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益生菌联合膳食纤维的肠内营养对重型颅脑损伤患者术后营养状况、免疫功能和肠黏膜屏障功能的影响*

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摘要 目的:观察重型颅脑损伤患者术后经膳食纤维的肠内营养联合益生菌干预后,患者免疫功能、肠黏膜屏障功能以及营养状况的变化。**方法:**选取2016年6月~2020年5月期间我院收治的重型颅脑损伤患者136例。根据入院顺序奇偶法分为对照组68例和研究组68例,对照组给予膳食纤维的肠内营养干预,研究组在对照组的基础上联合益生菌干预,对比两组格拉斯哥昏迷量表(GCS)评分、营养状况、免疫功能、肠黏膜屏障功能及并发症发生情况。**结果:**两组干预14d后白蛋白(ALB)、血红蛋白(Hb)、转铁蛋白(TR)均较干预前升高,且研究组较对照组高($P<0.05$)。两组干预14d后免疫球蛋白G(IgG)、免疫球蛋白A(IgA)、免疫球蛋白M(IgM)均较干预前升高,且研究组较对照组高($P<0.05$)。两组干预14d后总超氧化物歧化酶(T-SOD)、谷胱甘肽过氧化物酶(GSH-PX)均较干预前升高,且研究组较对照组高($P<0.05$),丙二醛(MDA)较干预前降低,且研究组较对照组低($P<0.05$)。两组干预14d后GCS评分升高,且研究组较对照组高($P<0.05$)。研究组的并发症发生率低于对照组($P<0.05$)。**结论:**益生菌联合膳食纤维的肠内营养干预可有效改善重型颅脑损伤术后患者营养状况、免疫功能和肠黏膜屏障功能,同时还可减少并发症发生率,改善患者预后。

关键词:益生菌;膳食纤维;肠内营养;重型颅脑损伤;营养状况;免疫功能;肠黏膜屏障功能

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Effects of Enteral Nutrition of Probiotics Combined with Dietary Fiber on Nutritional Status, Immune Function and Intestinal Mucosal Barrier Function in Patients with Severe Craniocerebral Injury after Operation*

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ABSTRACT Objective: To observe the changes of immune function, intestinal mucosal barrier function and nutritional status of patients with severe craniocerebral injury after enteral nutrition with dietary fiber combined with probiotics intervention. **Methods:** 136 patients with severe craniocerebral injury who were admitted in our hospital from June 2016 to May 2020 were selected. They were divided into 68 cases of control group and 68 cases of study group according to admission sequence parity method, the control group was given enteral nutrition with dietary fiber intervention, while the study group was treated with probiotics intervention on the basis of the control group, the Glasgow coma (GCS) score, nutritional status, immune function, intestinal mucosal barrier function and complications were compared between the two groups. **Results:** The levels of albumin (ALB), hemoglobin (Hb), transferrin (TR) in the two groups at 14 d after intervention were higher than before intervention, and the study group was higher than that of the control group ($P<0.05$). The levels of immunoglobulin G (IgG), immunoglobulin A (IgA), immunoglobulin M (IgM) in the two groups at 14 d after intervention were higher than before intervention, and the study group was higher than that of the control group ($P<0.05$). The levels of total superoxide dismutase (T-SOD), glutathione peroxidase (GSH-Px) in the two groups 14d after intervention were higher than before intervention, and the study group was higher than that of the control group ($P<0.05$), and malondialdehyde (MDA) was lower than before intervention, and the study group was lower than that of control group ($P<0.05$). GCS scores of the two groups increased 14d after intervention, and the study group was higher than that of the control group ($P<0.05$). The incidence of complications in the study group was lower than that of the control group ($P<0.05$). **Conclusion:** Enteral nutrition of probiotics combined with dietary fiber intervention can effectively improve the nutritional status, immune function and intestinal mucosal barrier function of patients with severe craniocerebral injury after operation, and can reduce the incidence of complications at the same time, improve the prognosis of patients.

Key words: Probiotics; Dietary fiber; Enteral nutrition; Severe craniocerebral injury; Nutritional status; Immune function; Intestinal mucosal barrier function

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前言

颅脑损伤是指因暴力直接或间接作用于头部引起颅脑组织的损伤,重型颅脑损伤是指伤后昏迷 6 小时以上或再次昏迷者,该患者病情危重^[1]。由于重型颅脑损伤患者处于昏迷状态,机体在较长的一段时间内无法摄入饮食,极易出现营养不良现象,导致患者免疫力低下,影响病情恢复^[2]。此外,重型颅脑损伤患者可产生病理性应激,肠黏膜遭受缺血 - 再灌注损伤,危及患者生命^[3,4]。现有研究证实添加膳食纤维的肠内营养可稳定患者内环境^[5,6],但因重型颅脑损伤常存在营养吸收障碍,肠内营养物质无法彻底吸收,受限程度大,因此,尽可能地提高膳食纤维的肠内营养效果对于改善重型颅脑损伤患者预后具有积极的意义。益生菌具有修复胃肠道黏膜屏障、纠正肠道菌群紊乱、增加免疫力等功能的作用^[7]。本研究对我院接收的重型颅脑损伤术后患者给予膳食纤维的肠内营养联合益生菌干预,效果显著,现报道如下。

