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醒脾养儿颗粒联合双歧杆菌三联活菌散对轮状病毒腹泻患儿免疫功能、心肌酶指标和血清 IL-6、CRP 的影响 *

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摘要 目的:观察醒脾养儿颗粒联合双歧杆菌三联活菌散对轮状病毒腹泻患儿免疫功能、心肌酶指标和血清白介素-6(IL-6)、C反应蛋白(CRP)的影响。**方法:**选取2018年1月到2021年1月期间我院接收的92例轮状病毒腹泻患儿。根据随机数字表法将患儿分为对照组和研究组,各为46例。对照组患儿接受双歧杆菌三联活菌散治疗,研究组患儿接受醒脾养儿颗粒联合双歧杆菌三联活菌散治疗,均治疗3d。观察两组疗效,记录不良反应发生情况。观察并对比两组患儿免疫功能[免疫球蛋白(Ig)M、IgG和IgA]、心肌酶指标[磷酸肌酸激酶(CK)、乳酸脱氢酶(LDH)、肌酸激酶同工酶(CK-MB)]和血清IL-6、CRP的变化情况。**结果:**研究组的临床总有效率为91.30%(42/46),高于对照组患者的71.74%(33/46),差异有统计学意义($P<0.05$)。两组治疗3d后血清IgM、IgG、IgA水平较治疗前升高,且研究组的改善程度优于对照组($P<0.05$)。两组治疗3d后血清LDH、CK、CK-MB水平较治疗前降低,且研究组的改善程度优于对照组($P<0.05$)。两组治疗3d后血清IL-6、CRP水平较治疗前降低,且研究组的改善程度优于对照组($P<0.05$)。两组患儿均未见明显不良反应发生。**结论:**醒脾养儿颗粒联合双歧杆菌三联活菌散治疗轮状病毒腹泻患儿,可提高免疫力,减轻心肌损伤,降低血清IL-6、CRP水平,安全有效。

关键词:醒脾养儿颗粒;双歧杆菌三联活菌散;轮状病毒腹泻;免疫功能;心肌酶指标;IL-6;CRP

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Effects of Xingpi Yanger Granule Combined with Bifidobacterium Triple Viable Powder on Immune Function, Myocardial Enzyme Indexes, Serum IL-6 and CRP in Children with Rotavirus Diarrhea*

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ABSTRACT Objective: To observe the effects of Xingpi Yanger granule combined with Bifidobacterium triple viable powder on immune function, myocardial enzyme indexes, serum interleukin-6(IL-6) and C-reactive protein(CRP) in children with rotavirus diarrhea. **Methods:** 92 children with rotavirus diarrhea who were received in our hospital from January 2018 to January 2021 were selected. According to the random number table method, the children were divided into control group and study group, with 46 cases in each group. The children in the control group were treated with Bifidobacterium triple viable powder, and the children in the study group were treated with Xingpi Yanger granule combined with Bifidobacterium triple viable powder, all patients were treated for 3 days. The curative effects of the two groups were observed and the adverse reactions were recorded. The changes of immune function [immunoglobulin (Ig) m, IgG and IgA], myocardial enzyme indexes [phosphocreatine kinase (CK), lactate dehydrogenase (LDH), creatine kinase isoenzyme (CK-MB)] and serum IL-6 and CRP were observed and compared between the two groups. **Results:** The total clinical effective rate in the study group was 91.30% (42/46), which was higher than 71.74% (33/46) in the control group ($P<0.05$). The levels of serum IgM, IgG and IgA in the two groups were higher than those before treatment, and the improvement degree of the study group was better than that of the control group ($P<0.05$). The levels of serum LDH, CK and CK-MB in the two groups were lower than those before treatment, and the improvement degree of the study group was better than that of the control group ($P<0.05$). The levels of serum IL-6 and CRP in the two groups were lower than those before treatment, and the improvement degree of the study group was better than that of the control group ($P<0.05$). There were no significant adverse reactions in both groups. **Conclusion:** Xingpi Yanger granule combined with Bifidobacterium triple viable powder in the treatment of children with rotavirus diarrhea can improve immunity, reduce myocardial injury and reduce the levels of serum IL-6 and CRP, which is safe and effective.

