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# 急性失血患者中早期输注冷沉淀治疗对凝血功能的影响\*

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**摘要 目的:**探讨急性失血患者中早期输注冷沉淀治疗对凝血功能的影响。**方法:**收集江苏省中医院(南京中医药大学附属医院) 2015 年 9 月-2019 年 8 月收治的 80 例急性失血患者的临床资料,将患者按照住院号排序后取随机数字后分为研究组(40 例)和对照组(40 例),其中对照组给予常规输注血小板治疗,研究组给予早期输注冷沉淀凝血因子治疗,观察两组凝血功能变化及临床指标。**结果:**两组患者均顺利完成相应的输注治疗,无终端、退出、输注中死亡等异常情况。研究组治疗的总有效率显著高于对照组( $P<0.05$ )。两组患者输血前的凝血酶原时间(Prothrombin time, PT)、部分活化凝血酶时间(Activated partial thromboplastin time, APTT)、纤维蛋白原(Fibrinogen, Fbg)、血小板(blood platelet, PLT)、凝血酶时间(thrombin time, TT)水平组间差异无统计学意义( $P>0.05$ );输血 24 h 后两组患者的 TT、PT、APTT 均降低, Fbg、PLT 水平升高,并且研究组的变化幅度大于对照组变化幅度( $P<0.05$ )。研究组患者的有效止血率、平均止血时间、24 h 悬浮红细胞续用量与对照组相比,有显著差异( $P<0.05$ )。**结论:**急性失血患者中早期输注冷沉淀治疗可改善患者的凝血功能,起到较好止血效果,值得临床推广应用。

**关键词:**急性失血者;早期输注冷沉淀;凝血功能;影响

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## Effect of Early Infusion Cryoprecipitate on Blood Coagulation in Patients with Acute Blood Loss\*

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**ABSTRACT Objective:** To investigate the effect of early infusion cryoprecipitate on blood coagulation in patients with acute blood loss. **Methods:** The clinical data of 80 patients with acute blood loss admitted from September 2016 to August 2019 in our hospital were collected. The patients were randomly divided into study group (40 cases) and control group (40 cases). In the control group, conventional infusion platelet therapy was given. The study group was given early infusion of cryoprecipitate factor, and the changes of coagulation function and clinical indicators were observed. **Results:** Two groups of patients successfully completed the corresponding infusion therapy, and there were no abnormalities such as terminal, withdrawal, and death during infusion. The total effective rate of treatment in the study group was significantly higher than that in the control group ( $P<0.05$ ). There were no differences in the levels of TT, PT, APTT, Fbg and PLT between the two groups before blood transfusion ( $P>0.05$ ). After 24 h of transfusion, the TT, PT and APTT of the two groups were decreased, and the levels of Fbg and PLT were decreased. The increase was greater in the study group than in the control group, and the difference was statistically significant ( $P<0.05$ ). The effective hemostasis rate, mean hemostasis time, and 24-hour suspension of red blood cells in the study group were significantly different from those in the control group ( $P<0.05$ ). **Conclusion:** Early infusion of cryoprecipitate in patients with acute blood loss can improve the coagulation function of patients and play a better hemostasis effect, which is worthy of clinical application.

**Key words:** Acute blood loss; Early infusion cryoprecipitate; Coagulation function; Influence

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### 前言

急性失血是临床常见的危重症之一,失血量占全身血量的 20%,主要外科创伤所引起大血管破裂、腹外伤导致肝脾、胃内

脏损伤,内科消化道出血,产科出血等引起,在临床中起病较急,血容量及红细胞迅速下降,对患者的生命造成了极大的威胁<sup>[1]</sup>。长期以来,临床抢救急性失血者时,多采用短期快速扩容,并以输注全血或者红细胞为主,不仅浪费了血液资源,而且还减少了稀释性血小板及凝血因子,延长抢救时间,影响抢救效果<sup>[2,3]</sup>。同时,急性输注与常规输血不同,因此,在抢救急性失血

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者时,应充分认识到急性输血与常规输血的差别,合理利用血液成分,及时为患者补充血小板及凝血因子,改善预后<sup>[45]</sup>。冷沉淀含丰富的纤维蛋白原结合蛋白和第八因子,其中纤维蛋白原结合蛋白能够抗感染、促进创伤组织的修复和愈合,第八因子对严重创伤后大出血的患者有止血作用,因此,本文现将急性失血患者中早期输注冷沉淀治疗对凝血功能的影响,希望为临床治疗急性出血患者提供更多的帮助,现报告如下。

