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内镜下注射聚桂醇与组织胶治疗肝硬化食管胃底静脉曲张的疗效观察

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摘要 目的:探讨内镜下注射聚桂醇与组织胶治疗肝硬化食管胃底静脉曲张的疗效。**方法:**选择我院于2014年2月~2015年12月间收治的肝硬化食管胃底静脉曲张患者共88例,经随机数字表法将患者分为观察组及对照组各44例。给予观察组内镜下注射聚桂醇与组织胶治疗,给予对照组内镜下注射碘化油与组织胶治疗。统计两组患者手术中组织胶总用量,注射点数及平均每点组织胶用量。治疗14d后行胃镜检查,评价两组患者疗效,统计两组患者再出血、再出血死亡情况与不良反应情况。**结果:**观察组组织胶总用量、平均每点组织胶用量均低于对照组,差异均有统计学意义($P<0.05$);治疗6个月后观察组疗效总有效率高于对照组,差异均有统计学意义($P<0.05$)。两组注射点数、再出血发生率、再出血死亡率及并发症发生率比较无统计学差异($P>0.05$)。**结论:**经内镜下注射聚桂醇与组织胶治疗肝硬化食管胃底静脉曲张安全有效,治疗费用低,值得推广。

关键词: 内镜;聚桂醇;组织胶;肝硬化;食管胃底静脉曲张

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Esophageal and Gastric Varices in Patients with Liver Cirrhosis: Curative Effect of Endoscopic Injection of Polidocanol and Tissue Adhesive

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ABSTRACT Objective: To investigate the effect of endoscopic injection of Polidocanol and tissue adhesive on esophageal and gastric varices in patients with liver cirrhosis. **Methods:** A total of 88 patients with liver cirrhosis accompanied by esophageal and gastric varices, who were admitted to Affiliated Drum Tower Hospital of Medical College of Nanjing University from February 2014 to December 2015, were selected and randomly divided into observation group(n=44) and control group(n=44). The observation group was treated with endoscopic injection of Polidocanol and tissue adhesive, while the control group was treated with endoscopic injection of lipiodol and tissue adhesive. The total amount of tissue adhesive, the number of injection points and the average amount of tissue adhesive in the two groups were recorded. After 14 days of treatment, gastroscopy was performed. The efficacy of the two groups of patients was evaluated. The numbers of rebleeding, rebleeding mortality and adverse reactions in the two groups were analyzed. **Results:** The total amount of tissue adhesive and the average amount of tissue glue in the observation group were lower than those in the control group, the differences were statistically significant ($P<0.05$). The total effective rate of the observation group was higher than that of the control group 6 months after treatment, the difference was statistically significant ($P<0.05$). There were no significant differences in the number of injection points, rebleeding rate, rebleeding mortality and adverse reactions rate between the two groups($P>0.05$). **Conclusion:** Using endoscopic injection of Polidocanol and tissue adhesive to treat the patients with liver cirrhosis accompanied by esophageal and gastric varices has good safety, good curative effect and low treatment costs, which is worthy of clinical promotion.

Key words: Endoscopic; Polidocanol; Tissue adhesive; Liver cirrhosis; Esophageal and gastric varices

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前言

肝脏疾病起病隐匿,通常无明显的症状及体征,因此多数肝硬化患者在经确诊时已是中晚期,合并有多种并发症如感染、肝性脑病、腹水、食管胃底静脉曲张出血等,而食管胃底静脉曲张出血为肝硬化患者较为常见、较为严重的并发症之一,如不能及时进行救治可能导致患者死亡^[1,2]。研究表明,肝硬化

患者中发生食管胃底静脉曲张的几率为30~60%,胃静脉曲张较食管静脉曲张的发生率低,但其死亡率更高,导致患者死亡主要原因为未能较好控制出血与再出血^[3,4]。近些年随着医疗水平的提高,食管胃底静脉曲张出血的死亡率明显降低,但短期(6周)的死亡率仍高达15%-20%^[5]。目前对于食管胃底静脉曲张治疗方法主要有内科治疗、介入治疗、外科手术治疗及内镜治疗等^[6,7]。文献表明,聚桂醇与组织胶在治疗食管胃底静脉曲张中具有较显著的效果^[8]。本次研究中我院经内镜下注射聚桂醇与组织胶治疗肝硬化食管胃底静脉曲张,旨在为临床治疗肝硬化食管胃底静脉曲张提供参考。

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1 资料与方法

1.1 一般资料

选择我院于2014年2月~2015年12月间收治的肝硬化食管胃底静脉曲张患者共88例,纳入标准:均存在肝硬化病史,且既往多次出血;经电子胃镜检查并确诊为食管胃底静脉曲张;未经门脉高压介入治疗、未经内镜治疗者;排除标准:严重心、肝、肾等重要器官功能不全者;拒绝接受内镜治疗者;存在聚桂醇、组织胶禁忌症者;并发恶性肿瘤者。经随机数字表法将患者分为观察组及对照组各44例。观察组中男29例,女15例,年龄40~68岁,平均 (56.67 ± 6.54) 岁;肝脏储备功能Child-pugh分级中A级14例,B级15例,C级15例,对照组中男28例,女16例,年龄37~67岁,平均 (55.87 ± 6.79) 岁;肝脏储备功能Child-pugh分级中A级13例,B级16例,例C级15例,两组患者年龄、性别、Child-pugh分级比较差异无统计学意义($P>0.05$)。

