

doi: 10.13241/j.cnki.pmb.2021.05.039

双歧杆菌三联活菌胶囊与血必净注射液联合治疗术后早期炎性肠梗阻的疗效及对肠黏膜功能的影响

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摘要 目的:研究双歧杆菌三联活菌胶囊与血必净注射液联合治疗术后早期炎性肠梗阻(EPISBO)的疗效及对肠黏膜功能和肠壁黏膜炎症的影响。**方法:**选择从2018年10月到2020年8月在医院接受治疗的EPISBO患者100例作为观察对象,按随机数表法将其分成观察组及对照组各50例,两组均常规治疗,对照组另给予血必净注射液,观察组在对照组的用药基础上再增用双歧杆菌三联活菌胶囊。两组均治疗7d,对比两组疗效,胃肠功能相关指标,肠黏膜功能相关指标,肠壁黏膜炎症指标,以及不良反应。**结果:**观察组的总有效率为98.00%,明显高于对照组的84.00%(均 $P<0.05$)。观察组的胃肠功能相关指标均分别明显优于对照组(均 $P<0.05$)。治疗7d后,两组的丙二醛(MDA)、二胺氧化酶(DAO)及乳酸(D-Lac)水平均明显低于治疗前,且观察组又低于对照组($P<0.05$)。两组的超氧化物歧化酶(SOD)水平明显高于治疗前,且观察组又高于对照组($P<0.05$)。治疗7d后两组的内毒素(LPS)、C反应蛋白(CRP)、肿瘤坏死因子- α (TNF- α)、白细胞介素-6(IL-6)及IL-1 β 水平均明显低于治疗前,且观察组又低于对照组($P<0.05$)。两组的不良反应相比,差异不显著($P>0.05$)。**结论:**应用双歧杆菌三联活菌胶囊联合血必净注射液治疗EPISBO的疗效和安全性均较好,且对肠黏膜功能和肠壁黏膜炎症具有较好的改善作用,值得推广。

关键词:双歧杆菌三联活菌胶囊;血必净注射液;术后早期炎性肠梗阻;疗效;肠黏膜功能;肠壁黏膜炎症

中图分类号:R574.2 文献标识码:A 文章编号:1673-6273(2021)05-982-05

Effect of Bifidobacterium Triple Living Bacteria Capsule and Xuebijing Injection on Early Postoperative Inflammatory Small Bowel Obstruction and Its Effect on Intestinal Mucosa Function Inflammation

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ABSTRACT Objective: To study the efficacy of Bifidobacterium Triple living bacteria capsule and Xuebijing injection on early postoperative inflammatory small bowel obstruction (EPISBO) and its effect on intestinal mucosa function and intestinal mucosa inflammation. **Methods:** From October 2018 to August 2020, 100 patients enrolled in Rongxian People's Hospital with EPISBO were randomly divided into observation group ($n=50$) and control group ($n=50$) by random digital table method. The two groups were given conventional therapy, the control group was given Xuebijing injection, and the observation group was added bifidobacterium triple living bacteria capsule on the basis of the medicine used in the control group. The therapeutic effect, gastrointestinal function related index, intestinal mucosa function related index, intestinal mucosa inflammation related index and adverse reactions was compared between the two groups. **Results:** The total effective rate of the observation group was 98.00%, which was significantly higher than that of the control group of 84.00%(all $P<0.05$). The gastrointestinal function related index in the observation group was significantly better than those in the control group ($P<0.05$). After 7 days treatment, the levels of malondialdehyde (MDA), diamine oxidase (DAO) and lactic acid (D-Lac) in the two groups was significantly lower than those before treatment, and the level in the observation group was lower than that in the control group ($P<0.05$). The level of superoxide dismutase (SOD) in the two groups was significantly higher than that before treatment, and the level in the observation group was higher than that in the control group ($P<0.05$). The levels of endotoxin (LPS), C reactive protein (CRP), tumor necrosis factor- α (TNF- α), interleukin-6 (IL-6) and IL-1 β in the two groups was significantly lower than those before treatment 7 days after treatment. And the observation group was lower than the control group ($P<0.05$). There was no significant difference in adverse reactions between the two groups ($P>0.05$). **Conclusion:** Bifidobacterium triple living bacteria capsule combined with Xuebijing injection is effective and safe in the treatment of EPISBO, and it can improve the function of intestinal mucosa

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(收稿日期:2020-08-28 接受日期:2020-09-23)

and inflammation of intestinal mucosa, so it is worth popularizing.