## 1 资料与方法

### 1.1 一般资料

纳入标准<sup>[67]</sup>:① 患者均符合输血治疗适应症;② 患者均明确的诊断和病情评估;收缩压 <13.3 kPa,脉压 <4.0 kPa,心脏指数 <2.5L/(min·m<sup>2</sup>);③ 自愿参与此次研究。排除标准:① 严重心肝肾肾功能不全;② 先天性凝血功能紊乱;③ 妊娠期及哺乳期妇女;④ 精神病;⑤ 依从性差,不配合或者拒绝参加研究者。

收集我院 2015 年 9 月-2019 年 8 月收治的 80 例急性失血患者,将患者按照住院号排序后取随机数字后分为研究组(40 例)和对照组(40 例)。对照组:男性 27 例,女性 13 例;年龄 20-86 岁,平均年龄(46.78±5.34)岁;失血原因:13 例恶性肿瘤出血,17 例由溃疡引起的消化道出血,10 例肝硬化胃底静脉曲张出血。研究组:男性 26 例,女性 14 例;年龄 23-88 岁,平均年龄(47.78±5.14)岁;失血原因:恶性肿瘤出血 12 例,由溃疡引起的消化道出血 16 例,肝硬化胃底静脉曲张出血 12 例。两组基础资料无统计学意义( $P>0.05$ )。

### 1.2 研究方法

表 1 两组治疗效果对比(例,%)

Table 1 Comparison of treatment effects between the two groups(n,%)

| Groups        | n  | Excellence | Effective | No avail | Total effective rate |
|---------------|----|------------|-----------|----------|----------------------|
| Control group | 40 | 20         | 10        | 10       | 30 (75.00)           |
| Study group   | 40 | 23         | 14        | 3        | 37 (92.50)*          |

Note: compared with the control group, \* $P<0.05$ .

### 2.2 急性失血患者血输注量的比较

各类患者的血凝效果比较无统计学意义( $P>0.05$ ),见表 2。

### 2.3 输血前后凝血功能比较

两组输血前的 TT、PT、APTT、Fbg、PLT 水平比较无统计学意义( $P>0.05$ );输血 24 h 后两组的 TT、PT、APTT 均降低,Fbg、PLT 升高,且研究组的变化幅度大于对照组( $P<0.05$ ),见表 3。

### 2.4 临床指标比较

研究组的有效止血率、平均止血时间、24 h 悬浮红细胞续用量与对照组相比,有统计学意义( $P<0.05$ )。见表 4。

## 3 讨论

在常规治疗的基础上,对照组:给予常规输注血小板治疗。若患者血小板计数小于  $50\times 10^9/L$ ,可考虑血小板输注。根据血小板计数、患者出血情况一次性给予 1-2 个治疗量血小板治疗,快速输完。研究组:给予早期输注冷沉淀凝血因子治疗,在临床治疗开始前 1 h 输入冷沉淀 10-20U 凝血因子<sup>[8]</sup>。并根据患者出血及凝血情况,决定是否继续使用。

### 1.3 观察指标

两组治疗的疗效判断:显效:治疗后 1 d 内各项体征稳定,未出现出血;有效:治疗后 1-3 d 内各项体征稳定,未出现出血;无效:治疗 3 d 后各项体征波动大,出现出血现象。

两组凝血功能、有效止血率、平均止血时间、24 h 悬浮红细胞续用量<sup>[9]</sup>。凝血功能。包括凝血酶原时间凝血酶原时间(Prothrombin time,PT)、部分活化凝血酶时间(Activated partial thromboplastin time,APTT)、纤维蛋白原(Fibrinogen,Fbg)、血小板(blood platelet,PLT)、凝血酶时间(thrombin time,TT)。

### 1.4 统计学方法

采用 SPSS19.0,计量资料以( $\bar{x}\pm s$ )表示,行 t 检验;计数资料用(%)表示,采用  $\chi^2$  检验。 $P<0.05$  有统计学意义。

## 2 结果

### 2.1 两组治疗效果的比较

两组患者均顺利完成相应的输注治疗,无终端、退出、输注中死亡等异常情况。研究组治疗的总有效率显著高于对照组( $P<0.05$ ),见表 1。

急性失血患者在急性输血中,一般采用库存血,但是止血效果不佳<sup>[10,11]</sup>,库存血通常在 2℃-6℃ 保存 24 h 之后,血液不稳定的 V、VIII、XI 因子已减少<sup>[12,13]</sup>。此时患者丢失了大量的血小板和凝血因子<sup>[14]</sup>,过多输入库存血能引起稀释性血小板减少症<sup>[15]</sup>。之前本研究的作者治疗产后大失血时,给予患者全血,创面仍然渗血,但是采取冷沉淀治疗后,出血得到了有效控制<sup>[16]</sup>。因此,在抢救急性失血患者中,应充分认识急性输血的凝血异常<sup>[17]</sup>。