表 1 两组患者一般资料比较

Table 1 Comparison of general data of patients between the two groups

Groups	Male / Female	Age (years)	Course of disease (h)	Cause of injury		
				Falling from height	Traffic accident	Strike
Control group(n=68)	37/31	45.91± 5.26	1.41± 0.24	19	31	18
Study group(n=68)	40/28	45.66± 6.25	1.37± 0.26	22	30	16
t/ χ^2	0.269	0.252	0.932		0.352	
P	0.604	0.0801	0.353		0.686	

1.2 方法

两组入院后均给予预防感染、脱水、维持水电解质平衡、降低颅内压、控制血压等基础干预。待机体循环、呼吸、水电解质相对稳定、酸碱平衡的情况下即可开始营养支持干预。对照组给予膳食纤维的肠内营养干预,使用常规管道喂养肠内营养混悬液(无锡纽迪希亚制药有限公司生产,国药准字 H20010285,规格:500 mL/瓶)基础上加用膳食纤维,肠内营养混悬液按 100-125 mL/h 的滴速通过喂养管到胃,第 1 d 用量为两瓶,后逐渐增加用量,但最大用量不宜超过 8 瓶。膳食纤维用法用量:按每 500 mL 肠内营养混悬液添加复合膳食纤维 7.5 g,其中不溶性膳食纤维:可溶性膳食纤维 =2:1,能量密度为 1.0 kcal/mL,空肠营养管匀速泵入,第 1 d 营养泵速度 30~50 mL/h,鼻饲 500 mL;第 2 d 营养泵速度 50~60 mL/h,增加至 1000 mL;第 3 d 营养泵速度 50~10 mL/h,加至 1500~2000 mL,随后维持此剂量,共干预 14 d。研究组在对照组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,每片重 0.5 g)干预,630 mg 双歧杆菌四联活菌片研磨水化后自鼻饲管内注入,3 次/d,连用 14 d。

1.3 观察指标

(1)于患者干预前、干预 14 d 后抽取 6 mL 清晨空腹静脉血,经离心半径 12.5 cm,4100 r/min 离心 14 min,取上清液待测。采用西班牙 BioSystems 公司生产的 A15 特种蛋白分析仪

1 资料与方法

1.1 一般资料

选取 2016 年 6 月~2020 年 5 月期间我院收治的重型颅脑损伤患者 136 例。纳入标准:(1)经头颅 CT 或 MRI 检查证实,且为闭合性颅脑损伤;(2)预计生存期 ≥ 1 个月;(3)格拉斯哥昏迷量表(Glasgow coma scale,GCS)^[8]评分 ≤ 8 分;(4)伤后 6 h 内入院;(5)患者家属知情本次研究并签署同意书。排除标准:(1)颅脑损伤前存在营养不良者;(2)合并影响营养和代谢及糖尿病患者;(3)合并其他部位严重出血和复合性损伤者;(4)既往有消化道疾病或手术史;(5)合并心肝肾等重要脏器的器质性病变者;(6)无法进行肠内营养干预者;(7)合并严重免疫功能异常者。根据入院顺序奇偶法随机分为对照组 68 例和研究组 68 例,两组一般资料均衡可比($P>0.05$),见表 1。本研究已获得医院伦理学委员会批准进行。

检测免疫球蛋白 A (Immunoglobulin A,IgA)、免疫球蛋白 G (Immunoglobulin G,IgG)、免疫球蛋白 M(Immunoglobulin M,IgM)水平。采用 Roche E170 全自动电化学发光免疫分析仪检测转铁蛋白(transferrin,TR)、白蛋白(albumin,ALB)、血红蛋白(hemoglobin,Hb)。采用酶联免疫吸附试验检测丙二醛(malondialdehyde,MDA)、总超氧化物歧化酶(Total superoxide dismutase,T-SOD)、谷胱甘肽过氧化物酶(Glutathione peroxidase,GSH-PX)水平,所用试剂盒购自深圳子科生物科技有限公司。(2)记录两组干预期间并发症发生情况。(3)于干预前、干预 14 d 后采用 GCS 评估患者病情严重程度。GCS 包括言语、睁眼和运动 3 个方面,最低分 3 分,最高分 15 分,分数越低,昏迷程度越严重。

