

doi: 10.13241/j.cnki.pmb.2016.32.026

# 内镜下喷洒蛇毒血凝酶与金属钛夹治疗不明原因消化道出血的临床疗效比较\*

王沁易<sup>1</sup> 刘哲<sup>2</sup> 张煦<sup>1△</sup> 张征<sup>1</sup> 李彦生<sup>1</sup>

(1 宝鸡市中医医院 消化内科 陕西 宝鸡 721000 2 延安大学附属医院 心血管内科 陕西 延安 716000)

**摘要** 目的 探讨内镜下喷洒蛇毒血凝酶与金属钛夹治疗不明原因消化道出血的临床疗效。方法 选取2013年8月至2015年12月本院收治的不明原因消化道出血患者82例,随机分为对照组和实验组,每组41例。对照组给予内镜下喷洒蛇毒血凝酶治疗,实验组给予金属钛夹止血治疗。观察两组患者经止血治疗后即时止血时间、外科手术率、输血量、症状消失时间和临床疗效、再出血率和出血量。结果 实验组即时止血率明显高于对照组,输血量低于对照组( $P < 0.05$ );实验组呕血消失时间、潜血转阴时间和引流液变清时间均小于对照组( $P < 0.05$ );实验组痊愈率、总有效率高于对照组( $P < 0.05$ );两组之间再出血率和出血量比较差异无统计学意义( $P > 0.05$ )。结论 金属钛夹较内镜下喷洒蛇毒血凝酶对不明原因消化道出血具有更好的临床疗效,且再出血率较低。

**关键词** 蛇毒血凝酶;金属钛夹;即时止血率;临床疗效;再出血率

中图分类号:R573.2 文献标识码:A 文章编号:1673-6273(2016)32-6309-04

## Comparison of the Clinical Efficacy of Endoscopic Spray Snake Venom and Metal Titanium Clip in the Treatment of Obscure Gastrointestinal Bleeding\*

WANG Qin-yi<sup>1</sup>, LIU Zhe<sup>2</sup>, ZHANG Xu<sup>1△</sup>, ZHANG Zheng<sup>1</sup>, LI Yan-sheng<sup>1</sup>

(1 Department of internal medicine, Baoji Hospital of traditional Chinese medicine, Baoji, Shaanxi, 721000, China;

2 Department of internal medicine, Yan'an University Affiliated Hospital, Yan'an, Shaanxi, 716000, China)

**ABSTRACT Objective:** To investigate the clinical efficacy of endoscopic spray snake venom and metal titanium clip in the treatment of obscure gastrointestinal bleeding. **Methods:** 82 patients with obscure gastrointestinal bleeding from August 2013 to December 2015 in our hospital were collected and randomly divided into the control group and the experimental group with 41 cases in each group. Patients in the control group were treated by endoscopic spray snake venom treatment; while patients in the experiment group were treated by metal titanium clip hemostatic treatment. The hemostatic instant hemostatic time, rate of surgery, blood transfusion amount, symptoms disappeared time and clinical efficacy were observed between two groups. **Results:** After treatment by the second solution, the instant hemostasis rate of experimental group was significant higher than that of the control group, the blood transfusion amount was lower than that of the control group ( $P < 0.05$ ); the hematemesis disappeared time, occult blood clearance time and drainage liquid cleared time of the experimental group were less than those of the control group ( $P < 0.05$ ); the cure rate and total effective rate of the experimental group were higher than those of the control group ( $P < 0.05$ ). No statistically significant difference was found in the bleeding rate and bleeding amount between two groups ( $P > 0.05$ ). **Conclusion:** Metal titanium clip had better clinical efficacy and lower bleeding rate than endoscopic spray snake venom in the treatment of obscure gastrointestinal bleeding.