血小板能够止血和维护血管壁完整性<sup>[18]</sup>。冷沉淀含有大量的第八因子,纤维蛋白原、纤维结合蛋白,输入后可迅速提升凝

表 2 急性失血患者血输注量的比较( $\bar{x}\pm s$ )

Table 2 Comparison of blood transfusions in patients with massive blood loss ( $\bar{x}\pm s$ )

| Patient                                               | FFP (mL)     | LPRC (mL)    | PC-2 (n)     |
|-------------------------------------------------------|--------------|--------------|--------------|
| Gastric cancer bleeding (n=25)                        | 98.34± 31.23 | 56.34± 21.12 | 75.34± 21.23 |
| Esophagorrhagiablood (n=33)                           | 80.23± 19.12 | 54.34± 19.23 | 69.34± 20.14 |
| Bleeding from varicose veins of gastric fundus (n=22) | 81.23± 20.14 | 56.34± 20.14 | 70.14± 21.23 |

表3 输血前后凝血功能比较( $\bar{x} \pm s$ )Table 3 Comparison of coagulation function before and after transfusion ( $\bar{x} \pm s$ )

| Groups        | TT (s)      |             | PT (s)      |             | APTT (s)    |             | Fbg (g/L)   |            | PLT ( $10^9/L$ ) |             |
|---------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|------------|------------------|-------------|
|               | Before      |             | Before      |             | Before      |             | Before      |            | Before           |             |
|               | blood       | After 24 h  | blood       | After 24 h  | blood       | After 24 h  | blood       | After 24 h | blood            | After 24 h  |
|               | transfusion |             | transfusion |             | transfusion |             | transfusion |            | transfusion      |             |
| Control group | 26.34 $\pm$ | 22.56 $\pm$ | 18.23 $\pm$ | 15.45 $\pm$ | 41.25 $\pm$ | 35.78 $\pm$ | 1.42 $\pm$  | 0.32       | 2.67 $\pm$       | 41.23 $\pm$ |
| (n=40)        | 3.25        | 3.15*       | 3.15        | 3.78*       | 7.56        | 4.6*        | 0.15*       |            | 10.34            | 9.15        |
| Study group   | 27.56 $\pm$ | 18.78 $\pm$ | 18.90 $\pm$ | 12.78 $\pm$ | 41.90 $\pm$ | 30.23 $\pm$ | 1.42 $\pm$  | 0.15       | 3.23 $\pm$       | 40.34 $\pm$ |
| (n=40)        | 3.16        | 2.03*       | 3.12        | 3.01**      | 7.16        | 4.15**      | 0.23**      |            | 9.15             | 7.34**      |

Note: compared with the same group before transfusion, \* $P < 0.05$ , compared with the 24 h control group, \*\* $P < 0.05$ .

表4 输注后的临床指标比较( $\bar{x} \pm s$ )Table 4 Comparison of clinical indicators ( $\bar{x} \pm s$ )

| Groups              | Hemostasis rate(%) | Hemostasis time(h) | 24-hour suspended red blood cell continuation(U) |
|---------------------|--------------------|--------------------|--------------------------------------------------|
| Control group(n=40) | 30(75.00)          | 7.45 $\pm$ 2.12    | 13.23 $\pm$ 4.23                                 |
| Study group(n=40)   | 37(92.50)*         | 3.24 $\pm$ 1.56*   | 8.34 $\pm$ 3.14*                                 |

Note: compared with the control group, \* $P < 0.05$ .

