjects and methods

2.1 General subject information

A total of 116 patients with severe traumatic fractures admitted were selected in this study. These patients were randomly divided into study group and control group with 58 patients per group using the random number table (**Supplementary Table 1**). In the study group, there were 30 males and 28 females, with a mean age of 34.26 ± 1.21 years (31–37 years),

an average weight of 65.34 ± 3.15 kg (58–71 kg), and an average height of 168.24 ± 5.26 cm (153–177 cm). There were 22 cases of femur and tibia-fibula fractures, 18 cases of tibia-fibula and ulna-radius fractures, 15 cases of femur and humerus fractures, and 3 cases of humerus and ulna-radius fractures. Causes of trauma included traffic injuries (n = 31), crush injuries (n = 14), fall injuries (n = 11), and others (n = 2). General clinical data were comparable for both two patient groups.

2.1.1 Inclusion criteria

(1) Patients who meet the criteria for severe trauma: Injury severity score (ISS) is >16 on the Abbreviated Injury Scale (AIS); (2) Has bone fractures; (3) Underwent open reduction and internal fixation; (4) Patients who are conscious and have normal cognition; (5) Patients who signed the informed consent form.

2.1.2 Exclusion criteria

(1) Open bone fractures; (2) Impaired central nervous system; (3) Severe stress response during treatment.

2.2 Methods

All participants received basic integrative therapy, including symptomatic treatment of injuries, open reduction internal fixation surgery for limb fractures, blood transfusion and fluid replacement to stabilize the circulatory system, and protective mechanical ventilation to maintain normal respiration and correct symptoms of hypoxia. In addition, hemostasis, analgesia, sedation, and measures to prevent gastrointestinal hemorrhage and infection were also provided.

2.2.1 Study group

Patients were intramuscularly injected with one unit of hemocoagulase solution for injection (Manufacturer: Zhaoke Pharmaceutical (Hefei) Co., Ltd., Anhui province, China; Approval document no.: CYFYLL2022494; NMPA approval no. H20060895; Strength: 1 mL: 1 unit) at 30 min before surgery. Patients were also intravenously injected with one unit of hemocoagulase solution for injection at 15 min before incision and on the evening of the day of surgery and 1 d after surgery.

2.2.2 Control group

Patients were given the same dose of normal saline in the same manner at the same time points as the study group.

2.3 Observation parameters

The bleeding time, coagulation time, perioperative bleeding volume, blood transfusion volume, hematology and coagulation parameters of the two groups were observed and compared.

(1) Hematology parameters include hemoglobin (Hb) and platelet count (PLT);

(2) Coagulation parameters include thrombin time (TT), fibrinogen (Fib), prothrombin time (PT), and activated partial thromboplastin time (APTT).

(3) Collect venous blood (2 mL) from patients before and at 24 h after surgery and the relevant parameters were measured using the Sysmex XE-2100 Automated Hematology System (Sysmex, Kobe, Japan) in strict accordance with the instrument procedures.

2.4 Statistical analysis

Statistical analysis was performed using SPSS (version 14.0, IBM, Chicago, IL, USA). Measured data was expressed as mean ± standard deviation ($\bar{x} \pm s$) and compared using the independent sample t-test between groups and paired t-test within a group. Count data was expressed as a percentage (%) and compared using a χ^2 test. $p < 0.05$ was considered statistically significant.

3. Results

3.1 Comparison of bleeding time and coagulation time in the study and control groups

The bleeding time and coagulation time were not significantly different between the study and control groups before surgery. However, the bleeding time and coagulation time were significantly shorter in the study group than that in the control group at 24 h after surgery (both $p < 0.05$) (Table 1).

3.2 Comparison of perioperative bleeding volume and blood transfusion volume in the study and control groups

Intraoperative bleeding volume, 24 h postoperative drainage volume, and blood transfusion volume were significantly lower in the study group than that in the control group (all $p < 0.05$) (Table 2).

3.3 3.3 Comparison of hematology parameters in the study and control groups

Hematology parameters, including Hb level and PLT level, were similar between the two groups before surgery (all $p < 0.05$). However, levels of hematology parameters at 24 h post-surgery were significantly higher in the study group than in the control group (all $p < 0.05$) (Table 3).

