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生长抑素联合双歧杆菌四联活菌治疗急性胰腺炎的效果及对肠粘膜屏障功能的影响 *

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摘要 目的:探究生长抑素联合双歧杆菌四联活菌治疗急性胰腺炎的效果及对肠粘膜屏障功能的影响。**方法:**选取 2015 年 8 月~2018 年 8 月我院收治的急性胰腺炎患者 98 例,根据患者入院先后顺序分为两组。对照组患者给予生长抑素治疗,观察组在对照组的基础上联合双歧杆菌四联活菌片治疗。比较两组患者的临床治疗效果,临床症状和指标的恢复时间及胃肠动力的恢复情况,治疗前后 D-乳酸、二胺氧化酶(DAO)和尿乳果糖和甘露醇的比值(L/M)水平的变化。**结果:**治疗后,观察组患者的总有效率显著高于对照组($P<0.05$),腹痛、腹胀、腹膜刺激征、血淀粉酶和尿淀粉酶恢复正常时间均显著短于对照组($P<0.05$)。治疗后,两组患者的血清 D-乳酸、DAO 和 L/M 水平均较治疗前显著下降,且观察组以上指标均显著低于对照组($P<0.05$)。此外,观察组患者的腹内压显著低于对照组,肠鸣音恢复时间显著短于对照组,胃肠减压引流量显著低于对照组($P<0.05$)。**结论:**与单用生长抑素相比,生长抑素联合双歧杆菌四联活菌可更迅速缓解急性胰腺炎患者的临床症状及指标,恢复胃肠动力,并显著改善患者的肠粘膜屏障功能,利于患者的康复。

关键词:生长抑素;双歧杆菌四联活菌;急性胰腺炎;肠粘膜屏障功能

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Clinical Efficacy of Somatostatin Combined with Bifidobacteria Tetraploid Live Bacteria in the Treatment of Acute Pancreatitis and Its Effect on the Intestinal Mucosal Barrier Function*

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ABSTRACT Objective: To investigate the efficacy of somatostatin combined with bifidobacteria tetraploid live bacteria in the treatment of acute pancreatitis and its effect on the intestinal mucosal barrier function. **Methods:** 98 cases of patients with acute pancreatitis admitted to our hospital from August 2015 to August 2018 were selected and divided into two groups according to the order of admission. The control group was given somatostatin, and the observation group was treated with bifidobacteria tetraplactis tablets on the basis of control group. The clinical treatment effect, clinical symptoms and indicators recovery time, gastrointestinal motility recovery, changes of D-lactic acid, DAO and L/M levels before and after treatment were compared between the two groups. **Results:** After treatment, the total effective rate of observation group was significantly higher than that of the control group ($P<0.05$). Patients in the observation group had significantly shorter recovery time for abdominal pain, abdominal distension, peritoneal irritation, blood amylase and urine amylase than those in the control group ($P<0.05$). After treatment, the serum D-lactic acid, DAO and L/M levels in both groups were significantly lower than those before treatment, and the above indicators in the observation group were significantly lower than those in the control group ($P<0.05$). In addition, the intra-abdominal pressure of patients in the observation group was significantly lower than control group, the recovery time of intestinal rumble was significantly shorter than control group, and the drainage volume of gastrointestinal decompression was significantly lower than control group ($P<0.05$). **Conclusion:** Compared with somatostatin alone, Somatostatin combined with bifidobacterium tetrabalone can more quickly relieve the clinical symptoms and indicators of patients with acute pancreatitis, restore the gastrointestinal motility and significantly improve the intestinal mucosal barrier function, which is conducive to the recovery of patients.

