

doi: 10.13241/j.cnki.pmb.2017.05.020

免疫营养素对恶性梗阻性黄疸胆道支架植入术后感染发生率的影响*

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摘要 目的:探讨免疫营养素对恶性梗阻性黄疸患者胆道支架植入术后感染的发生情况及临床预后的影响。**方法:**选择 2013 年 2 月到 2016 年 1 月选择在我院诊治的恶性梗阻性黄疸患者 156 例,据入院顺序分为观察组与对照组各 78 例,两组均行 PTCD+胆道金属支架植入术,观察组入院当日开始给予免疫营养制剂(在普通低脂饮食基础上添加鱼油脂肪酸和复方谷氨酰胺肠溶胶囊)口服,对照组入院当日开始给予普通低脂饮食,两组均治疗 5 d,观察两组预后情况。**结果:**两组术后 15 d 的 CD4⁺ 值都明显高于术后 1 d(P<0.05),观察组术后 15 d 的 CD4⁺ 值也明显高于对照组(P<0.05),两组不同时间点的 CD8⁺ 值对比差异无统计学意义(P>0.05)。观察组与对照组术后 15 d 的血清 IL-6 和 TNF- α 值都明显低于术后 1 d(P<0.05),观察组术后 15 d 的血清 IL-6 和 TNF- α 值也明显低于对照组(P<0.05)。观察组术后感染发生率为 5.1%,明显低于对照组的 20.5%(P<0.05)。**结论:**胆道支架植入术前应用免疫营养素可改善恶性梗阻性黄疸患者的免疫功能,抑制炎症反应,从而减少感染的发生率,促进患者的康复。

关键词:免疫营养素;胆道支架植入术;恶性梗阻性黄疸;感染;免疫

中图分类号:R657.4;R735.8 **文献标识码:**A **文章编号:**1673-6273(2017)05-882-04

Effect of Immune Nutrients on the Incidence of Infection after Biliary Stent Implantation in Patients with Malignant Biliary Obstruction*

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ABSTRACT Objective: To investigate the effects of immune nutrients on the incidence of infection after biliary stent implantation in patients with biliary stent implantation. **Methods:** From February 2013 to January 2016, 156 malignant obstruction jaundice patients were selected in our hospital and randomly divided into the observation group and the control group with 78 patients in each group, both groups were given biliary stent implantation, the observation group was given immunonutrition formula including fish oil fatty acids and glutamine compound enteric coated capsules in the general diet, the control group was treated by general diet from the beginning after admission, both groups were treated for 5 days. **Results:** On the 15th day after operation, the CD4⁺ values of both groups were significantly higher than those on the 1st day after operation (P<0.05), and the CD4⁺ value of observation group was significantly higher than that of the control group (P<0.05). No significant difference was found in the CD8⁺ value between two groups at different time points(P>0.05). On the 15th day after operation, the serum IL-6 and TNF- α levels in both groups were significantly lower than those on the 1st day after operation (P<0.05), and the serum IL-6 and TNF- α levels of observation group were significantly lower than those of the control group (P<0.05). The infection rate of observation group after operation was 5.1%, which was obviously lower than that of the control group of 20.5%(P<0.05). **Conclusion:** Immune nutrition applied before biliary stent implantation could effectively improve the immune function, inhibit the release of inflammatory factors, decrease the infection and further promote the patient's recovery.

Key words: Immune nutrients; Biliary stent implantation; Malignant obstructive jaundice; Infection; Immunity

Chinese Library Classification(CLC): R657.4; R735.8 **Document code:** A

Article ID: 1673-6273(2017)05-882-04

前言

恶性梗阻性黄疸(malignant obstructive jaundice, MOJ)是一类肝胆外科常见的病症,在我国的发病率当前有明显增加的趋势^[1]。外科手术是目前治疗恶性梗阻性黄疸最有效的方式之一,特别是通过胆道支架植入减黄治疗^[2]。但由于 MOJ 患者存在免疫力低下、肠粘膜屏障损伤、肠液逆流等不良因素,胆道

支架植入术后常常因为严重感染并发症而造成患者围手术期死亡^[3]。我科每年收治大量的晚期 MOJ 患者,每年因胆道支架植入术后感染消耗大量医疗资源^[4],保护 MOJ 患者肠道功能、减轻肠粘膜屏障损伤成为预防术后感染的关键因素^[5]。近年来,肠内免疫营养治疗有了很大的进展,其中含 ω -3 鱼油脂肪酸(ω -3PUFAs)和谷氨酰胺的免疫营养素当前应用比较多^[6-8]。本研究旨在建立规范化的术前免疫营养支持的临床方案,以降低恶

* 基金项目:首都市民健康项目培育课题(Z131100006813010)

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(收稿日期:2016-09-21 接受日期:2016-10-20)

性梗阻性黄疸行胆道支架植入术减黄后的感染及脓毒症的发生率,进而降低病死率。现报道如下。

1 资料与方法

1.1 研究对象

选择 2013 年 2 月到 2016 年 1 月在我院诊治的恶性梗阻性黄疸患者 156 例。根据入院顺序分为观察组与对照组各 78 例,两组的性别、年龄、病因、体重指数等基础资料对比差异无统计学意义($P>0.05$)。见表 1。

