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内镜套扎术联合奥美拉唑、奥曲肽治疗食管静脉曲张出血的疗效及安全性

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摘要 目的:探究内镜套扎术联合奥美拉唑、奥曲肽治疗食管静脉曲张出血的疗效及安全性。方法:选取2014年5月至2016年5月于我院诊治的肝硬化合并食管静脉曲张出血患者127例,分为研究组和对照组。对照组在常规治疗的基础上予以奥美拉唑和奥曲肽治疗,研究组则在对照组基础上予以内镜下食管静脉曲张套扎术(EVL)治疗。分析比较两组患者的临床疗效、住院情况、不良反应的发生情况及治疗后再出血率。结果:研究组所有患者的均成功完成手术,未出现大出血情况,对照组有10例患者表现为呕血和黑便,其中1例患者转为手术治疗。治疗后,研究组的临床总有效率显著高于对照组($P<0.05$)。治疗期间,研究组的止血时间、输血量、住院天数和住院费用均显著少于对照组($P<0.05$),研究组和对照组分别有10例和7例患者出现了恶心呕吐、食管异物感、头昏、心悸、腹痛腹胀、大便次数增多和发热等不良反应,其中对照组的大便次数增多的发生率显著高于研究组($P<0.05$),而其余不良反应发生率和不良反应总发生率比较差异无统计学意义。治疗后1年随访时间内,无死亡患者,研究组在第0.5、1、3、6、12个月的再出血率均显著低于对照组($P<0.05$)。结论:内镜套扎术联合奥美拉唑、奥曲肽治疗食管静脉曲张出血的临床疗效明显,能够有效、快速止血,缩短住院天数,降低住院费用和再出血率,且安全性高。

关键词:食管静脉曲张出血;内镜套扎术;内镜下食管静脉曲张套扎术;奥美拉唑;奥曲肽;临床疗效

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The Efficacy and Safety of Endoscopic Esophageal Varix Ligation combined with Omeprazole and Octreotide in the Treatment of Esophageal Variceal Bleeding

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ABSTRACT Objective: To explore the efficacy and safety of endoscopic esophageal varix ligation (EVL) combined with omeprazole and octreotide in the treatment of esophageal variceal bleeding. **Methods:** 127 patients with cirrhosis complicated with esophageal variceal hemorrhage diagnosed and treated in our hospital from May 2014 to May 2016 were divided into the study group and the control group. The control group was treated with omeprazole and octreotide on the basis of conventional therapy, while the study group was treated with endoscopic esophageal variceal ligation (EVL) on the basis of control group. The clinical efficacy, hospitalization condition, incidence of adverse reactions and rebleeding rate after treatment of the two groups were analyzed. **Results:** All the patients in the study group were successfully operated. In the control group, 10 patients showed hematemesis and melena, among which 1 patient was treated with surgery. After treatment, the clinical efficacy of the study group was superior to the control group, and the difference was statistically significant ($P<0.05$). During the treatment period, the hemostasis time, blood transfusion time, hospital stay and hospitalization expenses of the study group were significantly lower than those of the control group ($P<0.05$). In the study group and the control group, 10 cases and 7 cases respectively had nausea and vomiting, esophageal foreign body sensation, dizziness, palpitations, pain, bloating, increased faeces frequency, fever and other adverse reactions, and the incidence of increased faeces frequency of control group was significantly higher than that of the study group ($P<0.05$), but the incidence of other adverse reactions and the total incidence showed no significant difference between two groups ($P>0.05$). The rate of rebleeding was significantly lower in the study group at 0.5, 1, 3, 6 and 12 months after treatment than those in the control group ($P<0.05$). **Conclusion:** Endoscopic ligation combined with omeprazole and octreotide was effective in the treatment of esophageal variceal bleeding, which could be effective, rapid hemostasis, reduce the hospital stay, hospitalization cost and rebleeding rate with high safety.