1.2 物品准备

260系列电子胃镜(Olympus公司),23G内镜注射针(日本Olympus公司生产)。组织胶经北京瞬康医用胶有限公司生产,规格0.5mL/支。碘化油经上海旭东海普药业有限公司生产,规格为10mL/支。聚桂醇经陕西天宇制药有限公司生产,规格为10mL/支。

1.3 治疗方法

给予观察组内镜下注射聚桂醇与组织胶治疗,具体方法为:经内镜找到靶静脉注射点,通常选取静脉曲张突起最高点或活动性出血点或白色血栓或明显红色征附近进行注射。采用聚桂醇-组织胶-聚桂醇的"改良三明治"法^[9]静脉注射,确认靶点后预充聚桂醇,出针后按聚桂醇、组织胶、聚桂醇的顺序迅速注入血管。聚桂醇、组织胶的用量视患者曲张静脉瘤体的大小而定,通常注射1~3点,聚桂醇每点注射量10~20mL,每

次聚桂醇用量不超过40mL,每点注入组织胶0.5~3mL,栓塞注射部位,迅速退针后采用10%葡萄糖液5mL冲洗导管避免组织胶堵塞注射针,检查血管是否变硬,如果尚未变硬,则需重复注射,直至目标血管完全变硬。给予对照组内镜下注射碘化油与组织胶治疗,具体方法基本同观察组,确认靶点后预充碘化油,出针后按碘化油、组织胶、碘化油的顺序迅速注入血管。碘化油、组织胶的用量视患者曲张静脉瘤体的大小而定,通常注射1~3点。两组患者术后均常规禁食6~12h,两周内流质饮食,严密观察是否存在出血情况。

1.4 观察指标

统计两组患者手术中组织胶总用量,注射点数及平均每点组织胶用量。治疗14d后行胃镜检查,评价两组患者疗效,之后1、3、6个月再行胃镜复查。疗效评价标准^[9]:显效:静脉曲张基本或完全消失,无红色斑。有效:肉眼可见静脉曲张明显缓解,口径较细,存在数量较少的红色斑。无效:静脉曲张情况无明显改善,有大量红色斑,存在出血或渗血的情况。总有效率=(显效例数+有效例数)/总例数。术后随访3个月,统计两组患者再出血情况、再出血死亡情况与不良反应情况。

1.5 统计学方法

采用SPSS20.0软件对数据进行处理,计数资料由n(%)表示,两组数据比较经由 χ^2 检验,计量资料由 $(\bar{x} \pm s)$ 表示,两组比较经由t检验; $P<0.05$ 代表差异有统计学意义。

2 结果

2.1 两组组织胶总用量,注射点数及平均每点组织胶用量情况比较

观察组组织胶总用量、平均每点组织胶用量均低于对照组,差异均有统计学意义($P<0.05$);两组注射点数差异无统计学意义($P>0.05$)。见表1。

表1 两组组织胶总用量,注射点数及平均每点组织胶用量情况比较

Table 1 Comparison of total amount of tissue adhesive, the number of injection points and the average amount of tissue adhesive in the two groups

Groups	n	Total amount of tissue adhesive (mL)	Injection points (points)	Average amount of tissue adhesive (mL)
Observation group	44	1.54 $\pm$ 0.57	1.32 $\pm$ 0.42	1.09 $\pm$ 0.48
Control group	44	2.32 $\pm$ 0.65	1.37 $\pm$ 0.37	1.74 $\pm$ 0.56
t		10.864	1.075	10.612
P		0.000	0.283	0.000

2.2 两组患者疗效情况

治疗14d后、1月后、3月后两组患者疗效比较差异无统计学意义($P>0.05$);治疗6月后观察组疗效总有效率高与对照组,差异均有统计学意义($P<0.05$)。见表2。

2.3 两组患者再出血情况、再出血死亡情况与不良反应情况比较

观察组中发生再出血8例,再出血发生率为18.18%,其中排胶出血4例,食管静脉曲张再出血2例,胃底静脉曲张再出血1例,1例出血原因不明。再出血死亡1例,再出血死亡率为

2.27%。对照组中发生再出血9例,再出血发生率为20.45%,其中排胶出血4例,食管静脉曲张再出血1例,胃底静脉曲张再出血2例,2例出血原因不明。再出血死亡2例,再出血死亡率为4.55%。两组再出血发生率与再出血死亡率比较差异均无统计学意义($\chi^2=0.073$, $P=0.787$; $\chi^2=0.345$, $P=0.557$)。观察组术后随访出现发热2例,注射部位溃疡7例,并发症发生率为20.45%。对照组术后随访出现发热3例,注射部位溃疡9例,并发症发生率为27.27%。两组并发症发生率比较差异无统计学意义($\chi^2=0.563$, $P=0.453$)。