Key words: Bifidobacterium Triple living bacteria capsule; Xuebijing injection; EPISBO; Curative effect; Intestinal mucosal function; Intestinal mucosa inflammation

Chinese Library Classification(CLC): R574.2 **Document code:** A

Article ID:1673-6273(2021)05-982-05

前言

术后早期炎性肠梗阻(EPISBO)作为一种临床外科十分常见的术后继发性疾病,其病因通常认为和术中长时程的肠管不当性外置暴露及广泛性肠管黏连经电刀松解,亦或是小肠排列术等有关操作的实施密切相关^[1,2]。患者常因手术刺激导致无菌性炎症反应,出现肠壁的黏连充血及肠液、组织液的渗出,致使肠管麻痹且蠕动不佳,最终引起 EPISBO^[3,4]。对于此病的治疗,当前多选择应用血必净注射液等治疗,其具有调节免疫、抗炎、抗氧化应激、改善凝血、改善微循环等作用,疗效较好,但仍具有较大的提升空间^[5,6]。双歧杆菌三联活菌胶囊是调节肠道微生态的重要益生菌制剂,可较好地调节肠道免疫,抑制机体肠道内的有害菌形成内毒素,并可维持肠道稳态,对肠黏膜功能的改善与恢复具有较好的促进作用,但关于其参与治疗 EPISBO 的报道较少^[7,8]。本文通过研究双歧杆菌三联活菌胶囊与血必净注射液联合治疗 EPISBO 的疗效及对肠黏膜功能和肠壁黏膜炎症的影响,旨在为临床治疗 EPISBO 提供科学的治疗方案参考及详实的数据支持,现报道如下。

1 资料和方法

1.1 临床资料

选择从 2018 年 10 月到 2020 年 8 月在医院接受治疗的 EPISBO 患者 100 例作为观察对象。纳入标准:(1)符合 EPISBO 有关诊断标准^[9];(2)有近期的腹部手术史者;(3)年龄 ≥ 18 岁;(4)患者或其家属已知情同意,且已签署同意书者。排除标准:(1)有腹内疝或肠管成角畸形者;(2)有肠扭转或肠套叠者;(3)有严重的心、肝、肾等器官的严重功能障碍者;(4)有血液疾病者;(5)有恶性肿瘤者。按随机数表法将其分成观察组及对照组各 50 例,两组的一般资料相比,差异不显著($P>0.05$),见表 1。本次研究已得到医院内伦理委员会的评审通过。

1.2 研究方法

两组患者均常规予以止痛和胃肠减压,以及抗感染和维持水、电解质的平衡及营养支持等措施。对照组另给予血必净注射液(天津红日药业公司,国药准字:Z20040033)静滴,将 50 mL 药液添加至 100 mL 的生理盐水中,2 次/d。观察组在对照组的基础上,增用双歧杆菌三联活菌胶囊(上海信谊药厂,国药准

字:S10950032,规格:0.21 g/粒),剂量为 3 粒/次,2 次/d。对两组均连续治疗 7d。

1.3 观察指标

对比两组疗效,胃肠功能相关指标,肠黏膜功能相关指标,肠壁黏膜炎症指标,以及不良反应。(1)肠壁黏膜炎症指标检测,分别在治疗前及治疗后 7d 提取患者的腹腔引流液 4mL,通过日本日立公司的 7600 型全自动生化反应分析仪及酶联免疫吸附法测定 C 反应蛋白(CRP)、肿瘤坏死因子- α (TNF- α)、白细胞介素-6(IL-6)、白细胞介素-1 β (IL-1 β),应用鲎试剂偶氮显色法测定 LPS。(2)肠黏膜功能相关指标,在治疗前及治疗后 7d 提取患者的空腹静脉血 4 mL,给予 10 min 3000 r/min 的离心后将血清提出,通过硫代巴比妥酸法检测丙二醛(MDA),通过黄嘌呤氧化酶法测定超氧化物歧化酶(SOD),通过分光光度法检测二胺氧化酶(DAO)及乳酸(D-Lac)水平。上述试剂盒均购自上海的酶联生物科技公司,在实施检测操作时应严格遵守说明书的步骤进行处理。

1.4 疗效评价

显效:患者的腹痛腹胀及排气排便有关症状及体征已明显改善,且胃肠减压量的改善幅度超过 50%;有效:患者的腹痛腹胀及排气排便有关症状及体征有所缓解,且胃肠减压量的改善幅度为 30%~49%;无效:患者的腹痛腹胀及排气排便有关症状及体征无变化,或加重,且胃肠减压量也未改善。计算总有效率=(显效+有效)/总例数 $\times 100\%$ 。

1.5 统计学方法

通过 SPSS21.0 统计软件实施处理分析,计数资料用(n,%)表示,其比较予以 χ^2 检验。计量资料用($\bar{x}\pm s$)表示,其比较予以 t 检验, $P<0.05$ 为差异有统计学意义^[10]。