**Key words:** Snake venom blood; Metal titanium clip; Instant hemostasis rate; Clinical efficacy; Rebleeding rate

Chinese Library Classification(CLC): R573.2 Document code: A

Article ID: 1673-6273(2016)32-6309-04

### 前言

不明原因消化道出血是指通过胃镜、结肠镜以及钡餐等检查后仍不能确定出血原因,存在反复、持续性发作的消化道出血<sup>[1]</sup>。临床分为不明原因隐性出血和不明原因显性出血,前者以缺铁性贫血和大便隐血阳性为主要特征,后者以肉眼可见血便、黑便以及呕血等为主要特征<sup>[2]</sup>。不明原因消化道出血占有消化道出血的5%左右,以胃肠道血管畸形导致的不明原因消

化道出血最为常见<sup>[3]</sup>,因其诊断困难,临床止血效果差而导致死亡率较高<sup>[4]</sup>。近年来,随着胶囊内镜以及双气囊小肠镜等内窥镜检查技术的发展,不明原因消化道出血的诊断和治疗水平明显提高<sup>[5]</sup>。内镜下喷洒蛇毒血凝酶和金属钛夹是治疗上消化道出血的常用治疗方案,临床操作技术已经成熟,其安全性及治疗有效率均较高<sup>[6]</sup>。但将内镜下喷洒蛇毒血凝酶和金属钛夹用于治疗不明原因消化道出血的报道却较为少见。因此,本研究通过观察内镜下喷洒蛇毒血凝酶和金属钛夹治疗不明原因消化

\* 基金项目 陕西省自然科学基金项目(1208085MC53)

作者简介:王沁易(1980-),女,硕士研究生,主治医师,研究方向:胃肠病、肝病、消化内镜下治疗等相关研究,电话:13379185440

△通讯作者:张煦(1982-),女,本科,主治医师,研究方向:急诊内科临床研究,电话:18591058298

(收稿日期:2016-06-15 接受日期:2016-06-30)

道出血患者,以明确两种治疗方案的临床疗效。

### 1 资料与方法

#### 1.1 临床资料

选择 2013 年 8 月至 2015 年 12 月于我院消化科以不明原因消化道出血为诊断收入院的患者 82 例,男性 40 例,女性 42 例,年龄(53.17± 7.16)岁,病程(12.11± 1.15)天。将 82 例患者根据随机数字表法随机分为实验组和对照组。其中,实验组 41 例,男性 20 例,女性 22 例,年龄(52.09± 7.55)岁,体重(65.69± 8.36)kg,病程(11.72± 1.18)天,不明原因隐性出血 30 例,不明原因显性出血 11 例;对照组 41 例,男性 20 例,女性 22 例,年龄(54.77± 6.11)岁,体重(66.02± 7.19)kg,病程(12.89± 1.13)天,不明原因隐性出血 32 例,不明原因显性出血 9 例。两组患者病程临床分型等一般情况无统计学差异(P>0.05),具有可比性。

纳入及排除标准 (1)参照 2005 年颁布的《现代消化道出血诊治指南》中关于不明原因消化道出血的诊断标准而拟定以下纳入标准:①患者均以黑便、便隐血阳性或吐血等出血的临床症状入院;②患者经胃镜、结肠镜以及消化道钡餐均未明确诊断出血病灶;③患者年龄为 18~75 岁之间;④患者近 1 周内未使用其他有关抗凝血或止血性药物;⑤患者自愿参与本研究,并签订知情同意书。(2)排除标准:①患者不符合诊断标准或纳入标准;②患者为恶性肿瘤导致的继发性出血;③患者同时伴有心、肝、肾等器官严重功能不全者;④妊娠期或哺乳期女性;⑤患者伴有血友病等凝血机制异常性疾病者;⑥对本研究所用蛇毒血凝酶存在过敏反应者。

#### 1.2 方法

严格参照 2005 年颁布的《现代消化道出血诊治指南》中关于不明原因消化道出血的常规治疗原则予以治疗,两组患者均在入院后完善相关入院检查,二级护理,避免辛辣饮食,少食多餐,食物以松软易消化为主,注意休息。失血量较大出现低血容量休克者及时予以扩容、输血、升高血压等抢救治疗,实时监测血压、心率等生命体征。予奥美拉唑口服防止应激性溃疡出现,治疗过程中出现其他并发症及时予以对症处理。

