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鱼肝油酸钠联合普萘洛尔对肝硬化消化道出血的疗效及 对应激反应的影响*

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摘要 目的:研究鱼肝油酸钠联合普萘洛尔对肝硬化消化道出血的疗效及对应激反应的影响。**方法:**选取2016年9月至2017年8月我院收治的83例肝硬化消化道出血患者,根据患者入院顺序先后分为观察组(n=43例)和对照组(n=40例)。对照组使用鱼肝油酸钠注射液,观察组联合普萘洛尔片。比较两组患者临床疗效,丙二醛(MDA)、超氧化物歧化酶(SOD)、血清胆碱酯酶水平,临床症状改善情况,止血和半年内再出血情况,不良反应。**结果:**治疗后,观察组临床有效率显著高于对照组($P<0.05$)。治疗前,两组患者MDA、SOD、胆碱酯酶水平比较差异($P>0.05$),治疗后,观察组的MDA水平低于对照组($P<0.05$),SOD、胆碱酯酶水平高于对照组($P<0.05$)。治疗前,两组患者心率、静脉压比较无差异($P>0.05$),治疗后,观察组的心率低于对照组($P<0.05$),静脉压高于对照组($P<0.05$)。观察组的止血时间和再出血率少于对照组($P<0.05$)。观察组的不良反应率低于对照组($P<0.05$)。**结论:**鱼肝油酸钠联合普萘洛尔能有效改善肝硬化消化道出血患者的应激反应和临床症状,临床疗效良好,安全性高。

关键词:鱼肝油酸钠;普萘洛尔;肝硬化;消化道出血;应激反应

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Effect of Sodium Morrhuate Sodium and Propranolol in Treatment of Liver Cirrhosis with Gastrointestinal Hemorrhage and Its Effect on Stress Response*

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ABSTRACT Objective: To study the effect of sodium morrhuate combined with propranolol on cirrhosis of gastrointestinal bleeding and its effect on stress response. **Methods:** Eighty-three patients with cirrhosis and gastrointestinal hemorrhage who were admitted to our hospital from September 2016 to August 2017 were selected, and divided into observation group (n=43) and control group (n=40) according to the order of admission. The control group used sodium morrhuate injection, and the observation group combined with propranolol tablets. Comparing the clinical efficacy of two groups of patients, malondialdehyde (MDA), superoxide dismutase (SOD), serum cholinesterase levels, improvement of clinical symptoms, hemostasis and re-bleeding within six months, adverse reactions. **Results:** After treatment, the clinical effectiveness of the observation group was higher than the control group ($P<0.05$). Before treatment, there was no significant difference in MDA, SOD and cholinesterase levels between the two groups ($P>0.05$). After treatment, the MDA level in the observation group was lower than the control group ($P<0.05$). The level of SOD, cholinesterase was higher than the control group ($P<0.05$). Before treatment, there was no significant difference in heart rate and venous pressure between the two groups ($P>0.05$). After treatment, the heart rate of the observation group was lower than the control group ($P<0.05$), and the venous pressure was higher than the control group ($P<0.05$). The hemostatic time and rebleeding rate in the observation group were less than those in the control group ($P<0.05$). The adverse reaction rate in the observation group was lower than the control group ($P<0.05$). **Conclusion:** The combination of sodium morrhuate and propranolol can effectively improve the stress response and clinical symptoms of patients with cirrhosis and gastrointestinal bleeding. The clinical efficacy is good and the safety is high.