血因子水平<sup>[19,20]</sup>。激活内源凝血系统,加快血小板通过 vWF 黏附到胶原蛋白上<sup>[21]</sup>,增强血小板黏附性。当体内的纤维蛋白原含量增高,进一步加快凝血途径,纠正凝血异常<sup>[22,23]</sup>。另外冷沉淀中的高浓度纤维结合蛋白,能清除非毒物质、炎症,促进创伤的愈合<sup>[24]</sup>。同时也能在细胞表面形成网状结构,为产生胶原、清除病灶区的炎性产物、加速创面愈合创造了较好的条件<sup>[25,26]</sup>。采用早期输血冷沉淀治疗急性失血患者,及时补充了血小板和凝血因子,患者各项凝血指标显著改善,止血效果明显<sup>[27]</sup>。本研究显示研究组治疗的总有效率显著高于对照组,说明早期输注冷沉淀能有效的缩短凝血与出血时间,加速康复,从而提高治疗效率。本研究研究组的 TT、PT、APTT、Fbg、PLT 显著缩短,早期输注冷沉淀的有效止血率明显增高,平均止血时间明显缩短,24 h 内悬浮红细胞续用量显著减少<sup>[28]</sup>。表明早期输注冷沉淀可缩短凝血酶原时间及部分凝血活酶时间,改善凝血功能,促进止血功能。分析其原因是早期输注冷沉淀有显著的止血效果,同时能够补充急性出血患者血小板和大量凝血因子,有效的提高了患者的凝血功能,显著的升高血小板数,促进止血<sup>[29,30]</sup>。本研究也存在一定的不足,未研究两者联合治疗急性失血患者,在后期研究中,应进一步扩大研究样本,进一步证实研究的可靠性,为临床治疗提供有效参考依据。

综上所述,急性失血患者在救治时,应在积极补充血容量时,给予早期补充纤维蛋白原、凝血因子等。尤其对于凝血异常患者,采用冷沉淀来进一步补充消耗的凝血因子。通过早期输注冷沉淀可提高患者血液中的凝血因子和纤维蛋白原的含量,辅助血小板增强凝血功能,重建凝血机制,具有临床推广应用的价值。

#### 参考文献(References)

- [1] Feng Q, Zhu F, Li C, et al. Effect of Frequency of Platelet Apheresis on Coagulation Function in Donors: A Prospective Cohort Study [J]. Indian J Hematol Blood Transfus, 2019, 12(2): 1-6
- [2] Poreba M, Mostowik M, Aleksander Siniarski. Treatment with

high-dose n-3 PUFAs has no effect on platelet function, coagulation, metabolic status or inflammation in patients with atherosclerosis and type 2 diabetes[J]. Cardiovasc Diabetol, 2017, 16(1): 50-70

- [3] Junfeng L, Deren W, Yao X, et al. Association between Coagulation Function and Cerebral Microbleeds in Ischemic Stroke Patients with Atrial Fibrillation and/or Rheumatic Heart Disease [J]. Aging Dis, 2017, 8(2): 131-132
- [4] Schoeman RM, Rana K, Danes N, et al. A Microfluidic Model of Hemostasis Sensitive to Platelet Function and Coagulation [J]. Cell Mol Bioeng, 2017, 10(1): 3-15
- [5] Li S, Gao Y, Shao M, et al. Association between coagulation function and patients with primary angle closure glaucoma: a 5-year retrospective case-control study[J]. BMJ Open, 2017, 7(11): e016719
- [6] Li F, He M, Yang M, et al. Alteration of heat shock protein 20 expression in preeclamptic patients and its effect in vascular and coagulation function[J]. Front Med, 2018, 12(5): 542-549
- [7] Laurençot, Philippe. Mass-conserving solutions to coagulation-fragmentation equations with nonintegrable fragment distribution function[J]. Quarter Appl Mathem, 2018, 76(4): 767-785
- [8] Liu JQ, Yang SJ, Chen JQ, et al. Effect on changes of blood coagulation function, cytokines and immune function in patients undergoing laparoscopic radical gastrectomy for gastric cancer [J]. Journal of Hainan Medical University, 2017, 23(1): 104-108
- [9] Xiao W, Aimin D, Naqiang L, et al. Inflammation Is Associated With Platelet Coagulation Function Rather Than Enzymatic Coagulation Function in Patients With Takayasu Arteritis [J]. Int Heart J, 2017, 58(4): 589-592
- [10] Yozova ID, Howard J, Henke D, et al. Comparison of the effects of 7.2% hypertonic saline and 20% mannitol on whole blood coagulation and platelet function in dogs with suspected intracranial hypertension - a pilot study[J]. BMC Vet Res, 2017, 13(1): 185-204
- [11] Takeyama M, Nogami K, Matsumoto T, et al. Possible assessment of coagulation function and haemostasis therapy using comprehensive