3.4 Comparison of coagulation parameters in the study and control groups

Coagulation parameters were not significantly different between the two groups before and at 24 h after surgery. However, Fib level was significantly decreased in both groups at 24 h post-surgery ($p < 0.05$) (**Supplementary Table 2**).

4. Discussion

Previous clinical studies [11, 12] have shown that patients with severe limb trauma are often hypercoagulable due to abnormal changes in the coagulation system. Both intrinsic coagulation factors and extrinsic coagulation pathways are considered to play a role in this phenomenon, with the latter being a key contributing factor. Therefore, activation of extrinsic coag-

TABLE 1. Comparison of bleeding time and coagulation time ($\bar{x} \pm s$).

Group	N	Bleeding time (s)		t value	*p* value	Coagulation time (s)		t value	*p* value
		Pre-surgery	24 h post-surgery			Pre-surgery	24 h post-surgery		
Study group	58	116.34 ± 15.23	108.02 ± 11.25	3.3464	0.0011	354.24 ± 20.20	334.25 ± 16.52	5.8340	<0.001
Control group	58	115.91 ± 14.97	116.05 ± 14.99	0.0503	0.9599	355.64 ± 19.98	354.26 ± 18.63	0.3847	0.7012
t value	—	0.1533	3.2630	—	—	0.3753	6.1203	—	—
p value	—	0.88	<0.001	—	—	0.71	<0.001	—	—

TABLE 2. Comparison of perioperative bleeding volume and blood transfusion volume ($\bar{x} \pm s$).

Group	N	Intraoperative bleeding volume (mL)	24 h postoperative drainage volume (mL)	Blood transfusion volume (mL)
Study group	58	526.34 ± 22.32	92.16 ± 8.10	123.16 ± 11.02
Control group	58	963.14 ± 47.14	158.28 ± 11.03	264.28 ± 19.11
t value	—	63.7798	36.7969	48.7194
p value	—	<0.001	<0.001	<0.001

TABLE 3. Comparison of hematology parameters ($\bar{x} \pm s$).

Group	N	Hb (g/L)		t value	*p* value	PLT (10^9/L)		t value	*p* value
		Pre-surgery	24 h post-surgery			Pre-surgery	24 h post-surgery		
Study group	58	131.24 ± 9.23	121.93 ± 8.25	5.7274	<0.001	183.84 ± 7.26	173.25 ± 6.22	8.4362	<0.001
Control group	58	132.03 ± 8.96	101.24 ± 7.94	19.5868	<0.001	184.00 ± 8.05	160.24 ± 5.14	18.9457	<0.001
t value	—	0.4677	13.7614	—	—	0.1124	12.2793	—	—
p value	—	0.64	<0.001	—	—	0.91	<0.001	—	—

Hb: hemoglobin; PLT: platelet count.

ulation pathway is an important method for initiating blood coagulation during clinical treatment in patients with severe limb trauma. When an individual is healthy, the relevant substances in the blood, including platelets, various coagulation factors and anticoagulation factors, are in a relatively stable equilibrium [13]. However, this equilibrium is disrupted when an individual experiences trauma, especially severe trauma. During acute severe bone fracture, rupture of local blood vessel wall disrupts the equilibrium among coagulation, anticoagulation and fibrinolysis, ultimately leading to hemorrhage [14, 15]. In the case of minor trauma, intrinsic coagulation factors can be self-activated to promote coagulation. On the other hand, since patients with severe traumatic fractures have more severe and complicated trauma, drug intervention is required to activate extrinsic coagulation pathway to achieve effective hemostasis.

Given that wound and incisions are a source of bleeding in patients undergoing orthopedic surgery, it is also necessary to consider the effect of hemostatic agent on perioperative coagulation functions of the patient when selecting a reasonable hemostatic agent. This is because patients may develop hypercoagulability due to postoperative pain and inflammation. In addition, since bone fracture patients require long-term bed rest after surgery, the incidence of venous thrombosis can be greatly increased if hypercoagulability cannot be effectively controlled. Therefore, the impact on coagulation function is an important factor to be considered when choosing a hemostatic agent [16, 17].