(1) 对照组:通过胃镜或直肠镜行内镜下喷洒蛇毒凝血酶

(邦亭,沈阳新马药业有限公司,批准文号:国药准字 H20030204)治疗,将 2U 蛇毒凝血酶以 50 mL 生理盐水稀释后,在内镜下喷洒于出血局部。

(2)实验组:予内镜下金属钛夹治疗。在内窥镜直视下找到出血病灶,经内镜钳道将推送器送出内镜前端,用金属钛夹将出血部位以及附近组织紧箍以阻断血液供应。

#### 1.3 观察指标及检测方法

1.3.1 即刻止血率、输血量和外科手术率 即刻止血成功判定标准:内镜下分别经两种方案止血治疗,在 5 min 即无活性性出血,以及患者查血常规可见血红蛋白计数持续性下降得到控制。

1.3.2 症状消失时间 两组患者经内镜治疗后,详细记录其引流液变清、呕血消失、潜血转阴的时间,以评价两种治疗方案对患者出血量的影响。

1.3.3 临床疗效 痊愈:患者 24 h 内引流液变清,吐血或黑便等临床症状消失,大便隐血阴性;显效:患者 24 h 内引流液变清,吐血或黑便等临床症状明显缓解,大便隐血弱阳性;有效:患者 24 h 内引流液仍未见清,但可在 72 h 内转清,吐血或黑便等临床症状好转,大便隐血仍可见阳性;无效:患者 72 h 后引流液仍为血性,呕血和(或)便血症状未见明显缓解或加重。

1.3.4 再出血情况和出血量 治疗结束一个月内对患者进行随访,并记录经治疗后出现再出血的例数以及出血量。再次出血判定标准:患者出现呕血、便血等症状,或大便隐血试验阳性,或血常规可见血红蛋白计数下降。

#### 1.4 统计学分析

所有数据经统计学软件 SPSS19.0 予以分析,症状消失时间、输血量和出血量等指标选取  $\bar{x} \pm s$  表示,检验方式采用 t 检验,治疗有效率、即刻止血率和外科手术率等指标用率表示,检验方式采用  $\chi^2$  检验,以 P<0.05 认定差异有统计学意义。

### 2 结果

#### 2.1 两组即刻止血率、输血量和外科手术率的比较

实验组即刻止血率高于对照组,输血量低于对照组(P<0.05);但两组外科手术率比较,差异无统计学意义(P>0.05)。见表 1。

表 1 两组患者即刻止血率、输血量和外科手术率的比较( $\bar{x} \pm s$ )

Table 1 Comparison of the immediate hemostasis rate, blood transfusion, and surgical rate between two groups( $\bar{x} \pm s$ )

Groups	n	Immediate hemostasis rate (n, %)	Surgical procedures rate (n, %)	Blood transfusion(mL)
Control group	41	35(85.37)	2(4.88)	383.88± 46.77
Experimental group	41	40(97.56)	1(2.44)	359.25± 50.11
$\chi^2/t$		4.352	1.621	2.301
P		0.036	0.073	0.024

#### 2.2 两组患者症状消失时间比较

实验组患者呕血消失时间、潜血转阴时间和引流液变清时间均短于对照组,差异具有统计学意义(P<0.05)。见表 2。

#### 2.3 两组患者临床疗效的比较

实验组患者痊愈率(39.02%)高于对照组(24.39%),总有效

率(97.56%)高于对照组(85.37%),无效率(2.44%)低于对照组(14.43%)(P<0.05)。见表 3。

#### 2.4 两组患者再出血情况和出血量比较

治疗后一个月内,对照组和实验组发生再出血例数分别为 2 例和 4 例,但两组再出血率及再出血量比较均无统计学差异

表 2 两组患者症状消失时间比较( $\bar{x} \pm s$ )Table 2 Comparison of the symptom disappearance time between two groups( $\bar{x} \pm s$ )

