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# 高剂量生长抑素、奥美拉唑联合止血芳酸治疗急性上消化道出血合并凝血功能障碍患者的临床效果*

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**摘要 目的:**探讨高剂量生长抑素、奥美拉唑联合止血芳酸治疗急性上消化道出血合并凝血功能障碍患者的临床效果及安全性。**方法:**选择我院 2014 年 1 月~2017 年 12 月收治的 92 例急性上消化出血合并凝血功能障碍的患者，并按随机数表法将其分为对照组和研究组。对照组予以常规剂量生长抑素、奥美拉唑联合止血芳酸治疗，研究组予以高剂量生长抑素治疗，其余奥美拉唑及止血芳酸用法同对照组。治疗后，比较两组的临床疗效、止血情况、住院时间，治疗前后血常规指标、凝血功能的变化及并发症的发生情况。**结果:**治疗后，研究组总有效率明显高于对照组[91.30% vs. 74.42%](P<0.05)，而平均止血时间、再止血率及住院时间均明显短于对照组(P<0.05)；两组白细胞计数(WBC)、部分活化凝血酶原时间(APTT)及凝血酶原时间(PT)均较治疗前明显下降，血红蛋白(Hb)、红细胞计数(RBC)、红细胞压积(Hct)及血小板计数(PLT)均较治疗前明显上升，且研究组以上指标变化较对照组更明显(P<0.05)。两组并发症的发生率比较差异均无统计学意义(P>0.05)。**结论:**高剂量生长抑素、奥美拉唑联合止血芳酸治疗急性上消化道出血合并凝血功能障碍的效果明显优于常规剂量生长抑素、奥美拉唑联合止血芳酸治疗，其能够更有效缩短止血时间，避免再出血，且未增加药物不良反应，安全性高。

**关键词:**急性上消化道出血；凝血功能障碍；高剂量生长抑素；奥美拉唑；止血芳酸；治疗效果

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# Clinical Effect of High Dose Somatostatin, Omeprazole Combined with Hemostasis on the Acute Upper Gastrointestinal Bleeding Patients combined with Coagulation Dysfunction*

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**ABSTRACT Objective:** To research the clinical effect and safety of high dose somatostatin, omeprazole combined with hemostasis on the acute upper gastrointestinal bleeding patients combined with coagulation dysfunction. **Methods:** 92 patients of acute upper gastrointestinal bleeding patients combined with coagulation dysfunction from January 2014 to December 2017. According to random number table method, thoes patients were divided into control group and research group, control group was treated with conventional dose somatostatin and omeprazole combined with hemostasis, and the research group was treated with high doses of somatostatin, and the remaining omeprazole and hemostasis were used the same as control group. After treatment, then clinical efficacy, hemostasis and hospitalization time, blood routine index, coagulation function before and after treatment, and complications between two group was compared. **Results:** After treatment, total effective rate in research group was obvious higher than control group (91.30% vs 74.42%) (P<0.05). While the average hemostatic time, rehemostasis rate and hospitalization time in research group were lesser than the control group (P<0.05). White blood cells (WBC), partial activation thrombin time (APTT) and prothrombin time (PT) were decreased than before treatment, hemoglobin (Hb), erythrocyte count (RBC), hematocrit (Hct) and platelet count (PLT) in both group were increased than before treatment, while the changes of the above indicators in the research group were more significant than those in the control group (P<0.05). Complication rate between the two groups was no statistically significant difference (P>0.05). **Conclusion:** Clinical effect of high dose somatostatin, omeprazole combined with hemostasis on the acute upper gastrointestinal bleeding patients combined with coagulation dysfunction is better than conventional dose somatostatin and omeprazole combined with hemostasis, can shorten the bleeding time, to avoid rebleeding, and did not increase the adverse drug reactions, high safety.

**Key words:** Acute upper gastrointestinal bleeding; Coagulation dysfunction; High dose somatostatin; Omeprazole; Hemostatic aromatic acid; Treatment effect

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## 前言

急性上消化道出血为内科常见危急重症之一,主要由屈氏韧带以上的胰管、胃及食管所致,以呕血及黑粪为主要表现。由于血容量的减少能够引起周围循环的改变，导致凝血功能障碍,因此发病率及死亡率均较高[1,2]。早期治疗可于短时间内止血,进一步争取有效的治疗时间[3]。既往多在积极处理原发病变基础上加以质子泵抑制剂控制出血,能够一定程度的改善患者凝血反应及血小板聚集功能,但部分患者的临床效果并不理想[4,5]。有关研究表明[6]在既往治疗基础上联合生长抑素和止血芳酸能够增强急性上消化道出血患者的止血效果。近年来,有研究显示[7]大剂量生长抑素有可能会提高止血效果,但目前临床上缺乏此类相关全面报道。本研究旨在分析高剂量生长抑素、奥美拉唑联合止血芳酸治疗凝血功能障碍合并急性上消化道出血患者的临床效果,以期为临床治疗提供理论依据。

