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Hypofibrinogenemia Caused by Hemocoagulase After Colon Polyps Excision

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Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Conflict of interest: None declared

Case series

Patient: —

Final Diagnosis: **Routine use of hemocoagulase for injection for the prevention of late-onset bleeding is not recommended for patients who have undergone excision of colon polyps. Hemocoagulase following excision of colon polyps can cause hypofibrinogenemia and even l**

Symptoms: **Hematochezia**

Medication: —

Clinical Procedure: **Three patients also had lower gastrointestinal bleeding**

Specialty: **Gastroenterology and Hepatology**

Objective: **Unusual or unexpected effect of treatment**

Background: In patients with large colon polyps, late-onset bleeding may be more likely to occur because of the larger cutting surface. In these patients, hemostatic agents may be applied to prevent the late-onset bleeding. A total of 7 patients developed hypofibrinogenemia caused by hemocoagulase following excision of colon polyps in our center from November to December 2015.

Case Report: Seven patients underwent excision of colon polyps in our center from November to December 2015. The cutting face was large in these patients after surgery; therefore, hemocoagulase was used to prevent potential late-onset bleeding. Evaluation of clotting function showed that the fibrinogen level was normal before surgery in all 7 patients. Hemocoagulase was intravenously administered twice daily beginning from postoperative day 1. Hypofibrinogenemia of varying severity occurred 2–4 d later. Three patients also had lower-gastrointestinal bleeding. After drug withdrawal and infusion of fibrinogen, blood fibrinogen level gradually returned to normal. In contrast, among 13 patients who had not received hemocoagulase treatment for preventing hemorrhage following excision of colon polyps, detection of blood fibrinogen before surgery and 2–4 d after showed normal results.

Conclusions: Routine use of Hemocoagulase For Injection for the prevention of late-onset bleeding is not recommended for patients who have undergone excision of colon polyps. Hemocoagulase following excision of colon polyps can cause hypofibrinogenemia and even lower-gastrointestinal bleeding.

MeSH Keywords: **Afibrinogenemia • Colonic Polyps • Gastrointestinal Hemorrhage**

Full-text PDF: <http://www.amjcaserep.com/abstract/index/idArt/902059>



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Background

Late-onset bleeding may occur after excision of colon polyps, with an incidence of 0.2–2%. In patients with large colon polyps, late-onset bleeding may be more likely to occur because of the larger cutting surface. In these patients, hemostatic agents may be applied to prevent the late-onset bleeding. Many snake-venom-based hemocoagulase products are available, including Reptilase, Hemocoagulase Atrox For Injection (based on venom of *Bothrops atrox*), Hemocoagulase For Injection (based on venom of *Agkistrodon halys [pallas]*), Slounase (based on viper venom), and Haemocoagulase Agkistrodon For Injection. A total of 7 patients developed hypofibrinogenemia caused by hemocoagulase (Hemocoagulase For Injection) following excision of colon polyps in our center from November to December 2015.

Case Report

Twenty patients underwent excision of colon polyps in our center in the 2 months from November to December 2015. Among them, the cutting face was large in 7 patients after surgery; therefore, hemocoagulase was used to prevent potential late-onset bleeding. Evaluation of clotting function showed that the fibrinogen level was normal before surgery in all 7 patients. Hemocoagulase was intravenously administered twice daily beginning from postoperative day 1. Hypofibrinogenemia of varying severity occurred 2–4 d later (Table 1). Three patients also had lower-gastrointestinal bleeding. After drug withdrawal and infusion of fibrinogen, blood fibrinogen level gradually returned to normal.

In contrast, among 13 patients who had not received hemocoagulase treatment for preventing hemorrhage following excision

of colon polyps, detection of blood fibrinogen before surgery and 2–4 d after showed normal results (Table 2).

Apparently, there was a significant difference between the average of pre-operation fibrinogen (Pre-op Fg) and post-operation fibrinogen (Post-op Fg) in 7 patients with hemocoagulase administration. There was no significant difference between the average of Pre-op Fg and Post-op Fg in 13 patients without hemocoagulase administration.

Discussion

Hemocoagulase For Injection is a mixture of thrombin-like and thromboplastin-like enzymes that are isolated, purified, and prepared from the venom of *Agkistrodon halys (pallas)*. The hemocoagulase acts only on the bleeding site and does not affect intravascular coagulation status. Thus, it has good targeting capability and does not trigger thrombosis. Thanks to its low required dosage and high safety, hemocoagulase has been widely used for visceral bleeding in departments of digestive medicine, respiratory medicine and neurology, and for controlling bleeding in various surgical procedures in departments of otolaryngology and head and neck surgery. Except for occasional mild allergic reactions, no other adverse reaction has been reported [1–5].