Key words: Sodium morrhuate; Propranolol; Liver cirrhosis; Gastrointestinal hemorrhage; Stress

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前言

在临床中肝硬化属于较为常见的慢性进行性肝病, 主要因多种病因而引发的肝功能弥散性受损, 早期缺乏明显的临床特征, 晚期主要表现为消化道出血, 同时患者还会出现突发性呕血、黑便、血容量降低等症状^[1-3]。消化道出血会导致肝功能衰竭或出血性休克, 严重者会面临死亡, 可见, 如何快速有效的予以止血处理, 降低出血有关的并发症显得颇为重要^[4]。普萘洛尔在预防消化道出血中的效果良好, 鱼肝油酸钠是常见的血管硬化剂, 是鱼肝油中各种脂肪酸钠盐的灭菌水溶液。本文就鱼肝油酸钠联合普萘洛尔对肝硬化消化道出血的疗效及对应激反应的影响进行分析。

1 资料与方法

1.1 临床资料

选取 2016 年 9 月至 2017 年 8 月我院收治的 83 例肝硬化消化道出血患者。纳入标准: ①既往存在确切的肝硬化病史; ②通过胃镜检查发现胃底静脉曲张或食管破裂; ③均未进行过手术治疗或内镜下治疗。排除标准: ①严重肾功能障碍者; ②消化性溃疡及消化道肿瘤患者; ③精神障碍者。根据患者入院顺序先后分为观察组 (n=43 例) 和对照组 (n=40 例)。观察组中男性 26 例, 女性 17 例; 年龄为 34~67 岁, 平均 (52.43±4.87) 岁; 肝硬化病程为 1~6 年, 平均 (3.15±0.87) 年; 肝硬化 Child 分级: 31 例 B 级, 12 例 C 级。对照组中男性 23 例, 女性 17 例; 年龄为 32~65 岁, 平均 (51.87±4.92) 岁; 肝硬化病程为 1~7 年, 平均 (3.21±0.92) 年; 肝硬化 Child 分级: 29 例 B 级, 11 例 C 级。两组患者年龄、肝硬化病程等方面比较无差异 ($P>0.05$)。

1.2 方法

均对所有患者予以对症、支持、止血、抑酸等内科综合治疗, 择期开展硬化剂治疗。对照组使用鱼肝油酸钠完成治疗, 经常规胃镜对静脉曲张的程度、位置予以观察, 将鱼肝油酸钠注射液 (生产厂家: 上海信谊金朱药业有限公司, 规格: 0.1 g: 2 mL, 生产批号: 20160214) 作为硬化剂, 使用曲张静脉内注射法, 在

静脉出血点下方注射 5~15 mL 鱼肝油酸钠注射液, 数秒后, 再在此静脉选取第 2 个注射点予以注射, 静脉注射完毕后, 保持注射针和内镜原位不动, 留针 10 s, 随之把注射针退至鞘中, 胃镜朝食管前方推送 3~4 cm, 针孔压迫 3~5 min, 出血便可停止。观察组在对照组治疗基础上联合普萘洛尔片 (生产厂家: 江苏亚邦爱普森药业有限公司, 规格: 10 mg×100 s, 生产批号: 20160414) 完成治疗, 10 mg/天, 3 次/天, 口服, 剂量均根据患者心律、血压、耐受情况予以调整。所有患者均连续治疗 3 d。

1.3 观察指标

评价患者临床疗效, 治疗后, 患者体征、临床症状均完全消失, 并且在 24 h 内血压恢复至正常状态, 出血停止则为显效; 患者体征、临床症状均呈现出显著好转, 治疗后 72 h 内血压趋于正常, 并且消化道出血有所控制则为有效; 患者体征、临床症状、血压、出血等指标均未获得改善, 治疗后 72 h 以上消化道依然持续出血则为无效^[5]。总有效 = 显效 + 有效。

分析两组患者治疗前、治疗 3 天后丙二醛 (MDA)、超氧化物歧化酶 (SOD)、血清胆碱酯酶水平, 分别在治疗前和治疗 3 天后收集两组患者 5 mL 空腹静脉血, 转速 1500 r/min, 离心 15 min, 离心半径 18 cm, 提取上层血清待测, 使用日立 7150 型生化自动分析仪及相关配套试剂盒检测 MDA、SOD、血清胆碱酯酶水平, 均根据试剂盒和仪器说明书完成本次操作。分析两组患者治疗前、治疗 3 天后心率、静脉压改善情况。比较两组患者止血时间和半年内再出血情况。分析两组患者不良反应。

