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CASE REPORT

The Effects of Hemocoagulase on Coagulation Factors in an Elderly Patient with Upper Gastrointestinal Hemorrhage: A Case Report

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ARTICLE HISTORY

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Abstract: ***Background*:** Hemocoagulase agkistrodon has been widely used for visceral bleeding, however, its adverse reaction has not been fully recognized.

***Case Report*:** We reported a 65-year-old female with upper gastrointestinal hemorrhage that caused severe coagulation disorder during her hospitalization. Transfusion of blood products can not improve coagulation function. Coagulation parameters returned to normal two days after discontinuation of hemocoagulase agkistrodon.

***Conclusion*:** So intravenous administration of hemocoagulase should be cautiously used for the treatment of gastrointestinal bleeding.

Keywords: Hemocoagulase agkistrodon, hypofibrinogenemia, gastrointestinal hemorrhage.

1. INTRODUCTION

In clinical practice, several kinds of hemostatic agents are available. There are many different hemocoagulases according to the source of purified thrombin-like and thromboplastin-like enzymes. The main mechanism of haemostasis is that fibrinogen is cleaved by releasing fibrinopeptide -A or both fibrinopeptide-A and -B, and then fibrin monomer is formed; moreover, activated factor Xa contributes to the formation of thrombin at the site of hemorrhage [1]. Hemocoagulase used in the study was purified from the venom of Chinese Agkistrodon blomhoffii ussurensis living in Changbai Mountain. It only releases fibrinopepide-A to form fibrin monomers and these monomers can be quickly broken down in normal vessels, however, on the bleeding sites, it can accelerate platelet aggregation and thrombus formation to achieve hemostasis [2].

Due to its low dosage and high safety, hemocoagulase has been widely used for visceral bleeding and controlling bleeding in various departments such as digestive medicine, respiratory medicine, *etc*. Although the safety of hemocoagulase is uncertain, no thrombosis or other short-term complications have been found. For upper gastrointestinal hemorrhage, it is also a treatment choice. At present, the adverse reactions caused by hemocoagulase are not well recognized. Here, we report a case of hypofibrinogenemia caused by hemocoagulase agkistrodon for the treatment of upper gastrointestinal bleeding.

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2. CASE REPORT

A 65-year-old female was admitted to our hospital due to hematemesis and melena. She had hypertension and colon and rectal cancer after surgery for eight years. She denied any history of liver or hematological diseases. She was rendered proton pump inhibitors, somatostatin and hemocoagulase agkistrodon for 3 IU/day.

However, gastrointestinal bleeding continued, and she developed melena once or twice every day. Her vital signs were unstable. Her heart rate was 110 bpm (beat per minute) and blood pressure was 160/80 mmHg. Considering her uncontrollable blood pressure, gastrointestinal endoscopy examination could not be performed temporarily. However, an abdominal computed tomography scan did not demonstrate the site or cause of bleeding. Disappointingly laboratory tests demonstrated significant blood coagulation disorder and progressively declined hemoglobin concentration and platelets count.

Laboratory results showed that hemoglobin concentration was 85 g/L, platelets count was 60×10^9/L, prothrombin time was 32.2 s, international normalized ratio was 3.07, activated partial thromboplastin time was 43.1s, fibrinogen was 0.60 g/L, and d-dimer was 20 mg/L. Coagulation disorder is mainly manifested as hypofibrinemia. During her hospitalization, red blood cell 12 units, fresh frozen plasma 1200 mL, cryoprecipitate 30 units, and human fibrinogen 3g were infused. However, the repeated laboratory parameters did not improve.

At that time, disseminated intravascular coagulation was highly suspected, therefore, we consulted hematologists. They suspected that coagulation disorders might be related to the use of hemocoagulase because this drug could consume

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Table 1. The effect of hemocoagulase on laboratory parameters.

-	Two Days After Hemocoagulase Administer	Two Days After Hemocoagulase Discontinuation
Hemoglobin (g/L)	85	89
Platelets ($\times 10^9$/L)	60	106
Prothrombin Time (S)	32.2	13.7
INR[a]	3.07	1.06
APTT[b](s)	43.1	34.8
Fibrinogen (g/L)	0.6	3.43
d-dimer (mg/L)	20	4.1

a refers to international normalized ratio; **b** refers to the activated partial thromboplastin time.

fibrinogen and further induce the coagulation system disorder. Thus, hemocoagulase was discontinued. Two days later, coagulation function was corrected (Table **1**). The Naranjo score was six.

3. DISCUSSION

Hemocoagulase is a hemocoagulative enzyme complex and it is applied to improve coagulation and prevent bleeding [3]. Hemocoagulase agkistrodon is a single component thrombin and has positive hemostasis effect on hemorrhagic diseases. Simultaneously, it may affect other related physiological processes such as blood coagulation, fibrinolysis, and platelet aggregation [4-5].

It exerts its hemostatic activity by releasing fibrinopeptide-A to form fibrin monomers and these monomers can be quickly broken down in normal vessels, however, on the bleeding sites, it can accelerate platelet aggregation and thrombus formation to achieve hemostasis [6-7]. Therefore, the risk of thrombus formation is lower than other hemocoagulases. However, several snake venoms have been reported to contain several components which have an impact on the body's coagulation process [8-11]. However, adverse reactions of hemocoagulase agkistrodon have not been paid enough attention. Wei *et al*. [12] reported that larger doses of hemocoagulase might lead to fibrinogen deficiency in patients with intracranial tumors after surgical treatment. Wang *et al.* [7] reported that fibrinogen levels significantly decreased after administering hemocoagulase for 4–5 days. One study reported routine use of hemocoagulase for patients who have undergone excision of colon polyps which may cause hypofibrinogenemia and even lower gastrointestinal bleeding [2]. Wang *et al*. [13] found that the plasma fibrinogen concentration was reduced by half after 4–5 days of hemocoagulase administration (2–4 IU daily). In our case, on the second day of hemocoagulase usage (3 IU daily), the coagulation parameters and platelet counts obviously declined and severe hypofibrinogenemia and decreased platelet counts and longed clotting time did not improve after infusing blood products. After hemocoagulase was stopped, the various laboratory indicators returned to normal gradually. So if the adverse reactions of hemocoagulase cannot be detected as soon as possible, the consequences will be serious and even fatal.

CONCLUSION

Clarification of its adverse reaction will enable us to apply it better in clinical practice as a hemostatic drug. It is recommended to avoid long-term and large dosage usage and coagulation function should be monitored during the procedure.

In conclusion, our case report suggests that intravenous administration of hemocoagulase should be cautiously used for the treatment of gastrointestinal bleeding, because it might induce hypofibrinogenemia and further exacerbate bleeding. Moreover, we should closely monitor the fibrinogen levels throughout the period of use.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

HUMAN AND ANIMAL RIGHTS

No Animals/Humans were used for studies that are the basis of this research.

STANDARD FOR REPORTING

The study followed the CARE guidelines.

CONSENT FOR PUBLICATION

Informed consent was obtained from the patient for this study.

AVAILABILITY OF DATA AND MATERIALS

The data supporting the findings of the article is available in the hospital record system at the third affiliated hospital of Sun Yat-Sen University.

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CONFLICT OF INTEREST

The author declares no conflict of interest, financial or otherwise.

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