Group	n	Hematemesis disappear (h)	Occult blood clearance (d)	Drainage fluid becomes clear (d)
Control group	41	26.52± 4.05	3.75± 0.41	6.79± 1.93
Experimental group	41	23.18± 3.12*	2.51± 0.33*	3.57± 1.59*
t		4.183	15.086	7.989
P		0.003	0.017	0.042

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

表 3 两组患者临床疗效的比较(n,%)

Table 3 Comparison of the clinical curative effect between two groups(n,%)

Groups	n	Cure	Excellence	Effective	Invalid	Clinical effect rate
Control group	41	10(24.39)	12(29.27)	13(31.71)	6(14.43)	35(85.37)
Experiment group	41	16(39.02)	14(34.15)	10(24.39)	1(2.44)	40(97.56)
X <sup>2</sup>						3.905
P						0.048

(P>0.05)。

### 3 讨论

消化道出血包括上消化道出血和下消化道出血,两者之间以十二指肠悬韧带以区分,消化道出血一般通过胃镜、结肠镜以及钡剂透视即可明确出血部位并及时施以止血治疗<sup>[7]</sup>。但在消化道出血中约有5%患者经上述检查方法后仍不能明确出血原因和位置,被称为不明原因消化道出血<sup>[8]</sup>。不明原因消化道出血患者可见便血、呕血、大便隐血阳性或持续的血红蛋白水平下降,出血量较大时会危及患者生命,应当及时确定出血部位以及止血治疗<sup>[9]</sup>。随着内窥镜诊疗技术的发展,不明原因消化道出血的确诊率明显提高,所导致患者死亡率随之降低。蛇毒血凝酶是提取自蛇毒的具有凝血酶相似作用的有效成分,具有止血和抗凝的药理作用<sup>[10]</sup>,但其与金属钛夹在用于治疗不明原因消化道出血的临床疗效比较仍鲜见报道。

对于消化道出血的治疗,及时有效的止血治疗是挽救患者生命、提高疗效的关键。实验组患者即时止血率高于对照组,输血量小于对照组,差异有意义,但两组之间外科手术率无差异。实验组患者采用金属钛夹止血的治疗方案,通过金属钛夹在患者出血部位及其附近组织血管钳住,停止了相应血液供应,而对照组则是将蛇毒血凝酶通过内窥镜喷洒于出血部位,需要药物吸收入血后才能起到止血、凝血的药理作用。说明金属钛夹止血方式更简单直接,因此实验组即时止血率高于对照组,而对照组尚需一定输血。实验组呕血消失时间、潜血转阴时间和引流液变清时间均低于对照组,说明实验组止血疗效更优于对照组,且表3中实验组治疗疗效更优于对照组。结果提示对于呕血、吐血以及便血等有明显可见出血的患者,病情较急,需要即时止血的患者,可以采用金属钛夹止血,能在最短时间内达到有效止血的目的,最大程度挽救患者生命。而对于仅有便隐血阳性或血红蛋白略有下降的患者,病情较轻,可采取内镜下喷洒蛇毒以达到止血目的。

治疗后1个月内,两组之间再出血率虽无统计学差异,其原因可能与实验组为应用金属钛夹将出血部位以及附近组织血管钳住,通过压迫、收缩出血局部血管,形成血小板凝聚效应,达到止血目的<sup>[11-13]</sup>。这是因为金属钛夹会在一定时间内脱落并沿消化道随粪便排出体外,若金属钛夹提前脱落,出血部位并未完全愈合则会导致再次出血<sup>[14]</sup>。这可能是实验组再出血患者例数高于对照组原因,但两组之间并无统计学差异,其具体是否有影响还需大样本研究。而蛇毒血凝酶可通过直接水解纤维蛋白原,释放血纤肽A。此外,蛇毒血凝酶凝血的药理作用不受肝素影响<sup>[15]</sup>。因此,对于长期应用肝素导致的凝血机制下降、出血倾向者,可用蛇毒血凝酶治疗,但其疗效尚需进一步深入研究。