1.4 统计学处理

本次实验数据用 spss11.5 软件包予以分析, 计量资料用均数±标准差 ($\bar{x} \pm s$) 表示, 组间比较行 t 检验, 计数资料和等级资料用 [n(%)] 表示, 组间比较采取 χ^2 检验, 临床疗效分析行秩和检验, $P<0.05$ 表明差异有统计学意义。

2 结果

2.1 临床疗效分析

治疗后, 观察组临床有效率高于对照组 ($P<0.05$), 见表 1。

表 1 临床疗效分析[n(%)]
Table 1 Clinical efficacy analysis[n(%)]

Groups	Remarkable effect	Effective	Invalid	Total effective
Observation group (n=43)	33 (76.74)	7 (16.28)	3 (6.98)	40 (93.02)
Control group (n=40)	13 (32.50)	15 (37.50)	12 (30.00)	28 (70.00)
u/ χ^2 value		u=4.062		$\chi^2=7.419$
P value		P=0.000		P=0.007

2.2 应激反应分析

治疗前, 两组患者 MDA、SOD、胆碱酯酶水平比较无差异 ($P>0.05$), 治疗后, 两组患者 MDA 水平低于治疗前 ($P<0.05$), SOD、胆碱酯酶水平高于治疗前 ($P<0.05$), 观察组的 MDA 水平低于对照组 ($P<0.05$), SOD、胆碱酯酶水平高于对照组 ($P<0.05$), 见表 2。

2.3 两组患者临床症状改善情况分析

治疗前, 两组患者心率、静脉压比较无显著差异 ($P>0.05$), 治疗后, 两组患者心率较治疗前显著降低 ($P<0.05$), 静脉压较治疗前显著上升 ($P<0.05$), 其中观察组的心率低于对照组 ($P<0.05$), 静脉压高于对照组 ($P<0.05$), 见表 3。

2.4 止血时间和再出血情况分析

观察组的止血时间和再出血率显著少于对照组 ($P<0.05$), 见表 4。

表 2 应激反应分析($\bar{x} \pm s$)
Table 2 Stress response analysis($\bar{x} \pm s$)

Groups	MDA(nmoL/L)		SOD(U/mL)		Cholinesterase(U/L)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group (n=43)	63.43± 6.81	29.54± 2.31	26.54± 2.41	44.87± 4.32	3241.45± 314.566	886.43± 671.32
Control group (n=40)	64.04± 6.87	38.75± 3.54	27.87± 2.53	36.04± 3.61	3253.76± 316.03	4135.78± 451.43
t value	0.406	14.133	2.453	10.064	0.178	21.738
P value	0.689	0.000	0.016	0.000	0.859	0.000

表 3 两组患者临床症状改善情况分析($\bar{x} \pm s$)
Table 3 Analysis of the improvement of clinical symptoms in the two groups($\bar{x} \pm s$)

Groups	HR(Times/min)		Venous pressure(cmH ₂ O)	
	Before treatment	After treatment	Before treatment	After treatment
Observation group(n=43)	113.43± 13.55	76.43± 7.35	3.32± 0.31	6.81± 0.69
Control group(n=40)	115.08± 14.14	97.43± 9.81	3.38± 0.38	4.14± 0.48
t value	0.543	11.087	0.791	20.320
P value	0.589	0.000	0.432	0.000

表 4 止血时间和再出血情况分析
Table 4 Analysis of hemostasis time and rebleeding

Groups	Hemostasis time(h)	Rebleeding
Observation group(n=43)	17.84± 2.05	2
Control group(n=40)	25.54± 3.12	9
t/ χ^2 value	13.377	5.743
P value	0.000	0.000