Key words: Somatostatin; Bifidobacteria tetraploid live bacteria; Acute pancreatitis; Intestinal mucosal barrier function

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前言

急性胰腺炎是消化系统常见的急腹症之一,是由于多种因素引起的胰酶激活而形成水肿、出血甚至坏死的局部炎症反应[1,2]。该病临床差异较大,多数患者为轻型,预后较好,约有15%~20%的患者发展为重型,可引起多器官功能衰竭等并发症,甚至死亡[3,4]。近年来,急性胰腺炎的发病率显著上升,死亡率约为10%,且几乎所有的死亡病例均为首发,严重危威胁患者的生命和健康[5]。

急性胰腺炎的发病机制复杂,与胆道疾病、酗酒和暴饮暴食等因素有关。正常情况下,机体有多重机制保护胰腺功能正常,当这种正常的防御功能遭到破坏时,胰酶增加、感染和胰管阻塞可引起胰液对胰腺和周围组织进行自身消化,进而引发胰腺炎[6-8]。大部分学者认为炎症、肠粘膜上皮过度凋亡、肠道功能紊乱等在胰腺炎的发生和发展过程中具有重要作用。该病的治疗不单是对于胰腺的局部治疗,更是对患者整体生理功能的维护[9-11]。生长抑素可减少胰腺的内外分泌,具有保护胰腺细胞的作用[12,13]。双歧杆菌四联活菌具有调节肠道菌群的作用,可提高肠道粘膜的防御功能。两者对于急性胰腺炎均具有较好的治疗作用,但关于二者联合用药的研究较少[14,15]。本研究主要题图了生长抑素联合双歧杆菌四联活菌治疗急性胰腺炎的临床效果和安全性,结果报道如下。

1 资料和方法

1.1 一般资料

选择我院2015年8月~2018年8月收治的急性胰腺炎患者98例,纳入标准:① 经临床检查和影像学检查确诊;② 发病后48h内入院;③ 知情同意并签署同意书;④ 入组前未经过治疗者。排除标准:① 合并消化性溃疡、肠穿孔及急性肠炎;② 有慢性胰腺炎病史;③ 合并胰腺其他疾病;④ 合并其他感染性疾病及其他功能障碍。根据患者入院先后顺序将患者分为两组,对照组50例,男28例,女22例;年龄35~68岁,平均59.32± 5.14岁;病程3~18h,平均9.58± 2.54h;其中胆源性27例,酒精性16例,脂肪源性7例;观察组48例,男27例,女21例;年龄34~66岁,平均58.56± 5.02岁;病程3~19h,平均9.97± 2.64h;其中胆源性25例,酒精性17例,脂肪源性6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

患者均给予禁食、持续胃肠减压、营养支持、纠正酸碱平衡和抑制胰酶分泌等常规对症治疗。对照组患者给予生长抑素(海南中和药业股份有限公司,国药准字H 20034150,3 mg)进行治疗,取6 mg生长抑素加入生理盐水中以250 μg/h的速度24小时持续微泵泵入。观察组在对照组的基础上联合双歧杆菌四联活菌片(杭州远大生物制药有限公司,国药准字S20060010,0.5 g)治疗,1.5 g水化后采用胃导管进行灌注,夹管2 h,3次/d。两组患者均连续治疗1周。

1.3 观察指标

① 治疗效果,显效:症状消失,血和尿淀粉酶恢复正常;有效:临床症状基本消失,血和尿淀粉酶基本恢复正常;无效:临床症状、血和尿淀粉酶未达到上述标准或加重需转手术治疗。② 临床症状及指标恢复时间,包括腹痛、腹胀、腹膜刺激征、血淀粉酶和尿淀粉酶。③ 血清D-乳酸、二胺氧化酶(DAO)和尿乳果糖甘露醇的比值(L/M)水平:分别于治疗前后采集两组患者的空腹静脉血3 ml,采用UV2800紫外分光光度计(上海舜宇恒平科学仪器有限公司生产)对D-乳酸和DAO水平进行测定,采用Alliance2695高效液相色谱仪(美国Waters公司生产)对(L/M)水平进行测定。④ 胃肠动力恢复情况,包括腹内压、肠鸣音恢复时间和胃肠减压引流量。