综上所述,金属钛夹治疗不明原因消化道出血较内镜下喷洒蛇毒血凝酶具有更好的临床疗效,且金属钛夹治疗方案具有更好的即时止血率和消除出血症状疗效。

#### 参考文献(References)

- [1] Rondonotti E, Marmo R, Petracchini M, et al. The American Society for Gastrointestinal Endoscopy (ASGE) diagnostic algorithm for obscure gastrointestinal bleeding: eight burning questions from everyday clinical practice [J]. Digestive and Liver Disease, 2013, 45(3): 179-185
- [2] Pioche M, Vanbiervliet G, Jacob P, et al. Prospective randomized comparison between axial-and lateral-viewing capsule endoscopy systems in patients with obscure digestive bleeding [J]. Endoscopy, 2014, 46(6): 479-484
- [3] Wang X, Liang H, Xu M, et al. Comparison between transsylvian-transinsular and transcortical-transtemporal approach for evacuation of intracerebral hematoma [J]. Acta Cirurgica Brasileira, 2013, 28(2): 112-118
- [4] Artigas J M, Martí M, Soto J A, et al. Multidetector CT angiography for acute gastrointestinal bleeding: technique and findings [J]. Radiographics, 2013, 33(5): 1453-1470

- [5] Ye L P, Zhang Y, Mao X L, et al. Submucosal tunneling endoscopic resection for small upper gastrointestinal subepithelial tumors originating from the muscularis propria layer[J]. *Surgical endoscopy*, 2014, 28(2): 524-530
- [6] Riccioni M E, Urgesi R, Cianci R, et al. Negative capsule endoscopy in patients with obscure gastrointestinal bleeding reliable: recurrence of bleeding on long-term follow-up [J]. *World J Gastroenterol*, 2013, 19(28): 4520-4525
- [7] Hylek E M, Held C, Alexander J H, et al. Major bleeding in patients with atrial fibrillation receiving apixaban or warfarin: The ARISTOTLE Trial (Apixaban for Reduction in Stroke and Other Thromboembolic Events in Atrial Fibrillation): Predictors, Characteristics, and Clinical Outcomes [J]. *Journal of the American College of Cardiology*, 2014, 63(20): 2141-2147
- [8] Haack A, Aragão G G, Novaes M R C G. Pathophysiology of cystic fibrosis and drugs used in associated digestive tract diseases[J]. *World Journal of Gastroenterology: WJG*, 2013, 19(46): 8552
- [9] Liu Y, Zhang H L, Zhang Y, et al. Digestive tract hemorrhage due to complications with gastrointestinal stromal tumor treated with sunitinib: A case report[J]. *Oncology letters*, 2013, 5(2): 699-701
- [10] Dicu D, Pop F, Ionescu D, et al. Comparison of risk scoring systems in predicting clinical outcome at upper gastrointestinal bleeding patients in an emergency unit[J]. *The American journal of emergency medicine*, 2013, 31(1): 94-99
- [11] Carbonero-Celis M J, Romero-Moriña H, Northrop-Sharp B, et al. Upper digestive tract hemorrhage in a child with heterotopic pancreas in a gastric diverticulum [J]. *Revista española de enfermedades digestivas: organo oficial de la Sociedad Española de Patología Digestiva*, 2013, 105(1): 54-55
- [12] Mönkemü ller K, Peter S, Toshniwal J, et al. Multipurpose use of the 'bear claw' (over the scope clip system) to treat endoluminal gastrointestinal disorders[J]. *Digestive Endoscopy*, 2014, 26(3): 350-357
- [13] Manta R, Galloro G, Mangiavillano B, et al. Over-the-scope clip (OTSC) represents an effective endoscopic treatment for acute GI bleeding after failure of conventional techniques [J]. *Surgical endoscopy*, 2013, 27(9): 3162-3164
- [14] Homma S, Suzuki A, Sato K. Pulmonary involvement in ANCA-associated vasculitis from the view of the pulmonologist [J]. *Clinical and experimental nephrology*, 2013, 17(5): 667-671
- [15] Zilberstein B, Jacob C E, Barchi L C, et al. Simplified technique for reconstruction of the digestive tract after total and subtotal gastrectomy for gastric cancer [J]. *ABCD. Arquivos Brasileiros de Cirurgia Digestiva (São Paulo)*, 2014, 27(2): 133-137