2.5 不良反应分析

所有患者在治疗后主要表现为腹水消退、白蛋白上升,治疗过程中有个别患者伴有胸痛、高热等症状,但均属于轻微型,经对症处理或停药后均有所缓解。在对照组中 5 例患者出现腹水价值,观察组中无腹水加重情况,两组患者腹水加重率比较具有差异性($P < 0.05$)。

3 讨论

肝硬化消化道出血发生的危险因素主要有门静脉压和腹腔内压升高而导致曲张静脉破裂,饮食习惯不良易导致曲张静脉受破,肝功能较差时在使用对胃黏膜会造成损伤的药物会给曲张的食管胃底静脉造成损害,情绪不良及过度劳累也会导致消化道出血^[6-9]。当前在治疗肝硬化消化道出血中主要以药物治疗为主,然而药物种类较多,疗效也有一定差异性,近年来在治疗肝硬化消化道出血中提出联合用药,以此提高临床疗效^[10-13]。

在预防和治疗肝硬化消化道出血中主要以药物治疗和硬化剂注射治疗为主,其中单硝酸异山梨酯和 β -受体阻滞剂是较为常见的药物^[14-17]。相关研究显示,相对于单纯硬化剂注射治疗,单纯使用普萘洛尔等非选择性 β -受体阻滞剂,其 1~2 年的再出血率较高,在预防消化道出血中经单纯的普萘洛尔治疗,

已逐渐被硬化剂注射所代替^[18-23]。鱼肝油酸钠属于血管硬化剂,注射至黏膜下,能导致局部组织出现无菌性坏死,随之逐渐被纤维结缔组织所取代,鱼肝油酸钠不会直接影响凝血,但和钙离子有亲和力,从而形成钙皂,使得内源性凝血机制受到激活,提升血液凝结速度^[24-27]。鱼肝油酸钠也会损伤静脉内膜的内皮细胞,促使静脉腔内形成混合血栓,有助于止血,同时能诱导血小板聚集,封堵受损的血管裂口,放缓血液流速,在一般创口及黏膜创口中能发挥止血效果^[28-31]。但在使用硬化剂过程中易出现腹水加重情况。本次研究结果显示,经单纯鱼肝油酸钠治疗后出现腹水加重的患者有 5 例,可能是因为注射硬化剂后门静脉血流上升,因此有必要联合能降低门静脉压力的药物进行治疗。普萘洛尔在心脏 β_1 受体中能发挥较强的阻断作用,能降低心率,减弱心肌收缩力,降低心肌自律性,使有效不应期延长,放慢传导速度,减少心输出量,增加外周阻力,减少门静脉血流,进而降低门脉压力。本次研究结果显示,鱼肝油酸钠联合普萘洛尔治疗者在半年内的再出血率显著低于单纯鱼肝油酸钠治疗者,同时联合治疗中无腹水加重情况发生,在某种程度上解决了单纯硬化剂会增加门静脉血流而导致腹水这一情况。

肝硬化患者伴有门静脉高压症,门静脉高压症高动力形成很大程度上和内脏动脉在血管收缩物质中的反应性有关,其中

肝硬化门静脉高压症患者伴有高氧化应激,MDA 水平显著上升^[32-35]。肝硬化患者伴有较低的胆碱酯酶水平,并且和病情显著有关,因此肝硬化病情及预后和胆碱酯酶水平有关,能有效评估疗效及预后。本次研究结果显示,肝硬化消化道出血患者经鱼肝油酸钠联合普萘洛尔治疗后,MDA 水平显著降低,SOD、胆碱酯酶水平显著上升,且改善效果优于单纯鱼肝油酸钠治疗者,提示联合治疗更能有效改善患者氧化应激反应。除此之外,联合治疗者心率、静脉压获得显著改善,提示联合治疗能有效改善患者临床症状,临床疗效良好。

总之,鱼肝油酸钠联合普萘洛尔能有效改善肝硬化消化道出血患者的应激反应和临床症状,临床疗效良好,安全性高。

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