Key words: Xingpi Yanger granule; Bifidobacterium triple viable powder; Rotavirus diarrhea; Immune function; Myocardial enzyme index; IL-6; CRP

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前言

婴幼儿腹泻是儿科的常见疾病之一,主要临床表现为呕吐、腹泻、发热等。引起婴幼儿腹泻的原因很多,大多数学者认可轮状病毒是婴幼儿腹泻发生的首要原因^[1]。轮状病毒腹泻除了可引起消化系统症状外,严重者还可引起心肌损伤,诱发脑炎,对患儿生长发育有较大影响^[2]。当前,临床中尚无轮状病毒腹泻特效药,多以纠正水电解质、酸碱平衡紊乱等对症治疗为主^[3]。双歧杆菌三联活菌散为常用的微生态制剂,可对肠道内的菌群失衡进行调节,从而有效抑制病原菌繁殖^[4],但部分患儿经双歧杆菌三联活菌散治疗后效果不佳,症状缓解较慢。醒脾养儿颗粒是由一点红、山柰茶、毛大丁草和蜘蛛香制成的中成药,具有固肠止泻、养血安神的功效^[5]。本研究观察了醒脾养儿颗粒联合双歧杆菌三联活菌散治疗轮状病毒腹泻患儿的疗效,以期为其临床治疗提供参考。

1 资料与方法

1.1 一般资料

选取 2018 年 1 月到 2021 年 1 月期间我院接收的 92 例轮状病毒腹泻患儿。诊断标准:参考《儿童腹泻病诊断治疗原则的专家共识》^[6]:镜检少量或无白细胞、无红细胞及脓细胞,患儿大便呈稀水样或蛋花样,轮状病毒抗原检查结果阳性。纳入标准:(1)治疗前未服用止泻药等药物;(2)对本次研究用药无过敏症者;(3)患儿监护人知情本次研究并签署了相关同意书。排除标准:(1)重度脱水的患儿;(2)合并肺、肝、肾等器官功能障碍的患儿;(3)伴有肺炎、阿米巴痢疾、先心病等疾病的患儿;(4)大便细菌检查显示合并其他感染的患儿;(5)伴有营养不良的患儿。根据随机数字表法将患儿分为对照组(双歧杆菌三联活菌散治疗)和研究组(醒脾养儿颗粒联合双歧杆菌三联活菌散治疗),各为 46 例。两组一般资料对比无差异($P>0.05$),见表 1。

表 1 两组患儿一般资料对比

Table 1 Comparison of general data between the two groups

Groups	Male/female	Age(year)	Course of disease (d)	Diarrhea(times/d)		
				<5	5~10	>10
Control group(n=46)	20/26	3.62± 0.55	3.91± 0.68	12	23	11
Study group(n=46)	22/24	3.65± 0.48	3.86± 0.52	14	22	10
χ^2/t	0.175	-0.279	0.396		0.223	
P	0.675	0.781	0.693		0.894	

1.2 方法

两组患儿均给予维持水电解质酸碱平衡、补液、补充维生素等基础治疗。在此基础上,对照组给予双歧杆菌三联活菌散(国药准字 S10970104,厂家:上海上药信谊药厂有限公司,规格:2 g)治疗,温水冲服,1 岁以内一次半包;1~5 岁一次 1 包;6 岁及以上一次 2 包;均一日 3 次。研究组患儿接受醒脾养儿颗粒(国药准字 Z20025415,厂家:贵州健兴药业有限公司,规格:每袋装 2 g)联合双歧杆菌三联活菌散治疗,其中双歧杆菌三联活菌散治疗方案参考对照组,醒脾养儿颗粒治疗方案如下:温水冲服。1 岁以内一次 1 袋,一日 2 次;1~2 岁一次 2 袋,一日 2 次;3~6 岁一次 2 袋,一日 3 次;7~14 岁一次 3~4 袋,一日 2 次。

两组患儿均治疗 3 d 后观察治疗效果,记录治疗期间的药物安全性情况。

1.3 疗效判定标准

无效:治疗 3 d 后,全身症状未改善甚至加重,粪便性状及次数无改变^[7]。有效:治疗 3 d 后,粪便性状及次数、全身症状均明显改善。显效:治疗 3 d 后,粪便性状及次数均恢复正常,全身症状消失。总有效率=(显效例数+有效例数)/总例数×100%。

1.4 观察指标

治疗前后收集所有患儿静脉血 6 mL,置于抗凝试管中,静置 0.5 h,3000 r/min 条件下离心 12 min,离心半径 13.5 cm,分离血清,低温条件下待用。采用酶联免疫吸附法检测白介素-6(IL-6)水平(试剂盒购自瑞士罗氏集团),采用免疫比浊法检

测 C 反应蛋白(CRP)水平(试剂盒购自株式会社日立制作所)。采用免疫比浊法检测血清免疫球蛋白(Ig)M、IgG 和 IgA 水平(试剂盒购自北京万泰生物药业股份有限公司)。使用美国贝克曼库尔特有限公司生产的 AU5800 全自动生化分析仪检测血清磷酸肌酸激酶(CK)、乳酸脱氢酶(LDH)、肌酸激酶同工酶(CK-MB)水平。