1.4 统计学方法

本研究数据均采用 SPSS25.0 软件进行统计学分析,计量资料用($\bar{x} \pm s$)表示,比较应用 t 检验,计数资料以率或比表示,采用 χ^2 检验, $P<0.05$ 表明差异具有统计学意义。

2 结果

2.1 两组营养状况对比

两组干预前 ALB、TR、Hb 组间对比无差异($P>0.05$),干预 14 d 后,两组 ALB、TR、Hb 均升高,且研究组较对照组高($P<0.05$),详见表 2。

表 2 两组营养状况对比($\bar{x} \pm s$, g/L)

Table 2 Comparison of nutritional status between the two groups($\bar{x} \pm s$, g/L)

Groups	ALB		TR		Hb	
	Before intervention	14 d after intervention	Before intervention	14 d after intervention	Before intervention	14 d after intervention
Control group(n=68)	34.56± 4.25	37.25± 4.43 ^a	1.53± 0.29	1.86± 0.38 ^a	104.27± 12.25	109.12± 16.35 ^a
Study group(n=68)	34.23± 3.67	41.43± 5.51 ^a	1.58± 0.22	2.27± 0.35 ^a	104.45± 10.34	118.15± 14.11 ^a
t	0.485	4.875	1.133	6.544	0.093	3.448
P	0.629	0.000	0.259	0.000	0.926	0.001

Note: Compared with before intervention, ^aP<0.05.

2.2 两组免疫功能指标对比

14 d 后, 两组 IgG、IgA、IgM 均升高, 且研究组较对照组高(P<0.05), 详见表 3。

两组干预前 IgG、IgA、IgM 组间对比无差异(P>0.05), 干预

表 3 两组免疫功能指标对比($\bar{x} \pm s$, g/L)

Table 3 Comparison of immune function indexes between the two groups($\bar{x} \pm s$, g/L)

Groups	IgG		IgA		IgM	
	Before intervention	14 d after intervention	Before intervention	14 d after intervention	Before intervention	14 d after intervention
Control group(n=68)	2.27± 0.35	2.81± 0.25 ^a	2.15± 0.19	2.76± 0.31 ^a	2.72± 0.26	3.26± 0.38 ^a
Study group(n=68)	2.21± 0.21	3.34± 0.26 ^a	2.19± 0.16	3.35± 0.35 ^a	2.77± 0.28	3.85± 0.35 ^a
t	1.212	12.117	1.328	10.406	1.079	9.417
P	0.228	0.000	0.286	0.000	0.282	0.000

Note: Compared with before intervention, ^aP<0.05.

2.3 两组肠黏膜屏障功能指标对比

且研究组高于对照组(P<0.05), MDA 较干预前降低, 且研究组较对照组低(P<0.05), 详见表 4。

两组干预前 MDA、T-SOD、GSH-PX 组间对比无差异(P>0.05), 两组干预 14d 后 T-SOD、GSH-PX 均较干预前升高,

表 4 两组肠黏膜屏障功能指标对比($\bar{x} \pm s$)

Table 4 Comparison of intestinal mucosal barrier function between the two groups($\bar{x} \pm s$)

Groups	MDA(mmol/L)		T-SOD(U/mL)		GSH-PX(U/mL)	
	Before intervention	14 d after intervention	Before intervention	14 d after intervention	Before intervention	14 d after intervention
Control group(n=68)	8.54± 0.26	5.91± 0.27 ^a	103.63± 10.15	124.31± 18.46 ^a	82.94± 9.63	104.71± 12.13 ^a
Study group(n=68)	8.51± 0.25	3.60± 0.23 ^a	103.29± 11.21	156.42± 19.12 ^a	82.53± 10.42	127.79± 14.19 ^a
t	0.567	53.706	0.185	9.963	28.359	10.188
P	0.571	0.000	0.853	0.000	0.000	0.000

Note: Compared with before intervention, ^aP<0.05.

2.4 两组干预前后 GCS 评分对比

干预前, 对照组的 GCS 评分为(6.38± 0.91)分, 研究组的 GCS 评分为(6.34± 0.87)分, 组间比较无差异(t=0.327, P=0.744); 干预 14 d 后, 对照组的 GCS 评分为(9.97± 0.93)分, 研究组的 GCS 评分为(13.62± 0.73)分, 两组干预 14d 后 GCS 评分较干预前升高(t=23.449, 52.860, 均 P=0.000), 且研究组较对照组高(t=16.972, P=0.000)。

2.5 两组并发症发生率对比

干预期间, 研究组并发症发生率为 4.41%(3/68), 分别为 1 例颅内感染、1 例肺部感染、1 例消化道出血; 对照组并发症发

生率为 14.71%(10/68), 分别为 2 例肺部感染、3 例消化道出血、1 例尿路感染、3 例颅内感染、1 例多器官功能障碍综合征, 研究组的并发症发生率低于对照组($\chi^2=4.301$, P=0.038)。