1.4 统计学方法

使用SPSS16.0对采集的数据实施分析,计数资料以率(%)的形式表示,组间比较采用卡方检验,计量资料以($\bar{x}\pm s$)的形式表示,组间比较采用t检验,以$P<0.05$为差异有统计学意义。

2 结果

2.1 两组患者临床治疗效果的比较

治疗后,观察组患者的总有效率显著高于对照组(97.92% vs. 80%,$P<0.05$),见表1。

表1 两组患者临床治疗效果的比较[例(%)]

Table 1 Comparison of the clinical therapeutic effect between two groups [n(%)]

Groups	Cases	Excellent	Valid	Invalid	Total effective rate
Control group	50	23(46.00)	19(38.00)	8(16.00)	42(80.00)
Observation group	48	35(72.92)	12(25.00)	1(2.08)	47(97.92)
x^2	-				5.687
P	-				0.031

2.2 两组患者临床症状及指标恢复时间的比较

观察组患者腹痛、腹胀、腹膜刺激征、血淀粉酶和尿淀粉酶恢复正常时间均显著短于对照组($P<0.05$),见表2。

2.3 两组治疗前后血清D-乳酸、DAO和L/M水平的比较

治疗前,两组患者的血清D-乳酸、DAO和L/M水平比较无统计学差异($P>0.05$),治疗后,两组血清D-乳酸、DAO和L/M水平均较治疗前显著下降,且观察组以上指标均显著低于对照组($P<0.05$),见表3。

2.4 两组患者的胃肠动力恢复情况的比较

观察组患者的腹内压显著低于对照组,肠鸣音恢复时间显著短于对照组,胃肠减压引流量显著低于对照组(P<0.05),详见表4。

表 2 两组患者临床症状及指标恢复时间的比较($\bar{x}\pm s$,d)

Table 2 Comparison of the recovery time of clinical symptoms and indicators between two groups($\bar{x}\pm s$, d)

Groups	Cases	Stomachache	Ventosity	Peritoneal irritation	Blood amylase	Urine amylase
Control group	50	4.25± 1.02	3.31± 0.87	4.12± 1.04	6.51± 1.85	8.79± 2.13
Observation group	48	2.55± 0.62	1.58± 0.41	1.77± 0.48	4.21± 1.05	6.42± 1.12
t	-	10.015	12.671	14.454	7.607	6.933
P	-	＜0.001	＜0.001	＜0.001	＜0.001	＜0.001

表 3 两组患者治疗前后的血清 D- 乳酸、DAO 和 L/M 水平的比较($\bar{x}\pm s$)

Table 3 Comparison of the serum D-lactic acid, DAO and L/ M levels between two groups before and after treatment($\bar{x}\pm s$)

Groups	Cases	D-lactic acid(μg/mL)		DAO(U/mL)		L/ M	
		Before treatment	Aftertreatment	Before treatment	Aftertreatment	Before treatment	Aftertreatment
Control group	50	11.52± 3.36	8.55± 2.13*	5.77± 1.55	3.55± 0.98*	0.44± 0.09	0.25± 0.41*
Observation group	48	10.98± 3.02	7.18± 2.04*	5.84± 1.62	2.87± 0.81*	0.47± 1.02	0.10± 0.22*
t	-	0.836	-3.249	-0.219	-3.736	-0.203	2.269
P	-	0.405	0.002	0.827	＜0.001	0.840	0.026

注：与治疗前相比，*P＜0.05。

Note: Compared with before treatment, *P＜0.05.