- coagulation assays in a patient with acquired haemophilia A [J]. Haemophilia, 2017, 23(1): e46-e50
- [12] Jia, Rui, Li, et al. Incidence, influencing factors, and prognostic impact of intraoperative massive blood loss in adolescents with neuromuscular scoliosis: A STROBE-compliant retrospective observational analysis[J]. Med, 2017, 96(11): e6292
- [13] Hongju L, Bin L, Xuerong Y, et al. Preoperative risk factors for massive blood loss in adrenalectomy for pheochromocytoma[J]. Oncotarget, 2017, 8(45): 79964-79970
- [14] M C A Müller, Ponjee GAE. Using thromboelastography to measure coagulation following massive blood loss[J]. Ned Tijdschr Geneeskd, 2017, 161(29): D1380
- [15] Lange ND, Schol P, Marcus Lancé, et al. Restrictive Versus Massive Fluid Resuscitation Strategy (REFILL study), influence on blood loss and hemostatic parameters in obstetric hemorrhage: study protocol for a randomized controlled trial[J]. Trials, 2018, 19(1): 166-185
- [16] Miyashima Y, Iwamuro M, Shibata M, et al. Prediction of Disseminated Intravascular Coagulation by Liver Function Tests in Patients with Japanese Spotted Fever[J]. Int Med, 2017, 57(2): 197-202
- [17] Li W, Wang YR, Song W, et al. The changes of plasma coagulation function in patients with glioma and its correlation with malignant grade of glioma[J]. Zhonghua Yi Xue Za Zhi, 2018, 98(5): 336-339
- [18] Feng Q, Zhu F, Li C, et al. Effect of Frequency of Platelet Apheresis on Coagulation Function in Donors: A Prospective Cohort Study[J]. Indian J Hematol Blood Transfus, 2019, 20(2): 1-6
- [19] Bilecen S, de Groot JA, Kalkman CJ, et al. Effect of Fibrinogen Concentrate on Intraoperative Blood Loss Among Patients With Intraoperative Bleeding During High-Risk Cardiac Surgery: A Randomized Clinical Trial[J]. Jama, 2017, 317(7): 738-747
- [20] Koch KU, Tietze A, Aanerud J, et al. Effect of ephedrine and phenylephrine on brain oxygenation and microcirculation in anaesthetised patients with cerebral tumours: study protocol for a randomised controlled trial[J]. Bmj Open, 2017, 7(11): e018560
- [21] Abramov D, Haglund NA, Salvo TGD. Effect of Milrinone Infusion on Pulmonary Vasculature and Stroke Work Indices: A Single-Center Retrospective Analysis in 69 Patients Awaiting Cardiac Transplantation[J]. Am J Cardiovasc Drugs, 2017, 17(6): 1-8
- [22] Crochemore T, Savioli FA. Thromboelastometry-guided hemostatic therapy for hemorrhagic shock in the postoperative period of vascular surgery: a case report[J]. J Med Case Rep, 2018, 12(1): 153-154
- [23] Markowitz J, Hyams JS, Adedokun OJ, et al. Tu1864 - The Effect of Immunogenicity Measured with a Drugtolerant Assay on Loss of Response and Infusion Reactions in Pediatric IBD Patients Treated with Infliximab in the Develop Registry [J]. Gastroenterology, 2018, 154(6): S1041
- [24] Pan F, Zhang R, Wang G, et al. Effect of hydroxyethyl starch 130/0.4 on blood loss and coagulation in patients with recent exposure to dual antiplatelet therapy undergoing off-pump coronary artery bypass graft surgery[J]. Jpn Circ J, 2011, 75(10): 2397-2402
- [25] Sargent N, Roy A, Simpson S, et al. A protocol for management of blood loss in surgical treatment of peritoneal malignancy by cytoreductive surgery and hyperthermic intraperitoneal chemotherapy [J]. Transfus Med, 2016, 26(2): 118-122
- [26] Stayer SA, Schwartz RE, Pasquariello CA, et al. Pediatric orthotopic liver transplantation: potential predictors of intraoperative blood loss and coagulation status monitoring [J]. Pediatr Surg Int, 1995, 10(5): 317-321
- [27] Bachir NM, Rockey DC. M1543: Endoscopic Findings Thought to Be a Source of Blood Loss in Patients With Iron Deficiency Anemia Do Not Correlate With Stool Blood[J]. Gastrointest Endosc, 2010, 71(5): AB250-AB250
- [28] Obinwanne KM, Fredrickson KA, Mathiason MA, et al. Incidence, treatment, and outcomes of iron deficiency after laparoscopic Roux-en-Y gastric bypass: a 10-year analysis [J]. J Am Coll Surg, 2014, 218(2): 246-252
- [29] Duchesne JC, Jr MSN, Cotton BA, et al. Damage control resuscitation: the new face of damage control [J]. J of Trauma, 2010, 69(4): 976-990
- [30] Zhou D, Luo Y L, Luo S H, et al. The Effect of Diagnostic Blood Loss on Anemia and Transfusion Among Postoperative Patients With Congenital Heart Disease in a Pediatric Intensive Care Unit[J]. J Pediatr Nurs, 2017, 38(20): 62-67