## 1 资料与方法

### 1.1 一般资料

选择我院 2014 年 1 月 ~2017 年 12 月收治的 92 例凝血功能障碍合并急性上消化出血患者。入选标准[8]:48 h 内伴严重呕血和黑便等上消化道出血表现,大便潜血实验呈阳性,并经纤维胃镜检查明确诊断为急性上消化道出血，且伴凝血功能障碍;非妊娠或者哺乳阶段;近期无质子泵抑制剂使用史;心肝肾等器官无明显病变;无手术指征;性别不限。排除标准:曾伴血液系统病变;呼吸道出血;上消化道周边出血;内镜检查提示静脉曲张性出血或者喷射样出血;休克状态;伴幽门梗阻、穿孔等严重溃疡并发症;伴十二指肠、胃或者食管切除史;免疫功能低下、恶性肿瘤;对本研究药物过敏者。

按随机数表法将所有患者分为对照组和研究组。对照组男 27 例,女 19 例;年龄 30~68 岁,平均(49.42± 8.11)岁;平均 24 h 内出血量(1214.60± 38.29);疾病类型:十二指肠溃疡出血 10 例,急性出血性胃炎 19 例,急性胃黏膜病变 17 例。研究组男 26 例,女 20 例;年龄 30~68 岁,平均(48.01± 9.53)岁;平均 24 h 内出血量(1230.17± 34.76);疾病类型:十二指肠溃疡出血 10 例,急性出血性胃炎 21 例,急性胃黏膜病变 15 例。两组一般资料比较差异无统计学意义(P>0.05),具有可比性。

### 1.2 治疗方法

患者入院后均积极进行生命体征检测,并予以禁食、原发症处理、静脉补充血容量,保持呼吸道通畅等常规治疗。对照组予以常规剂量生长抑素、奥美拉唑联合止血芳酸治疗,首次静脉注射 250 μg 生长抑素(规格:3 mg/ 支,20131124,常州四药制药有限公司),再持续静脉泵注 250 μg/h 生长抑素 +500 mL0.9%氯化钠溶液(规格:500 mL:4.5g/ 瓶,20131008,广东利泰制药股份有限公司)，控制滴速为 4.1 mL/h,qd。静脉滴注 40 mg 奥美拉唑(规格:40 mg/ 支,20130914,阿斯利康制药有限公司),bid;静脉滴注 0.6 g 止血芳酸(规格:0.1:10 mL,2013721,扬州中宝制药有限公司)+500 mL10%葡萄糖注射液(规格:500 mL:25 g,20130418,山东齐都药业有限公司),qd,均持续治疗 5 d。研究组予以高剂量生长抑素治疗，首次静脉注射 500 μg 生长抑素,再静脉泵注 500 mL 0.9%氯化钠 +500 μg/h 生长抑素,控制滴速为 8.2 mL/h,持续治疗 5d,其余奥美拉唑及止血芳酸用法同对照组。

### 1.3 观察指标

**1.3.1 临床疗效评估** 于治疗第 5 d 时评估临床疗效,记录止血时间(胃管引出液变清、无血,粪便由黑色转至黄色,粪便潜血试验转至阴性)、再止血(经治疗后未见出血征象,但 72h 内再见出血征象或者内镜证实再出血)及住院时间和并发症发生情况。治疗后 24~48 h 内临床表现消失,心率及血压维持稳定,大便潜血实验呈阴性，胃镜检查提示出血停止为显效；治疗后 48~72 h 内临床表现大致消失,心率及血压恢复稳定,大便潜血试验提示阴性,胃镜提示出血减少为有效;治疗 72 h 后仍可见黑便等表现,心率及血压有波动为无效[8]。

**1.3.2 生化指标测定** 于治疗前及治疗 5 d 时抽取患者 2 mL 静脉血,常规处理后保存待检。以全自动生化分析仪测定白细胞计数(WBC)、血红蛋白(Hb)、红细胞计数(RBC)水平,试剂盒均来自南京森贝伽生物科技有限公司。选择全自动血凝仪测定红细胞压积(Hct)、血小板计数(PLT)、部分活化凝血酶原时间(APTT)及凝血酶原时间(PT)水平,试剂盒均来自上海经科化学科技有限公司。