表 2 两组患者疗效情况[n(%)]

Table 2 Curative effect of the patients in the two groups [n (%)]

Groups	Time	n	Excellence	Effective	Invalid	Total effective rate
Observation group	14d after treatment	44	23	14	7	37(84.09)
	1 month after treatment	44	22	14	8	36(81.81)
	3 months after treatment	44	22	13	9	35(79.54)
	6 months after treatment	44	20	14	10	34(77.27)
Control group	14d after treatment	44	21	14	9	35(79.54)
	1 month after treatment	44	20	13	11	33(75.00)
	3 months after treatment	44	19	12	13	31(70.45)
	6 months after treatment	44	18	11	15	29(65.90) [#]

Note: compared with the observation group, [#]P<0.05.

3 讨论

食管、胃底静脉曲张均为肝硬化门脉高压症较为常见且严重的并发症^[10]。文献研究显示,食管静脉曲张首次出血患者的死亡率高达 30%以上,再出血发生率达 80%^[11,12]。胃底静脉曲张的发病率虽较食管静脉曲张低,但发生出血时其危险性更高,胃底静脉曲张存在诸多分支,血流速度较食管曲张更快,因此死亡率也高于食管静脉曲张^[13,14]。当上述两种情况同时发生则更难治疗,目前仍无统一的治疗方案。积极控制胃底食管静脉曲张,防止出血与再出血情况是目前延长肝硬化患者生存期的重要手段^[15]。内镜介入是目前国内外均较为普遍用于治疗胃底食管静脉曲张出血的方法,主要包括曲张静脉注射组织粘合剂、硬化注射术以及曲张静脉套扎术等^[16,17]。临床研究表明,硬化注射术以及曲张静脉套扎术的效果均不显著,内镜下注射组织胶为近几年普遍用于治疗胃底静脉曲张出血的首选的方法,术后止血率超过 90%^[18]。组织胶在治疗食管胃底静脉曲张中虽广泛使用,但在操作、安全性与随访预后等方面报道不一,因此,对于食管胃底静脉曲张的治疗与预防方案存在一定的争议^[19]。

本次研究中我院经内镜下注射聚桂醇与组织胶治疗肝硬化食管胃底静脉曲张,结果显示两组注射点数、再出血发生率、再出血死亡率及并发症发生率差异均无统计学意义($P>0.05$)。提示经内镜下注射聚桂醇与组织胶治疗与传统的治疗方案安全性相当。由于食管胃底静脉曲张通常出血量大,单纯的使用组织胶无法良好的闭塞出血血管,因此临床中很少单独使用组织胶进行治疗^[20]。临床中多采用“三明治”注射法,即注射针内两头均为油性物质,中间为组织胶粘合剂。聚桂醇为一种两性分子,可与细胞膜脂作用,使血管内皮细胞受损,进一步促进炎症反应造使血管腔粘连,达到阻塞血管的目的。通常在两周后肉芽组织形成取代静脉血栓,三个月左右肉芽组织机化,静脉周围凝固坏死的粘膜进一步纤维化,使静脉覆盖层增加,增强了曲张静脉的张力。这样可有效的改善曲张静脉,同时还可预防曲张静脉再形成,达到预防曲张静脉再出血及再形成的目的。观察组组织胶总用量、平均每点组织胶用量均低于对照组,差异均有统计学意义($P<0.05$)。以上结果表明,注射聚桂醇与组织胶治疗方案可降低组织胶总用量。聚桂醇的价格远

远低于组织胶价格,因此采用注射聚桂醇与组织胶治疗可减少医疗费用,这对于临床中药物的选择特别是对经济条件差的基层医院具有重要意义^[21]。确认靶点后预充聚桂醇,可避免堵塞内镜活检孔道,充当了碘化油的作用。聚桂醇起效时间较慢,而胃静脉曲张血流量及血流速度较大,因此不易闭塞^[22]。组织胶与血液作用时间较短,在数秒内即可聚合固化,因此,最后推注的聚桂醇则有充分的时间与血液进行相互作用。聚桂醇、组织胶的用量视患者曲张静脉瘤体的大小而定,通常注射 1~3 点,注射后检查血管是否完全变硬,保证注射点不出血,如果发生拔针出血的情况,应及时进行补充注射。本次研究受条件限制,随访时间最长的为六个月,未对食管胃底静脉曲张长期疗效及再出血情况进行随访观察,因此对于注射聚桂醇与组织胶治疗长期安全性是否可靠还需进一步研究。

综上所述,经内镜下注射聚桂醇与组织胶治疗肝硬化食管胃底静脉曲张安全有效,治疗费用低,值得推广。

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