Hemocoagulase is a hemostatic agent extracted from *Bothrops jararaca* venom that is extensively used in general surgery, gynecology, and thoracic surgery. The clinical hemostatic effect of hemocoagulase has also been widely recognized by patients and clinicians [10, 18]. Previous studies [19, 20] have demonstrated that the application of hemocoagulase during hepatobiliary surgery can effectively reduce intraoperative bleeding volume without affecting the coagulation functions of patients. Furthermore, other studies [21, 22] have shown that injection of hemocoagulase into rabbits accelerated blood coagulation without affecting platelet concentration. A study by Nascimento da Costa *et al.* [23] found that hemocoagulase therapy does not confer the risk of deep vein thrombosis in the lower limb and is clinically safe and highly reliable in elderly patients.

Hemocoagulase plays both "thrombin-like" and "thromboplastin-like" roles in clinical practice [24, 25]. Hemocoagulase acts similarly to human thrombin in that it causes platelet aggregation and white thrombus formation at the bleeding site without affecting the patient's other healthy sites [26, 27]. On the other hand, hemocoagulase can also act as thromboplastin in the degradation of fibrin to fibrinopeptide A, which forms soluble fibrin I with fibrin to achieve coagulation in patients with injury-induced bleeding

[28, 29]. Collectively, these findings [30, 31] showed that the coagulation and hemostatic effects of hemocoagulase are specific only to the bleeding site and not to blood vessels in other healthy tissues.

In the present study, the 24 h postoperative bleeding time and coagulation time were significantly shorter in the study group than in the control group (both $p < 0.05$). Patients in the study group had significantly lower intraoperative bleeding volume, 24 h postoperative drainage volume, and blood transfusion volume than that in the control group (all $p < 0.05$). In addition, the levels of 24 h postoperative hematology parameters were markedly higher in the study group than in the control group (all $p < 0.05$). However, coagulation parameters were similar between the study and control groups both before and at 24 h after surgery. Further study revealed that administration of a small dose of hemocoagulase promoted local platelet aggregation and thrombus formation specifically at the site of vascular damage without disrupting the coagulation/fibrinolysis balance in the patients. Hemocoagulase does not activate fibrin stabilizing factor, indicating stable maintenance of overall coagulation function. Consistent with previous findings [32, 33], our results further confirmed the superior efficacy of hemocoagulase in the clinical treatment of severe traumatic fractures. Limitations of this study included a small sample size and a lack of patients with open fractures. Therefore, a large-cohort study of a wider patient population is warranted to determine the efficacy and scope of application of hemocoagulase.

5. Conclusions

In summary, hemocoagulase is a better hemostatic agent that can effectively reduce perioperative bleeding without affecting coagulation functions in patients with severe traumatic fractures. Therefore, hemocoagulase is a reliable treatment regimen in clinical practice.

AVAILABILITY OF DATA AND MATERIALS

The authors declare that all data supporting the findings of this study are available within the paper and any raw data can be obtained from the corresponding author upon request.

AUTHOR CONTRIBUTIONS

HYZ—designed the research study. HYZ, JYS, HMG, XML and JZW—performed the research. HYZ, JYS, HMG, XML and JZW—analyzed the data. HYZ, JYS, HMG, XML and JZW—wrote the manuscript. All authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethical approval was obtained from the Ethics Committee of the Affiliated Hospital of Chengde Medical University (Approval no. CYFYLL2022494). Written informed consent was obtained from a legally authorized representative(s) for anonymized patient information to be published in this article.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

SUPPLEMENTARY MATERIAL

Supplementary material associated with this article can be found, in the online version, at https://oss.signavitae.com/mre-signavitae/article/1677194327244062720/attachment/Supplementary%20material.docx.

REFERENCES

[1] Pottecher J, Lefort H, Adam P, Barbier O, Bouzat P, Charbit J, *et al*. Guidelines for the acute care of severe limb trauma patients. Anaesthesia Critical Care & Pain Medicine. 2021; 40: 100862.

[2] Major Extremity Trauma Research Consortium (METRC). Outcomes following severe distal tibial, ankle, and/or Mid/Hindfoot trauma: comparison of limb salvage and transtibial amputation (OUTLET). Journal of Bone and Joint Surgery. 2021; 103: 1588–1597.

[3] Bunn C, Kulshrestha S, Di Chiaro B, Maduekwe U, Abdelsattar ZM, Baker MS, *et al*. A leg to stand on: trauma center designation and association with rate of limb salvage in patients suffering severe lower extremity injury. Journal of the American College of Surgeons. 2021; 233: 120–129e5.