Key words: Esophageal variceal bleeding; Endoscopic ligation; EVL; Omeprazole; Octreotide; Clinical efficacy

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前言

食管静脉曲张是门脉高压形成与发展的最终结果,食管静脉曲张破裂出血是肝硬化门脉高压最严重的并发症之一,首次出血死亡率达到 50%-70%,反复出血发生率为 80%,致残率、病死率高,临床治疗效果不甚理想^[1-3]。药物止血是静脉曲张出血的一线治疗方法,而内镜下治疗已经成为了食管静脉曲张出血的主要治疗方法之一^[4]。研究表明内镜下治疗是降低食管静脉曲张破裂出血的死亡率的主要途径之一,内镜联合药物治疗更能够有效降低死亡率^[5]。内镜下静脉曲张套扎术(EVL)多用于中度和重度静脉曲张的患者,具有疗效好、安全性高、费用低、并发症少、可反复进行、住院周期短等诸多优点^[6]。本雅非主要根据我科的诊治经验,研究了内镜套扎术联合奥美拉唑、奥曲肽治疗食管静脉曲张出血的疗效及安全性,以及患者住院期间的输血量、住院天数和住院费用和治疗后的再出血率,以期对肝硬化并食管静脉曲张出血的治疗提供参考。

表 1 两组患者基本资料对比(n, $\bar{x} \pm s$)

Table 1 Comparison of the basic data between two groups (n, $\bar{x} \pm s$)

Groups	年龄(Age)	性别(Gender)		肝功能 Child-Pugh 分级(Child-Pugh Stage)			食管静脉曲张程度 (Esophageal varices degree)	
		男	女	A	B	C	中度	重度
Study group (n1=77)	48.3 $\pm$ 9.9	43	34	15	45	17	22	55
Control group (n2=50)	50.2 $\pm$ 7.5	28	22	13	25	12	18	32

1.2 治疗方法

所有患者静卧休息、禁食、留置胃管,予以吸氧、心电监护,再给予抗休克、扩充血容量、保肝、营养支持等治疗,酌情予以输血。在此基础上对照组予以注射用奥美拉唑钠(生产厂家:江苏奥赛康药业股份有限公司,国药准字 H20059053,规格:40 mg/ 瓶)和醋酸奥曲肽注射液(生产厂家:北京百奥药业有限责任公司,国药准字 H20061309,规格:0.1 mg/ 支)治疗,先醋酸奥曲肽 0.1 mg 溶于生理盐水 20 mL 后静脉注射,之后以醋酸奥曲肽 0.05 mg/h 持续泵入,使用 5 天,奥美拉唑 40 mg 溶于生理盐水 100 mL 后静脉滴注,一天 3 次,使用 7 天。

在对照组的治疗基础上,研究组再予以内镜下食管静脉曲张套扎术(EVL)治疗,在奥美拉唑、奥曲肽治疗 12h 后进行,术前做好配血和急救准备,术中采取心电监护。在内镜下选取需要套扎的食管曲张静脉部位,在突出于黏膜表面的静脉根部,用六连发套扎器(生产厂家:美国威尔逊-库克医学公司)从下到上螺旋式上升结扎,尽可能接近目标结扎点并使套扎器充分吸引,保证静脉彻底断流,若过程中发生出血,需在结扎点下方曲张处结扎止血。手术结束后,继续进行对照组的药物治疗 3 d,补充血浆、白蛋白以利套扎形成的静脉球脱落愈合,输液速度不能过快,量不宜过多。

治疗过程中严密观察患者的生命体征、三大常规、肝肾功、大便次数等,治疗结束后复查胃镜。

1.3 评价指标

1.3.1 临床疗效 记录每名患者的止血时间,并分为 3 个等

1 资料与方法

1.1 研究对象

研究对象选自 2014 年 5 月 -2016 年 5 月期间我科收治的肝硬化合并食管静脉曲张出血患者共 127 例。按照患者及家属的意见将患者进行分组,同意内镜治疗的患者选为研究组,共 77 例,不同意内镜治疗的患者则选为对照组,共 50 例。纳入标准:(1)经临床、影像学、电子胃镜等检查确诊为肝硬化、门静脉高压合并食管静脉曲张破裂出血,符合第八版《内科学》中相关诊断标准;(2)无上消化道胃镜检查禁忌证;(3)全身情况可耐受,知情同意本研究,可配合治疗。排除标准:(1)采用 EVL 治疗患者的静脉曲张直径粗大 >1.4 cm,出血性休克、食管狭窄、食管扭曲、食管穿孔等;(2)合并严重感染、血液系统疾病、严重心、脑、肺、肾功能不全。比较研究组与研究组患者的基本资料,差异无统计学意义($P>0.05$),表明两组研究对象的可比性高,见表 1。