### 1.4 统计学分析

数据处理选用 SPSS18.0 软件进行,数据均符合正态分布,用($\bar{x}$± s)表示计量资料,组间比较选用独立样本 t 检验,用[例(%)]表示计数资料,组间比较采用 $x^2$ 检验,以 P<0.05 为差异有统计学意义。

## 2 结果

### 2.1 两组临床疗效的比较

治疗后,研究组总有效率为 91.3%,明显高于对照组,组间差异有统计学意义(P<0.05),见表 1。

表 1 两组临床疗效比较[例(%)]

Table 1 Comparison the clinical efficacy between two groups[n(%)]

| Groups | n | Effectiveness | Effective | Ineffective | Total effective rate |
|---|---|---|---|---|---|
| Control group | 46 | 15(32.61) | 20(43.48) | 11(23.91) | 35(76.09) |
| Research group | 46 | 24(52.17) | 18(39.13) | 4(8.70) | 42(91.30) |
| P | | | 0.024 | | 0.482 |

### 2.2 两组止血情况及住院时间的比较

研究组平均止血时间、再止血率及住院时间均短于对照组,差异有统计学意义(P<0.05),见表 2。

表 2 两组止血情况及住院时间的比较($\bar{x}\pm s$,例(%))

Table 2 Comparison the hemostasis and hospital stay between two groups($\bar{x}\pm s$, n(%))

| Groups | n | Average hemostasis time (h) | Re-bleed rate(%) | Hospital stay(d) |
|---|---|---|---|---|
| Control group | 46 | 30.95± 4.03 | 15() | 13.85± 1.90 |
| Research group | 46 | 19.61± 2.65 | 4(8.70) | 10.41± 1.24 |
| P | | 0.000 | 0.005 | 0.000 |

### 2.3 两组治疗前后血常规指标的比较

治疗前,两组血常规指标比较差异无统计学意义(P>0.05);治疗后,两组 WBC 均较治疗前显著下降,Hb 及 RBC 均较治疗前明显上升,且研究组 WBC 明显低于对照组,Hb 及 RBC均显著高于对照组,组间比较差异有统计学意义(P<0.05),见表3。

表 3 两组治疗前后血常规指标比较($\bar{x}\pm s$)

Table 3 Comparison of the blood routine index before treatment and after treatment between two groups ($\bar{x}\pm s$)

| Groups | n | WBC(× $10^9$/L) | | Hb(g/L) | | RBC(× $10^9$/L) | |
|---|---|---|---|---|---|---|---|
| | | Before treatment | After treatment | Before treatment | After treatment | Before treatment | After treatment |
| Control group | 46 | 9.54± 1.54 | 7.95± 1.06 | 85.53± 12.69 | 99.64± 14.50 | 2.69± 0.43 | 3.70± 0.42 |
| Research group | 46 | 9.90± 1.30 | 7.01± 0.87 | 89.04± 10.42 | 109.75± 12.63 | 2.84± 0.37 | 4.55± 0.57 |
| P | | 0.229 | 0.000 | 0.151 | 0.001 | 0.076 | 0.000 |

### 2.4 两组治疗前后凝血功能比较

治疗前,两组凝血功能比较差异无统计学意义(P>0.05);治疗后,两组 Hct 及 PLT 均较治疗前明显上升,APTT 及 PT 均较治理前显著下降,且研究组 Hct 及 PLT 明显高于对照组,APTT 及 PT 显著低于对照组,差异均有统计学意义(P<0.05),见表 4。

表 4 两组治疗前后凝血功能的比较($\bar{x}\pm s$)

Table 4 Comparison of the blood coagulation function before treatment and after treatment between two groups ($\bar{x}\pm s$)

| Groups | n | Hct(%) | | PLT(× $10^9$/L) | | APTT(s) | | PT(s) | |
|---|---|---|---|---|---|---|---|---|---|
| | | Before treatment | After treatment | Before treatment | After treatment | Before treatment | After treatment | Before treatment | After treatment |
| Control group | 46 | 25.11± 3.27 | 36.82± 4.11 | 94.11± 12.79 | 131.20± 16.70 | 38.41± 4.86 | 30.12± 4.15 | 15.69± 2.21 | 12.51± 1.49 |
| Research group | 46 | 24.60± 3.80 | 41.45± 6.52 | 90.10± 13.46 | 148.92± 19.63 | 39.95± 4.12 | 28.77± 3.29 | 16.21± 1.80 | 10.88± 1.26 |
| P | | 0.492 | 0.000 | 0.147 | 0.000 | 0.105 | 0.087 | 0.219 | 0.000 |