[4] Lefort H, Gil-Jardine C, Chauvin A. Guidelines for the acute care of severe limb trauma patients. European Journal of Emergency Medicine. 2021; 28: 339–340.

[5] Ho KM, Rao S, Nasim S, Rogers FB. Femoral venous catheterisation, lower limb pneumatic compression and venous thromboembolism after severe trauma: a substudy of the da Vinci trial. Anaesthesia and Intensive Care. 2021; 49: 74–76.

[6] Melendi G, Moreno RP, Hernández A, Hernández Y, Seligra C, Fain J, *et al*. Severe upper limb trauma related to escalator use. Pediatric case report. Archivos argentinos de pediatría. 2021; 119: e256–e260. (In Spanish)

[7] Arriaga AF, Bader AM. Severe pain after hip fracture repair in older adults: challenging a dominant narrative. Annals of Internal Medicine. 2022; 175: 1039–1040.

[8] Guo J CX, Lin Z, Jin L, Hou Z, Dong W, Zhang Y. Tight junction disruption through activation of the PI3K/AKT pathways in the skin contributes to blister fluid formation after severe tibial plateau fracture. Frontiers in Bioengineering and Biotechnology. 2022; 10: 946261.

[9] Ma R, Ren J, Zhang ZB, Men JL, Deng QJ. Effect of hemocoagulase agkistrodon on coagulation status in patients with traumatic brain injury *in vitro*. Zhonghua Yi Xue Za Zhi. 2021; 101: 586–590. (In Chinese)

[10] Liu Y, Li R, Tan C, Ma Y, Feng J, Xu Q, *et al*. Application of hemocoagulase bothrops atrox in the submucosal injection for endoscopic submucosal dissection: a preliminary trial. European Journal of Gastroenterology & Hepatology. 2021; 33: e681–e685.

[11] Rostagno C, Falchetti G, Rostagno AC, Mattesini A. TAVR in patients with hip fracture and severe aortic stenosis: how and when? Internal and Emergency Medicine. 2021; 16: 1419–1422.

[12] Costa ML, Achten J, Parsons NR. Five-year outcomes for patients sustaining severe fractures of the lower limb. The Bone & Joint Journal. 2022; 104-B: 633–639.

[13] Saito M, Moore-Lotridge SN, Uppuganti S, Egawa S, Yoshii T, Robinette JP, *et al*. Determining the pharmacologic window of bisphosphonates that mitigates severe injury-induced osteoporosis and muscle calcification, while preserving fracture repair. Osteoporosis International. 2022; 33: 807–820.

[14] Söreskog E, Lindberg I, Kanis JA, Åkesson KE, Willems D, Lorentzon M, *et al*. Cost-effectiveness of romosozumab for the treatment of postmenopausal women with severe osteoporosis at high risk of fracture in Sweden. Osteoporosis International. 2021; 32: 585–594.

[15] Lin YC, Hsu YC, Wu WT, Lee RP, Wang JH, Chen HW, *et al*. The incidence of severe urinary tract infection increases after hip fracture in the elderly: a nationwide cohort study. Scientific Reports. 2021; 11: 3374.

[16] González-Marcos E, González-García E., Rodríguez-Fernández P., González-Bernal J. J., Sánchez-González E., González-Santos J. Predictors of moderate or severe cognitive impairment at six months of the hip fracture in the surgical patient over 65 years of age. Journal of Clinical Medicine. 2022; 11: 2608.

[17] Li J, Wong RMY, Chung YL, Leung SSY, Chow SK, Ip M, *et al*. Fracture-related infection in osteoporotic bone causes more severe infection and further delays healing. Bone & Joint Research. 2022; 11: 49–60.

[18] Keni R, Gourishetti K, Kinra M, Nayak PG, Shenoy R, Nandakumar K, *et al*. Botrops derived hemocoagulase formulation a probable agent for diabetic wound healing. 3 Biotech. 2020; 10: 443.

[19] Tang J, Kang Y, Huang L, Feng X, Wu L, Peng Y. Neuroprotective effects of hemocoagulase agkistrodon on experimental traumatic brain injury. Brain Research Bulletin. 2021; 170: 1–10.