(上接第 6264 页)

- [7] American Diabetes A. Diagnosis and Classification of Diabetes Mellitus[J]. *Diabetes Care*, 2012, 35(Suppl 1): S64-S71
- [8] Tam LM, Kim J, Blumenthal RS, et al. Absolute coronary artery calcium score is the best predictor of non-calcified plaque involvement in patients with low calcium scores (1-100) [J]. *Atherosclerosis*, 2013, 230(1): 76-79
- [9] Han D, Lee JH, Hartaigh Bó , et al. Role of computed tomography screening for detection of coronary artery disease [J]. *Clinical Imaging*, 2016, 40(2): 307-310
- [10] McDermott MM, Liu K, Criqui MH, et al. Ankle-brachial index and subclinical cardiac and carotid disease: the multi-ethnic study of atherosclerosis[J]. *Am J Epidemiol*, 2005, 162(1): 33-41
- [11] Garcia M, Mulvagh SL, Bairey Merz CN, et al. Cardiovascular Disease in Women: Clinical Perspectives [J]. *Circ Res*, 2016, 118(8): 1273-1293
- [12] Chae CU, Derby CA. The menopausal transition and cardiovascular risk[J]. *Obstet Gynecol Clin North Am*, 2011, 38(3): 477-488
- [13] Kim C, Cushman M, Khodneva Y, et al. Risk of Incident Coronary Heart Disease Events in Men Compared to Women by Menopause Type and Race [J]. *Journal of the American Heart Association: Cardiovascular and Cerebrovascular Disease*, 2015, 4(7): e001881
- [14] Barrett-Connor E. Menopause, atherosclerosis, and coronary artery disease[J]. *Curr Opin Pharmacol*, 2013, 13(2): 186-191
- [15] Madhavan MV, Tarigopula M, Mintz GS, et al. Coronary artery calcification: pathogenesis and prognostic implications[J]. *J Am Coll Cardiol*, 2014, 63(17): 1703-1714
- [16] Alluri K, Joshi PH, Henry TS, et al. Scoring of coronary artery calcium scans: History, assumptions, current limitations, and future directions[J]. *Atherosclerosis*, 2015, 239(1): 109-117
- [17] Rodriguez-Granillo GA, Carrascosa P, Bruining N. Progression of coronary artery calcification at the crossroads: sign of progression or stabilization of coronary atherosclerosis? [J]. *Cardiovasc Diagn Ther*, 2016, 6(3): 250-258
- [18] Yeboah J, Young R, McClelland RL, et al. Utility of Nontraditional Risk Markers in Atherosclerotic Cardiovascular Disease Risk Assessment[J]. *J Am Coll Cardiol*, 2016, 67(2): 139-147
- [19] Tullios BW, Sung JH, Lee JE, et al. Ankle-Brachial Index (ABI), Abdominal Aortic Calcification (AAC), and Coronary Artery Calcification (CAC): the Jackson Heart Study [J]. *The international journal of cardiovascular imaging*, 2013, 29(4): 891-897
- [20] Criqui MH, McClelland RL, McDermott MM, et al. The ankle-brachial index and incident cardiovascular events in the MESA (Multi-Ethnic Study of Atherosclerosis)[J]. *J Am Coll Cardiol*, 2010, 56(18): 1506-1512
- [21] Hiramoto JS, Katz R, Ix JH, et al. Sex differences in the prevalence and clinical outcomes of subclinical peripheral artery disease in the Health, Aging, and Body Composition (Health ABC) study [J]. *Vascular*, 2014, 22(2): 142-148
- [22] Allison MA, Laughlin GA, Barrett-Connor E, et al. Association between the ankle-brachial index and future coronary calcium (the Rancho Bernardo study)[J]. *Am J Cardiol*, 2006, 97(2): 181-186