### 2.5 两组并发症发生情况的比较

两组并发症以心悸、恶心及短期眩晕为主,组间并发症的发生率比较差异无统计学意义(P>0.05),见表 5。

表 5 两组并发症发生情况的比较[例(%)]

Table 5 Comparison the incidence of complications between two groups[n(%)]

| Groups | n | Heart | Nausea | Short-term vertigo | Occurrence rate |
|---|---|---|---|---|---|
| Control group | 46 | 3(6.52) | 5(10.87) | 3(6.52) | 12(26.09) |
| Research group | 46 | 1(2.17) | 3(6.52) | 4(8.70) | 8(17.39) |
| P | | 0.307 | 0.459 | 0.694 | 0.312 |

## 3 讨论

急性上消化道出血病情复杂,凝血功能异常为其严重并发症之一[9]。急性上消化出血可减少血容量,导致凝血因子直接丢失,增加内皮细胞受损,影响机体凝血机制,诱导纤溶亢进[10,11]。同时,由于组织灌注不足,引起无氧代谢增强并分泌大量乳酸,导致酸中毒,进一步加剧凝血功能障碍,增加临床治疗难度[12,13]。

快速控制出血是其治疗的关键,现代医学表明止血效果和胃内 PH 水平有着良好相关性,酸性环境能够影响血浆凝血功能及血小板聚集所起的止血机制,因此抑酸药物可发挥一定的止血效果[14]。质子泵抑制剂的抑酸效果持久,能够避免胃壁细胞内外钙离子及氢离子交换,减少其消失[15]。奥美拉唑属质子泵抑制剂的常用药物,可改善胃内酸性环境,利于纤维蛋白凝块及血小板聚集的形成,产生稳定血痂[16]。但临床研究报道[17]其长期使用可能会增加胃肠道不适,影响止血疗效。既往研究显示联合用药可通过其协同作用,在减少药物副反应的同时提高作用效果。止血芳酸能够改善外循环所致的血小板功能损伤,避免血小板数量减少,缩短血液凝固时间,控制出血。

生长抑素属人工环状十四肽氨基酸,其生理效应和天然生长抑素有较高的相似性,能够于消化道上皮黏膜中发挥选择性作用,利于内脏血管收缩,减少内脏出血[18];且可增加食管下段括约肌压力,诱导其静脉丛收缩,减少循环血量,并可一定程度的抑制胃液及胃酸分泌,保护胃黏膜细胞,避免胃内容物反流,进一步增加止血作用,预防再出血发生。陈新贵[19]等研究表明生长抑素在内脏出血控制方面作用明显,且安全性高。临床研究报道[20]生长抑制素加大剂量使用能够提高止血成功率。为进一步明确其临床效果,本研究在常规奥美拉唑联合止血芳酸基础上加以高剂量生长抑制素,结果显示高剂量组总有效率显著高于常规剂量组,且平均止血时间、再止血率及住院时间均较短,说明高剂量生长抑制素可提高临床效果,考虑与其大剂量应用能够增加药效,维持胃内较高 PH 状态,发挥有效的止血作用,避免剂量过小所致的再出血情况,从而增强血液凝固功能有关。但目前临床较少纳入实验室指标的观察,因此结果有待进步考察[21]。

血常规检查中, 白细胞增多提示机体可能伴有炎症反应[22]。Hb 是血液中最多数量的血细胞,其生理功能主要是运输氧气,Hb 及 RBC 含量降低可说明机体组织可能伴有缺氧或者贫血。大量研究证实[23,24]及时评估患者凝血功能状态能够反映病情进展及风险程度,有利于预后的改善,Hct、PLT、APTT 及 PT 为其常用指标。本研究结果显示两组治疗后血常规及凝血功能均有改善,但高剂量组改善更明显,说明其更能有效调节机体状态,改善凝血功能障碍,原因可能与药物剂量较大更能抑制胃酸及消化酶分泌,改善酸性环境,避免血小板活性受到抑制,纠正凝血功能障碍[25]。同时,本研究结果显示两组并发症均以心悸、恶心及短期眩晕为主,且未引起严重不良后果,说明加大药物剂量未明显增加药物副反应,安全性较好[26]。但本研究由于纳入样本量较小,结果可能存在一定偏差,有待更多临床试验证实。

综上所述,高剂量生长抑素、奥美拉唑联合止血芳酸治疗急性上消化道出血合并凝血功能障碍的效果明显优于常规剂量生长抑素、奥美拉唑联合止血芳酸治疗,期能够更有效缩短止血时间,避免再出血,且未增加药物不良反应,安全性高。

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