[20] Kang BS, Kim YI, Hong S, Ban SS, Han WS, Kim BG. Decline in platelet function following administration of a snake venom-derived hemocoagulase in a patient with end-stage renal disease. Kidney Research and Clinical Practice. 2020; 39: 501–503.

[21] Torigoe K, Yamashita A, Abe S, Muta K, Mukae H, Nishino T. Effect of hemocoagulase on the prevention of bleeding after percutaneous renal biopsy. Toxins (Basel). 2022; 14: 223.

[22] Xian R, Wang C, Gong L, Hang B, Wang W, Zhang X, *et al*. A species-specific strategy for the identification of hemocoagulase agkistrodon halys pallas based on LC-MS/MS-MRM. Frontiers in Molecular Biosciences. 2022; 9: 831293.

[23] Nascimento da Costa T, Mota-da-Silva A, Colombini M, Moura-da-Silva AM, Medeiros de Souza R, Monteiro WM, *et al*. Relationship between snake size and clinical, epidemiological and laboratory aspects of Bothrops atrox snakebites in the western Brazilian Amazon. Toxicon. 2020; 186: 160–167.

[24] Lotto NP, de Albuquerque Modesto JC, Sant'Anna SS, Grego KF, Guarnieri MC, Lira-da-Silva RM, *et al*. The absence of thrombin-like activity in Bothrops erythromelas venom is due to the deletion of the snake venom thrombin-like enzyme gene. PLoS One. 2021; 16: e0248901.

[25] Kaido T, Yoda M, Kamijo T, Arai S, Yamauchi K, Okumura N. A novel variant fibrinogen, AalphaE11del, demonstrating the importance of AalphaE11 residue in thrombin binding. International Journal of Hematology. 2021; 114: 591–598.

[26] Reda S, Rühl H, Witkowski J, Müller J, Pavlova A, Oldenburg J, *et al*. PC deficiency testing: thrombin-thrombomodulin as PC activator and aptamer-based enzyme capturing increase diagnostic accuracy. Frontiers in Cardiovascular Medicine. 2021; 8: 755281.

[27] De-Simone SG, Lechuga GC, Napoleao-Pego P, Gomes LR, Provance DW Jr, Nirello VD, *et al*. Small angle X-ray scattering, molecular modeling, and chemometric studies from a thrombin-like (Lmr-47) enzyme of lachesis m. rhombeata venom. Molecules. 2021; 26: 3930.

[28] D'Alessandro E, Scaf B, Oerle R, Nieuwenhoven FA, Hunnik A, Verheule S, *et al*. Thrombin generation by calibrated automated thrombography in goat plasma: optimization of an assay. Research and Practice in Thrombosis and Haemostasis. 2021; 5: e12620.

[29] Pinheiro-Junior EL, Boldrini-França J, Takeda AAS, Costa TR, Peigneur S, Cardoso IA, *et al*. Towards toxin PEGylation: the example of rCollinein-1, a snake venom thrombin-like enzyme, as a PEGylated biopharmaceutical prototype. International Journal of Biological Macromolecules. 2021; 190: 564–573.

[30] Ogawa T, Tobishima Y, Kamata S, Matsuda Y, Muramoto K, Hidaka M, *et al*. Focused proteomics analysis of habu snake (*protobothrops flavoviridis*) venom using antivenom-based affinity chromatography reveals novel myonecrosis-enhancing activity of thrombin-like serine proteases. Frontiers in Pharmacology. 2021; 12: 766406.

[31] Belo AA, Naves de Souza DL, de Melo-Braga MN, Lopes de Souza L, Molina Molina DA, Vaz de Melo PD, *et al*. Production of a murine mAb against Bothrops alternatus and B. neuwiedi snake venoms and its use to isolate a thrombin-like serine protease fraction. International Journal of Biological Macromolecules. 2022; 214: 530–541.

[32] Huang Y, Zhou B, Zhang D, Chen Y. Serum levels of VWF, t-PA, TNF-alpha, and ICAM-1 in patients receiving hemocoagulase combined with platelet-rich plasma during total hip replacement. Genetics Research. 2022; 2022: 2766215.

[33] Kim TO, Kim MS, Kho BG, Park HY, Kwon YS, Kim YI, *et al*. Paradoxical pulmonary hemorrhage associated with hemocoagulase batroxobin in a patient with hemoptysis: a CARE-compliant case report. Medicine. 2021; 100: e24040.

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