1.5 统计学方法

以 SPSS19.0 软件进行统计分析。以($\bar{x} \pm s$)描述经检验符合正态分布的 IgM、LDH、CK 等计量资料,组间比较采用成组 t 检验,组内比较采用配对 t 检验。以[n(%)]描述疗效、不良反应发生率等计数资料,进行 χ^2 检验。 $P<0.05$ 表示有差异。

2 结果

2.1 疗效对比

研究组的临床总有效率为 91.30%(42/46),高于对照患者的 71.74%(33/46),差异有统计学意义($P<0.05$),见表 2。

2.2 免疫功能指标对比

两组治疗 3 d 后血清 IgM、IgG、IgA 水平较治疗前升高,且研究组的改善程度优于对照组($P<0.05$),见表 3。

2.3 心肌酶指标对比

两组治疗 3 d 后血清 LDH、CK、CK-MB 水平较治疗前降低,且研究组的改善程度优于对照组($P<0.05$),见表 4。

2.4 IL-6、CRP 对比

两组治疗 3 d 后血清 IL-6、CRP 水平较治疗前降低,且研究组的改善程度优于对照组($P<0.05$),见表 5。

表 2 两组疗效对比 [例(%)]

Table 2 Comparison of curative effects between the two groups [n(%)]

Groups	Remarkable effect	Effective	Invalid	Total effective rate
Control group(n=46)	12(26.09)	21(45.65)	13(28.26)	33(71.74)
Study group(n=46)	17(36.96)	25(54.35)	4(8.70)	42(91.30)
χ^2				5.845
P				0.016

表 3 免疫功能指标对比 ($\bar{x} \pm s$, g/L)Table 3 Comparison of immune function indexes ($\bar{x} \pm s$, g/L)

Groups	Time	IgM	IgG	IgA
Control group(n=46)	Before treatment	0.77 $\pm$ 0.15	5.98 $\pm$ 0.87	0.49 $\pm$ 0.08
	3 d after treatment	0.88 $\pm$ 0.14	7.55 $\pm$ 0.93	0.66 $\pm$ 0.12
	t1, P1	-3.636, 0.000	-8.361, 0.000	-7.995, 0.000
Study group(n=46)	Before treatment	0.73 $\pm$ 0.13	6.09 $\pm$ 0.92	0.52 $\pm$ 0.07
	3 d after treatment	1.02 $\pm$ 0.18	9.68 $\pm$ 0.84	0.89 $\pm$ 0.13
	t2, P2	-8.858, 0.000	-19.545, 0.000	-16.996, 0.000
	t3, P3	-4.164, 0.000	-11.528, 0.000	-8.817, 0.000

Note: t1 and P1 were the comparison within the control group, t2 and P2 were the comparison within the study group, t3 and P3 were the comparison between the control group and the study group after 3 days of treatment.

表 4 不同观察时间点的心肌酶指标对比 ($\bar{x} \pm s$, U/L)Table 4 Comparison of myocardial enzyme indexes at different observation time points ($\bar{x} \pm s$, U/L)

Groups	Time	LDH	CK	CK-MB
Control group(n=46)	Before treatment	341.91 $\pm$ 20.26	82.04 $\pm$ 7.44	51.97 $\pm$ 5.21
	3 d after treatment	297.18 $\pm$ 24.22	61.13 $\pm$ 6.32	34.19 $\pm$ 5.68
	t1, P1	9.608, 0.000	14.528, 0.000	15.646, 0.000
Study group(n=46)	Before treatment	342.11 $\pm$ 22.31	82.37 $\pm$ 8.39	51.34 $\pm$ 6.89
	3 d after treatment	261.23 $\pm$ 19.37	48.95 $\pm$ 6.57	27.49 $\pm$ 4.76
	t2, P2	18.566, 0.000	21.271, 0.000	19.316, 0.000
	t3, P3	7.862, 0.000	9.062, 0.000	6.132, 0.000

Note: t1 and P1 were the comparison within the control group, t2 and P2 were the comparison within the study group, t3 and P3 were the comparison between the control group and the study group after 3 days of treatment.

表 5 IL-6、CRP 对比 ($\bar{x} \pm s$)Table 5 Comparison of IL-6 and CRP ($\bar{x} \pm s$)

Groups	Time	IL-6 (pg/mL)	CRP (mg/L)
Control group(n=46)	Before treatment	18.43 $\pm$ 2.57	56.85 $\pm$ 5.63
	3 d after treatment	13.36 $\pm$ 2.18	35.41 $\pm$ 4.35
	t1, P1	10.204, 0.000	20.438, 0.000
Study group(n=46)	Before treatment	18.21 $\pm$ 2.38	56.57 $\pm$ 6.38
	3 d after treatment	9.44 $\pm$ 1.97	24.82 $\pm$ 3.55
	t2, P2	19.252, 0.000	29.494, 0.000
	t3, P3	9.048, 0.000	14.244, 0.000

Note: t1 and P1 were the comparison within the control group, t2 and P2 were the comparison within the study group, t3 and P3 were the comparison between the control group and the study group after 3 days of treatment.