级;无效:治疗 3 d 后出血无改善;有效:治疗 3d 内出血消失;显效:治疗 2 d 内出血消失。

1.3.2 住院情况 主要包括止血时间、输血量、住院天数、住院费用。

1.3.3 不良反应 详细记录患者在治疗期间的不良反应情况,计算不良反应发生率。

1.3.4 治疗后再出血率 对患者进行随访 1 年,复查胃镜,记录患者在治疗后第 0.5、1、3、6、12 个月的再出血率。

1.4 统计学分析

整理所有数据录入 SPSS 17.0 软件,数资料采用 χ^2 检验和 Mann-Whitney U 检验;计量资料以($\bar{x} \pm s$)表示,采用独立样本 t 检验,以 $P<0.05$ 为差异具有统计学意义。

2 结果

2.1 两组临床疗效的比较

研究组所有患者的手术均成功完成,未出现大出血情况,部分患者在手术中有微量渗血,药物喷洒处理后停止。对照组有 10 例患者表现为呕血和黑便,出血量 500-1400 mL,其中 1 例患者出血无法得到控制,转为外科手术治疗。治疗后,研究组总有效率为 97.4%,显著优于对照组(80%, $P<0.05$)。如表 2 所示。

2.2 两组住院情况的比较

治疗期间,研究组的止血时间、输血量、住院天数和住院费用均显著少于对照组($P<0.05$),如表 3 所示。

表 2 两组临床疗效比较

Table 2 Comparison on clinical effect of two groups

Groups	Ineffective	Effective	Obviously effective	Total effective rate
Study group(n1=77)	2	17	58	97.40%
Control group (n2=50)	10	18	22	80.00%

表 3 两组患者住院情况的比较($\bar{x} \pm s$)Table 3 Comparison of the hospitalization condition between two groups($\bar{x} \pm s$)

Groups	Hemostasis time (d) (止血时间, 天)	Blood transfusion amount (mL)(输血量, 毫升)	Hospitalization time (d) (住院天数, 天)	Hospitalization cost (yuan) (住院费用, 元)
Study group(n1=77)	1.3 $\pm$ 0.9*	168.8 $\pm$ 102.5*	21.4 $\pm$ 6.7*	9162.7 $\pm$ 823.5*
Control group (n2=50)	2.8 $\pm$ 1.3	410.5 $\pm$ 144.6	29.6 $\pm$ 5.9	14253.8 $\pm$ 568.4

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

2.3 两组不良反应发生情况的比较

治疗期间, 两组分别有 10 例和 7 例患者都出现了恶心呕吐、食管异物感、头昏、心悸、疼痛、腹胀、大便次数增多和发热等不良反应, 予以适当处理后均可缓解。其中对照组的大便次

数增多的发生率显著高于研究组($P < 0.05$), 而其余不良反应发生率和不良反应总发生率比较, 差异无统计学意义($P > 0.05$)。如表 4 所示。

表 4 两组患者不良反应发生率比较[n(%)]

Table 4 Comparison of the incidence of adverse reactions between two groups [n(%)]

Groups	Nausea, vomiting, esophageal foreign body sensation(恶心 呕吐、食管异物感)	Dizziness, palpitations(头 昏、心悸)	Pain, bloating (疼痛、腹胀)	Increased faeces frequency(大便 次数增多)	Fever(发热)	Others(其他)	Total incidence (总发生率)
Study group (n1=77)	4(5.19%)	3(3.90%)	6(7.79%)	2(2.60%)*	4(5.19%)	3(3.90%)	10(12.99%)
Control group (n2=50)	1(2.00%)	4(8.00%)	2(4.00%)	6(12.00%)	3(6.00%)	2(4.00%)	7(14.00%)

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

2.4 两组治疗后再出血率的比较

治疗后 1 年随访时间内, 无死亡患者, 研究组在第 0.5、1、

3、6、12 个月的再出血率均显著低于对照组 ($P < 0.05$)。如表 5 所示。

表 5 两组患者治疗后再出血率比较[例(%)]

Table 5 Comparison of the incidence of rebleeding after treatment between two groups [n(%)]

Groups	15 days after	1 month after	3 months after	6 months after	12 months after
Study group(n1=77)	11(14.29%)*	15(19.48%)*	13(16.88%)*	9(11.69%)*	12(15.58%)*
Control group (n2=50)	22(44.00%)	24(48.00%)	21(42.00%)	16(32.00%)	18(36.00%)