3 讨论

重型颅脑损伤患者多处于昏迷状态, 且机体处于高分解代谢状态, 易继发低蛋白血症, 致使脑损伤加重, 病死率极高^[9], 同时重型颅脑损伤还处于高应激状态, 除了会降低机体免疫力外, 严重者还会引起自主调节中枢下丘脑—垂体—肾上腺轴功能的紊乱, 导致肠黏膜屏障破坏、消化道出血等并发症^[10-12]。胃

肠作为人体内最大的细菌和内毒素聚集地,当肠粘膜屏障受损时,内毒素和细菌的入侵可引起全身失控性炎症反应、脓毒血症等,给患者生命健康带来严重威胁^[13-15]。以往常采用肠内营养支持辅助治疗重型颅脑损伤,可增强胃肠道黏膜消化与吸收功能,从而使得免疫状况好转^[16-18]。膳食纤维包括不可溶性膳食纤维和可溶性膳食纤维两种,其中不可溶性膳食纤维可促进肠道蠕动,预防肠黏膜萎缩^[19,20]。可溶性膳食纤维则在肠道中被细菌分解,促进受损肠黏膜恢复。临床试验证实膳食纤维联合肠内营养支持方案应用于重型颅脑损伤患者术后,可获得较好的疗效,有效促进机体恢复^[21]。动物实验也说明膳食纤维可保护重型颅脑损伤大鼠肠黏膜^[22],但也有报道显示肠内营养支持的方案仍不能完全避免胃肠黏膜废用性萎缩,临床效果有待提升^[23]。因此,临床学者们尝试在肠内营养的基础上联合促胃肠消化吸收功能的药物,益生菌作为临床常见的微生态制剂,可在一定程度上改善胃肠消化功能,近年来逐渐应用于肠胃营养支持治疗中。

重型颅脑损伤患者由于昏迷无法自主摄食,机体为供给基本代谢所需能量会加快分解体内营养物质,导致体内营养物质如蛋白质等快速消耗,而此时没有外源性营养物质的摄入会导致患者出现营养不良。ALB、TR、Hb 均属于蛋白质营养的一部分,可有效反映人体营养状况。本次研究结果显示,研究组干预后的营养状况改善效果更佳,表明益生菌联合膳食纤维的肠内营养可减缓患者营养状况恶化。益生菌是肠道内有益细菌的总称,可通过分解糖类产生乳酸,使肠道 pH 维持在适宜的酸度,促进营养吸收保持肠道健康,有利于纠正高分解代谢状态,进而改善营养状况^[24,25]。免疫球蛋白是反映机体免疫力的重要参考指标,其中 IgA 可抑制病原菌附着,发挥肠黏膜保护效果;IgM 具有中和病毒、溶解细菌等效果;IgG 可发挥抗感染免疫的效果;当机体发生营养不良时,体内代谢产生的能量不足,导致 IgA、IgG、IgM 分泌受到抑制,使机体向疾病状态趋近。GSH-PX、T-SOD 是体内清除氧自由基的重要酶,GSH-PX 水平降低可间接反映肠黏膜的损伤,MDA 可反映肠黏膜上皮细胞损伤程度和完整性。本研究中益生菌联合膳食纤维的肠内营养的干预方案在免疫功能和肠黏膜屏障功能指标的改善作用更为明显,这是因为益生菌可通过提高肠道免疫球蛋白水平,刺激肠道局部免疫,发挥免疫促进效果^[26,27],同时,益生菌定殖在人体内后,可通过改变宿主某一部位菌群组成从而调节宿主黏膜与系统免疫功能或通过调节肠道内菌群平衡,减少肠内细菌和内毒素易位,降低肠黏膜通透性,防止肠功能衰竭,促进患者恢复^[28]。白东等人^[29]的研究结果表明,重型颅脑损伤患者术后应用益生菌联合膳食纤维的肠内营养,可对肠黏膜屏障发挥较好的保护作用。两组干预后 GCS 评分均提高,且研究组的 GCS 评分更高,提示益生菌联合膳食纤维的肠内营养干预可进一步改善患者预后。另研究组的并发症发生率低于对照组,表明益生菌联合膳食纤维的肠内营养安全有效,可减少并发症发生率,可能是因为益生菌可促进营养物质的吸收,患者抵抗力得以更快恢复,对外界的刺激性反应减小,从而降低了并发症发生率^[30]。本次研究存在样本量偏少、未能设置随访观察患者远期预后等不足,有待后续进行多中心、大样本量的深入研究。

综上所述,益生菌联合膳食纤维的肠内营养可有效改善重型颅脑损伤患者术后营养状况、免疫功能和肠黏膜屏障功能,

同时还可减少并发症发生率,从而改善患者预后。

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