2.5 不良反应发生率对比

两组患儿均未见明显不良反应发生。

3 讨论

轮状病毒属于呼肠孤病毒科轮状病毒属, 传染性极强, 主要分型有 7 组, 其中仅 A、B、C 三组可引起人类的腹泻, 而在这之中, B、C 引发成人腹泻, A 则引发婴幼儿腹泻^[89]。婴幼儿胃肠道功能较弱, 抵抗力较差, 更容易感染轮状病毒^[10]。患儿感染轮状病毒后, 其空肠黏膜表皮绒毛细胞坏死、脱落, 进而影响机体水电解质的吸收, 增加胃肠蠕动, 从而引起腹泻症状^[11,12]。目前, 临床针对轮状病毒腹泻患儿的治疗主要为微生态制剂调理肠道菌群等常规对症支持治疗, 双歧杆菌三联活菌散常用于治疗腹泻及便秘, 其主要通过补充人体正常生理细菌, 从而有效抑制并清除肠道中的有害细菌^[13,14]。李碧莹等^[15]学者将益生菌用于婴幼儿轮状病毒性腹泻治疗中, 结果显示, 其可有效修复肠道屏障功能, 提高治疗效果。但通过研究发现^[16], 轮状病毒腹泻患儿在早期常常可见心肌酶指标异常升高情况, 而双歧杆菌三联活菌散在这方面并无改善作用。醒脾养儿颗粒是一种中成药, 其中的毛茛草及一点红共同发挥利水消肿, 凉血解毒的功效; 山桅茶清热消渴; 蜘蛛香活血行气; 以上药物可共同发挥理气醒脾、清热解暑、固肠止泻的作用^[17]。

本次研究结果显示, 相较于单用双歧杆菌三联活菌散治疗的患儿, 联合醒脾养儿颗粒治疗的患儿可获得更好的疗效, 且两组患儿均未见明显不良反应发生。主要是因为醒脾养儿颗粒能拮抗小肠运动亢进, 发挥固肠止泻作用。以往不少研究证实^[18,19], 轮状病毒感染下患儿的体液免疫处于抑制状态, 导致 IgM、IgG、IgA 处于低水平状态。本研究中醒脾养儿颗粒联合双歧杆菌三联活菌散治疗可有效提高 IgM、IgG、IgA 水平。究其原因, 双歧杆菌三联活菌散可减少肠道毒素的产生, 促进肠道正常生理功能恢复, 间接改善免疫功能^[20,21]。而醒脾养儿颗粒主要成分之一蜘蛛香可消食健胃、理气平痛, 治疗腹泻的同时还可改善患儿不喜饮食的症状, 尽量保证患儿足够的营养摄入, 从而改善其免疫功能^[22]。CRP 为急性时相蛋白, 可促进激活补体、吞噬细胞免疫功能、调节炎症过程^[23]。IL-6 是炎症反应的重要递质, 可促进炎症反应和诱导 CRP 生成^[24]。本研究中联合治疗控制炎症反应的效果优于单用双歧杆菌三联活菌散治疗者。这可能是因为醒脾养儿颗粒中的一点红主要成分为生物碱、黄酮、甾醇、酚类、挥发油和萜类、甾醇类、脂肪烷类等化合物, 具有抗肿瘤、抗氧化、抗炎镇痛、抑菌等广泛的药理作用^[25]。LDH^[26]、CK^[27]、CK-MB^[28,29]是心肌细胞内的酶, 心肌细胞受损时, 以上物质可被释放入血, 常被用作心肌受损的生物标志物。本研究中两组治疗 3d 后血清 LDH、CK、CK-MB 水平较治疗前降低, 且研究组的改善程度优于对照组, 提示醒脾养儿颗粒联合双歧杆菌三联活菌散治疗可减轻心肌损伤, 主要与醒脾养儿颗粒中的山桅茶含有皂苷、挥发油、萜类、木脂素、萜类化合物等有关, 其中皂苷可影响机体心脏收缩力, 发挥正性肌力作用^[30]。

综上所述, 醒脾养儿颗粒联合双歧杆菌三联活菌散治疗轮状病毒腹泻患儿, 疗效显著, 其治疗作用可能与提高免疫力, 减轻心肌损伤, 降低血清 IL-6、CRP 水平有关。

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