2 结果

2.1 两组疗效对比

观察组的总有效率为 98.00%,明显高于对照组的 84.00% (均 $P<0.05$),见表 1。

2.2 两组胃肠功能相关指标的对比

观察组的胃肠功能相关指标均分别明显优于对照组(均 $P<0.05$),见表 2。

表 1 两组疗效比较(n,%)

Table 1 Comparison of therapeutic effect between the two groups (n,%)

Groups	Cases	Remarkable effect	Effective	Ineffective	Total effective
Observation group	50	22(44.00)	27(54.00)	1(2.00)	49(98.00)
Control group	50	13(26.00)	29(58.00)	8(16.00)	42(84.00)
χ^2	-				5.983
P	-				0.014

2.3 两组肠黏膜功能相关指标的对比

治疗前两组的肠黏膜功能相关指标相比,差异不显著($P>0.05$)。治疗 7d 后,两组的 MDA、DAO 及 D-Lac 水平均明显低

于治疗前,且观察组又低于对照组($P<0.05$)。两组的 SOD 水平明显高于治疗前,且观察组又高于对照组($P<0.05$),见表 3。

表 2 两组胃肠功能相关指标比较($\bar{x}\pm s$)

Table 2 Comparison of gastrointestinal function related indexes between the two groups($\bar{x}\pm s$)

Groups	Cases	Gastrointestinal decompression volume (mL/d)	Disappearance time of abdominal distension (d)	Anal defecation time (d)	Disappearance time of nausea and vomiting (d)	Recovery time of bowel sounds(d)
Observation group	50	318.79±76.42	2.47±0.96	4.13±1.08	5.18±1.47	2.19±0.77
Control group	50	782.57±103.45	3.71±1.32	5.94±1.31	6.36±1.40	3.53±0.92
t	-	25.498	5.372	7.538	4.110	7.898
P	-	0.000	0.000	0.000	0.000	0.000

表 3 两组肠黏膜功能相关指标比较($\bar{x}\pm s$)

Table 3 Comparison of intestinal mucosa function related index between the two groups($\bar{x}\pm s$)

Groups	Cases	MDA (nmol/L)		SOD (IU/mL)		DAO (U/L)		D-Lac (mg/L)	
		before treatment	after 7d treatment	before treatment	after 7d treatment	before treatment	after 7d treatment	before treatment	after 7d treatment
Observation group	50	7.42±1.35	5.38±1.27*	51.24±7.98	62.97±9.14*	13.29±2.67	5.28±0.69*	10.58±3.45	6.44±1.36*
Control group	50	7.40±1.41	6.34±1.33*	51.26±8.02	58.83±9.25*	13.34±2.72	7.94±0.72*	10.62±3.53	8.76±1.50*
t	-	0.072	3.691	0.012	2.251	0.093	18.861	0.057	8.102
P	-	0.942	0.000	0.990	0.027	0.926	0.000	0.954	0.000

Note: compared with before treatment,* $P<0.05$.

2.4 两组肠壁黏膜炎症指标的对比

治疗前两组肠壁黏膜炎症指标相比,差异不显著($P>0.05$)。

治疗 7d 后两组的 LPS、CRP、TNF- α 、IL-6 及 IL-1 β 水平均明显低于治疗前,且观察组又低于对照组($P<0.05$),见表 5。

表 4 两组肠黏膜炎症相关指标比较($\bar{x}\pm s$)

Table 4 Comparison of intestinal mucosa inflammation related index between the two groups($\bar{x}\pm s$)

Groups	Cases	LPS (EU/mL)		CRP (mg/L)		TNF- α (ng/L)		IL-6 (ng/L)		IL-1 β (ng/L)	
		before treatment	after 7d treatment	before treatment	after 7d treatment	before treatment	after 7d treatment	before treatment	after 7d treatment	before treatment	after 7d treatment
Observation group	50	0.87±0.21	0.18±0.14*	10.87±1.54	3.39±0.52*	3.43±0.74	1.60±0.58*	79.18±13.47	59.33±15.19*	70.38±14.33	50.59±12.57*
Control group	50	0.89±0.24	0.31±0.15*	10.91±1.68	6.12±1.37*	3.41±0.80	2.12±0.53*	80.24±12.96	68.54±16.20*	71.17±15.61	58.63±13.99*
t	-	0.443	4.480	0.124	13.174	0.130	4.680	0.401	2.933	0.264	3.023
P	-	0.658	0.000	0.902	0.000	0.897	0.000	0.689	0.004	0.793	0.003

Note: compared with before treatment,* $P<0.05$.