The thrombin-like and thromboplastin-like enzymes in the hemocoagulase are similar enzyme substrates. They can directly act on the third phase of blood coagulation, promoting platelet aggregation at the site of vascular damage. Also, they release a series of clotting factors and platelet factors to degrade the Arg16–Gly17 scissional bonds in the amino acid chain of fibrinogen (Figure 1). They can release fibrinopeptide-A to form fibrin

Table 1. Blood fibrinogen values before surgery and 2–4 d after hemocoagulase administration for prevention of bleeding in patients who had undergone excision of colon polyps.

Patient no.	Time of drug application (days)	Bleeding	Pre-op Fg (g/L)	Post-op Fg (g/L)
1	2	Yes	3.78	0.49
2	2	Yes	3.34	0.95
3	4	Yes	3.84	0.50
4	2	Yes	3.89	0.40
5	2	No	2.68	1.50
6	2	No	2.68	1.23
7	2	No	2.91	1.26

Normal reference value: 2.0–4.0 g/L. Fg – fibrinogen; Pre-op – preoperative; Post-op – postoperative. Pre-op Fg vs. Post-op Fg, P value=0.0007, $P<0.05$, there are significant differences between the 2 groups (paired t test).

Table 2. Blood fibrinogen values before surgery and 2–4 d after surgery without hemocoagulase for prevention of bleeding in patients who had undergone excision of colon polyps.

Patient no.	Pre-op Fg	Post-op Fg
1	2.82	3.32
2	2.71	2.76
3	2.98	3.48
4	3.49	2.97
5	2.75	2.56
6	3.42	3.86
7	2.50	2.37
8	2.14	2.17
9	3.06	3.14
10	3.52	3.47
11	2.94	3.43
12	3.01	2.83
13	2.53	2.21

Normal reference value: 2.0–4.0 g/L. Fg – fibrinogen; Pre-op – preoperative; Post-op – postoperative. Pre-op Fg vs. Post-op Fg, P value=0.5757, $P>0.05$, there are no significant differences between the 2 groups (paired t test).

monomer I, but do not degrade fibrinopeptide B or directly activate coagulation factor XIII (fibrin stabilizing factor). As a result, only unstable fibrin monomers form. These monomers can quickly be broken down in normal vessels; therefore, the risk of thrombosis is low after intravenous injection of hemocoagulase. At the site of vascular injury, however, the instable soluble fibrin monomer I can be aggregated into fibrin I polymer and thus promote platelet aggregation, and accelerate platelet aggregation and thrombus formation, finally achieving hemostasis at the site of vascular injury [2–6].

Hemocoagulase exerts its hemostatic effect by hydrolyzing the A α chain of fibrinogen; therefore, it can continuously consume fibrinogen and lead to reduced plasma concentration.

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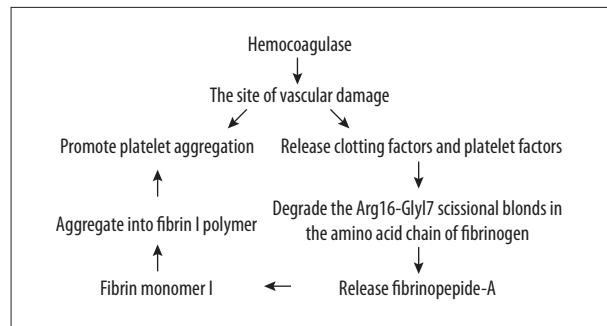


Figure 1. The action mechanism of hemocoagulase.

Wang et al. [6] found that the plasma fibrinogen concentration could be lowered by half after 4–5 d of hemocoagulase use (2–4 IU daily). According to the package insert of Hemocoagulase For Injection, this drug has potent activity in removing fibrinogen and thus lowering the blood fibrinogen level at a dose of 50–100 kU/dose. In our series, when the dose of hemocoagulase reached 50 kU, the coagulation function dramatically declined and the patients developed severe hypofibrinogenemia. After hemocoagulase was stopped and fibrinogen was supplemented intravenously, the blood fibrinogen level returned to normal.

Therefore, although only occasional anaphylactoid reactions are mentioned in package inserts and the literature as adverse reactions of Hemocoagulase For Injection, hypofibrinogenemia has been noted in our clinical practice. Patients may develop persistent oozing from the wound. More importantly, the dose that may cause hypofibrinogenemia is far lower than the 50–100 kU/dose, as indicated in the package insert. Therefore, routine use of Hemocoagulase For Injection for the prevention of late-onset bleeding is not recommended for patients who have undergone excision of colon polyps.

Conclusions

Routine use of Hemocoagulase For Injection for the prevention of late-onset bleeding is not recommended for patients who have undergone excision of colon polyps. Hemocoagulase following excision of colon polyps can cause hypofibrinogenemia and even lower-gastrointestinal bleeding.