表 4 两组患者的胃肠动力恢复情况的比较($\bar{x}\pm s$)

Table 4 Comparison of the recovery of gastrointestinal motility between two groups($\bar{x}\pm s$)

Groups	Cases	Intra-abdominal pressure(cmH_2O)	Bowel sounds recovery time(h)	Gastrointestinal decompression drainage(mL/d)
Control group	50	13.52± 3.64	15.02± 3.21	678.59± 135.47
Observation group	48	9.12± 2.85	10.03± 2.87	612.25± 125.32
t	-	6.677	8.101	2.514
P	-	＜0.001	＜0.001	0.014

3 讨论

完整的肠道粘膜屏障功能对于维持机体的内环境稳定和预防疾病的发生具有重要的意义，急性胰腺炎患者的肠粘膜屏障受损导致肠腔内的有害物质通过肠粘膜进入血液，引起细菌移位至各个器官组织，进一步加重病情并影响预后，是多脏器功能衰竭的主要原因，已越来越受到临床的重视[16-18]。研究显示菌群失调、炎性刺激、缺血再灌注和肠道动力障碍等是导致肠粘膜屏障功能损害的重要原因[19,20]。故对于急性胰腺炎治疗的关键是对于肠道粘膜屏障的保护，并调整内环境的稳定和循环功能[21]。

D 乳酸是肠道细菌产生的一种物质，急性胰腺炎患者的肠道粘膜通透性增加，D- 乳酸由肠道进入血液循环而使得其在外周血中的浓度增加，其水平可反映肠道粘膜通透性的变化[22,23]。DAO 主要存在于小肠粘膜及纤毛的上皮细胞中，当肠粘膜脱落时进入血液，在外周血中的水平升高，可反映肠粘膜的受损情况[24]。乳果糖主要经肠道吸收，甘露醇经细胞膜吸收，当肠道粘膜屏障遭到破坏时，其通透性增加，使得乳果糖的吸收增加，导致 L/M 水平升高[25]。本研究结果显示观察组患者治疗后的血清 D- 乳酸、DAO 和 L/M 水平均显著低于对照组，说明生长抑素联合双歧杆菌四联活菌可降低患者肠粘膜通透性，显著改善患者肠粘膜损伤，增强患者的肠粘膜屏障功能。双歧杆菌四联活菌由多种益生菌组成，可促进有益菌在肠道定植，恢复肠道菌群正常的结构，并在肠道表面形成一层生物膜，减少了细菌和毒素的吸收，从而提高患者的肠道粘膜屏障功能有关[26,27]。生长抑素可促进蛋白合成，纠正患者体内的负氮平衡，减轻对各器官的损伤，维持肠道粘膜的正常形态与结构，还能够改善患者的细胞功能，减轻胰腺水肿，促进肠道内皮细胞的愈合，从而减少了毒素对肠粘膜屏障的损害[28,29]。两者联合应用对患者肠道粘膜的屏障功能的恢复效果更好。

急性胰腺炎患者的炎症反应参与了胃肠动力障碍的发生和发展，同时缺血、缺氧是加重肠道动力障碍的重要原因[30]。本研究结果显示联合用药可显著改善患者的胃肠动力。双歧杆菌四联活菌还可以提肠道粘膜的防御功能，激发机体的免疫力，促进维生素的合成，进一步改善患者的肠道动力的恢复。生长抑素可促进机体的炎症和抗炎反应处于较低水平的平衡，进而提高患者的胃肠动力。另外生长抑素可抑制迷走神经的兴奋性并有效降低血流量，减少胰腺胰酶的分泌，对炎症起到延缓的作用[31]。两者联合应用对于患者胃肠动力的恢复效果更好。本研究中，联合用药的患者临床症状和指标改善时间短于单药治疗的患者，而总有效率高于单药治疗的患者，说明联合用药可显著提高临床治疗效果。这可能与联合用药可显著改善患者的 D- 乳酸、DAO 和 L/M 水平和肠道动力有关。

综上所述，与单用生长抑素相比，生长抑素联合双歧杆菌

四联活菌可更迅速缓解急性胰腺炎患者的临床症状及指标，恢复胃肠动力，并显著改善患者的肠粘膜屏障功能，利于患者的康复。

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