3 讨论

临床上,EPISBO 通常是患者在实施腹部外科手术,特别是胃肠外科术式治疗之后较易发生的一类亚急性并发症^[11,12]。其常易和急性肠梗阻以及绞窄型肠梗阻发生混淆,进而影响临床医师的正确判断而误诊误治^[13,14]。据数据显示,此病的发病率在术后肠梗阻中的占比大约为 20%,患者的肠壁水肿较为明显,且渗出较多,而肠袢间的粘连也比较致密,若未给予明确的诊断评估而盲目实施手术探查,则可能破坏患者的肠壁完整性,最终形成肠瘘^[15-17]。因此,对于 EPISBO 的治疗方案应以内科疗

法为主,选择科学的治疗方案有助于患者的预后康复,而非盲目手术探查,从而进一步使患者机体产生损伤。

本文结果显示,观察组的总有效率为 98.00%,明显高于对照组的 84.00%,且胃肠功能相关指标均分别明显优于对照组(均 $P<0.05$),这与 Wu 等人^[18,19]的报道结果基本一致,提示了观察组的疗效更好,且患者术后胃肠功能的恢复也更佳。中医认为,EPISBO 病位在肠,患者手术后通常具有气血虚弱和腑气不通,以及热邪郁闭和寒邪凝滞等情况,较易引起标实本虚和血瘀痛阻,因此治疗时需行气散结及通里攻下^[20-22]。观察组应用的血必净主要成分中,红花可活血通经和散瘀止痛,当归可润

肠通便和活血化瘀,川芎可活血祛瘀和行气开郁,还可祛风止痛,丹参可活血化瘀和通经止痛。赤芍可清热凉血和活血祛瘀^[23]。上述诸药联用,共奏活血化瘀及润肠止痛之功效,有助于患者临床症状的改善^[24,25]。双歧杆菌三联活菌胶囊作为一种富含嗜酸乳杆菌和粪肠球菌,以及双歧杆菌的常用活菌制剂,其可明显地调节患者的肠道菌群,并可帮助维持肠道内的稳态,与血必净联用最终有效地提升了治疗疗效,改善了患者的临床症状^[26,27]。MDA 和 SOD 作为临床常用的反映机体氧化应激的指标,其对患者的肠黏膜氧化应激损伤具有较好的提示作用。其中 MDA 属于脂质的过氧化反应性产物,能够体现机体中氧化反应的有关强度和速度^[28]。而 SOD 是对氧自由基进行清除的重要酶,其水平的高低能够体现出机体的抗氧化应激水平^[29]。D-Lac 及 DAO 是对肠黏膜功能进行评估的敏感指标,二者在机体中的水平越高往往代表着患者的肠黏膜功能也越差^[30]。本文发现,治疗 7d 后,观察组患者治疗后的肠黏膜功能改善程度优于对照组。究其原因,观察组应用的血必净能够帮助改善肠道血管内皮的功能,加速肠道超微结构自身损伤后的修复,并可诱导机体内的热休克蛋白形成,并保护血红素氧化酶的正常作用,抑制其过氧化损害,最终改善了肠黏膜的功能^[31]。而双歧杆菌三联活菌胶囊能够调整患者肠道菌群,促进肠道中优势菌群的不断增殖,并有效抑制病原菌的增多,降低肠源性内毒素的水平,最终有效促进了受损肠黏膜的恢复,提升了肠黏膜功能^[32]。此外,LPS、CRP、TNF- α 、IL-6 及 IL-1 β 均为炎症介质或炎症因子,此类指标在机体的炎症性疾病中均会表现出不同程度的升高状态,且炎症程度越高,通常水平会上升的越明显。其中 LPS 以往被认为属于全身炎症反应综合征的重要触发剂,过高的含量水平可导致较大的机体损害。CRP 作为急性时相反应蛋白,与炎症反应密切相关^[33]。IL-6 和 IL-1 β 均为促炎因子。本文发现,治疗 7d 后两组的 LPS、CRP、TNF- α 、IL-6 及 IL-1 β 水平均明显低于治疗前,且观察组又低于对照组 ($P<0.05$),这提示了观察组治疗后肠壁黏膜炎症状况得到了更好地改善。现代药理研究证实,血必净中含有的红花、川芎、丹参等中药材能够较好地调节机体中的炎症反应状况,干预 TNF- α 、IL-6 等炎症因子的正常表达,并可重建机体中促炎/抗炎介质的生态平衡,抑制相应的过氧化损害^[34,35]。同时,观察组应用的益生菌能够增加肠道的营养吸收,增大免疫功能,对肠黏膜具有保护作用,而对有害病原菌则有抑制作用,最终较好地缓解了患者术后的肠壁黏膜炎症。

综上所述,应用双歧杆菌三联活菌胶囊联合血必净注射液治疗 EPISBO 的疗效和安全性均较好,且对肠黏膜功能和肠壁黏膜炎症具有较好的改善作用,值得推广。

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