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

3 讨论

食管胃底静脉曲张是门脉高压持续作用的结果, 约有 95% 是由各种原因的肝硬化导致^[7]。门静脉高压导致门 - 体侧循环建立开放, 即门静脉系的胃左、胃短静脉与腔静脉系的奇静脉之间的胃底和食管粘膜下静脉开放。食管曲张静脉破裂出血通常出血量较大, 死亡率高, 且患者对于手术的耐受度较小^[8]。

内镜下静脉曲张套扎术是在内镜下用食管静脉曲张套扎器把安装在内镜头端的橡皮圈套扎在被吸入的曲张静脉上, 形成息肉状, 数天后自行脱落, 其目的是通过套扎曲张静脉阻断血流, 使曲张静脉消失或基本消失, 是现代治疗肝硬化食管静脉曲张主要而有效的手段^[9]。通过套扎术可以即时阻断曲张静

脉血流, 紧急止血, 随后套扎处静脉血栓形成、组织坏死、纤维化, 曲张静脉消失, 达到止血和减少再出血的作用^[10]。经套扎后局部组织形成浅溃疡, 随后逐渐被成熟的瘢痕组织取代。套扎术不会影响食管壁肌层, 不会使食管腔狭窄, 具有根除快、并发症少的特点, 但其最大的不足在于无法降低门静脉压力^[11,12]。生长抑素及其类似物用于治疗食管静脉曲张破裂出血是目前使用的药物中疗效最为确切的一种, 奥曲肽可以减少曲张静脉的血流量, 降低门脉压, 此外还能够增加食管下端括约肌张力, 抑制胃酸反流和胃蛋白酶分泌, 进一步促进止血^[13,14]。奥美拉唑作为质子泵抑制剂的代表药物, 能够通过强效抑制胃酸, 使患者的胃食管黏膜得到保护, 减少侵袭, 从而减少食管曲张静脉破损出血的发生^[15]。

一项 Meta 分析显示:与单独内镜下治疗相比,内镜联合药物治疗(奥曲肽、生长抑素等)能够提高止血率,而在死亡率或严重不良事件方面没有差异^[6]。本研究分析了内镜套扎术联合奥美拉唑、奥曲肽治疗食管静脉曲张出血的疗效及安全性,结果显示研究组所有患者的手术均成功完成,未出现大出血情况,部分患者在手术中有微量渗血,药物喷洒处理后停止。对照组有 10 例患者表现为呕血和黑便,出血量 500-1400 mL,其中 1 例患者出血无法得到控制,转为外科手术治疗。治疗后,研究组的止血时间和输血量均少于对照组,研究组的临床疗效优于对照组,可以更有效快速止血。治疗期间,且住院天数和住院费用均显著减少,患者恢复速度更快,更加经济、合理。治疗期间,研究组和对对照组分别有 10 例和 7 例患者都出现了恶心呕吐、食管异物感、头昏、心悸、疼痛、腹胀、大便次数增多和发热等不良反应,予以适当处理后均可缓解,两组的不良反应总发生率比较差异无统计学意义。套扎术治疗后患者可能会出现不同程度的胸骨后及上腹部疼痛,但多为一过性疼痛,持续 1-2 周后可自行消失,一般不需特殊处理,症状重者可适当应用一些镇静止痛药^[17-20]。

由于首次出血后的患者在 2 年中再出血的危险性为 80%,故应充分重视再出血的预防^[21-24]。内镜套扎术能阻断胃左静脉-食管静脉-腔静脉的出血侧支,但食管静脉血流阻断后胃冠状静脉及胃周围静脉丛血管扩张,血流增加,随时间延长复发率升高,故常需反复多次套扎巩固治疗^[25-27]。本研究中,治疗后 1 年随访时间内,无死亡患者,研究组在第 0.5、1、3、6、12 个月的再出血率均显著低于对照组。目前认为,EVL 是预防再出血的首选方法,但有较高的静脉曲张复发率,对细小曲张静脉治疗有一定困难^[28,29]。应当注意,在手术时需要从贲门齿状线开始套扎治疗,吸引适度、套扎,过早静脉球太小,橡皮圈易滑脱,过晚静脉球过大可能使静脉破裂引起大出血。

综上所述,内镜套扎术联合奥美拉唑、奥曲肽治疗食管静脉曲张出血的临床疗效明显,能够有效、快速止血,缩短住院天数,减少住院费用和再出血率,且安全性高。

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