纳入标准:符合恶性梗阻性黄疸的诊断标准(总胆红素超

过正常值上限,直接胆红素/总胆红素 $>50\%$;肝内伴或不伴有肝外胆管扩张,有恶性肿瘤性疾病所致的肝外胆管受侵或受压表现),适应胆道支架植入术;年龄 30-85 岁;无手术切除指征;签署知情同意书同意术前施行免疫营养支持治疗;研究得到医院伦理委员会的批准。

排除标准:合并严重心、肺、肾功能疾病者;胆道梗阻前合并病毒性肝炎等原发肝脏疾病致肝功能不全者;因胆道出血等其他非感染原因导致病情加重者;伴有十二指肠梗阻,术前不能口服者。

表 1 两组基础资料对比

Table 1 Comparison of the basic data between two groups

Indexs	Observation group(n=78)	Control group(n=78)	t/ χ^2	P
Sex (male/female)	40/38	44/34	0.210	>0.05
Age (years old)	66.55 $\pm$ 11.23	66.13 $\pm$ 9.82	0.287	>0.05
BMI(kg/m ²)	21.09 $\pm$ 3.91	21.88 $\pm$ 2.84	0.331	>0.05
Pathogeny(n)			0.076	>0.05
pancreatic cancer	20	22		
hilar cholangiocarcinoma	20	18		
Hilar metastatic carcinoma	10	8		
Gallbladder carcinoma	8	10		
Bile duct and carcinoma of ampulla	10	10		
Liver cancer	6	8		
Twelve finger cancer	4	2		

1.2 治疗方法

两组都均行经皮肝穿刺胆道金属自膨式金属支架植入术,支架置入成功后留置外引流,观察组:入院当日开始给予免疫营养制剂,在普通低脂饮食基础上添加 ω -3 鱼油脂肪酸(华瑞制药),每次 10 g,1 次/日,复方谷氨酰胺肠溶胶囊(成都地奥),每次 2 粒,3 次/日。对照组:入院当日开始给予普通低脂饮食,尽量控制两组在普通饮食上无差异。两组均治疗 5 d。5 天后行 PTCD+胆道支架植入术。

1.3 观察指标

所有患者入院次日晨、手术当日晨、术后 5 d、术后 15 d,分别检测细胞免疫功能(CD4⁺、CD8⁺值)和炎症因子(IL-6 和 TNF- α),由我院血液科实验室、本院检验科、本院中心实验室检测。

感染发生情况:观察与记录两组术后 15 d 发生的感染情

况,感染判断指标是术后 5 d 体温超过 38.5℃、或血常规白细胞、中性百分比超过正常值。

1.4 统计学分析

应用 SPSS 17.00 进行统计分析,计量数据采用 $\bar{x} \pm s$ 表示,对比采用重复测量资料的方差分析或者配对 t 检验;而计数资料采用两个样本率比较的卡方检验,以 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 两组治疗前后 CD4⁺ 和 CD8⁺ 值对比

两组术后 15 d 的 CD4⁺ 值都明显高于术后 1d ($P<0.05$),观察组术后 15 d 的 CD4⁺ 值也明显高于对照组($P<0.05$),两组不同时间点的 CD8⁺ 值对比差异无统计学意义($P>0.05$)。见表 2。

表 2 两组不同时间点的 CD4⁺ 和 CD8⁺ 值对比($\bar{x} \pm s$)

Table 2 Comparison of the CD4⁺ and CD8⁺ value between two groups at different time points ($\bar{x} \pm s$)

Groups	n	CD4 ⁺		t	P	CD8 ⁺		P
		1 d	15 d			1 d	15 d	
		postoperation	postoperation			postoperation	postoperation	
Observation group	78	24.29 $\pm$ 11.84	45.98 $\pm$ 8.14	11.844	<0.05	28.11 $\pm$ 4.29	27.49 $\pm$ 5.25	>0.05
Control group	78	23.89 $\pm$ 9.98	38.29 $\pm$ 9.13	7.983	<0.05	29.00 $\pm$ 3.49	28.11 $\pm$ 4.09	>0.05
P		>0.05	<0.05			>0.05	>0.05	

2.2 两组治疗前后血清 IL-6 和 TNF- α 水平对比

两组术后 15 d 的血清 IL-6 和 TNF- α 值都明显低于术后 1

d($P<0.05$),观察组术后 15 d 的血清 IL-6 和 TNF- α 值明显低于对照组($P<0.05$)。见表 3。

表 3 两组不同时间点血清 IL-6 和 TNF-α 值对比($\bar{x} \pm s$)

Table 3 Comparison of the serum IL-6 and TNF-α values between two groups at different time pointst($\bar{x} \pm s$)

Groups	n	IL-6(pg/mL)		P	TNF-α(ng/L)		P
		1 d postoperation	15 d postoperation		1 d postoperation	15 d postoperation	
Observation group	78	30.37± 20.78	14.56± 9.47	<0.05	56.39± 18.26	20.62± 9.08	<0.05
Control group	78	30.79± 14.69	18.71± 13.63	<0.05	56.88± 15.34	24.41± 11.54	<0.05
P		>0.05			>0.05		

2.3 两组术后感染情况对比

观察组术后感染发生率为 5.1%(4/78),明显低于对照组的 20.5%(16/78)。见表 4。

表 4 两组术后感染情况对比(n)

Table 4 Comparison of the incidence of postoperative infection between two groups (n)

Groups	n	Incidence of infection
Observation group	78	5.1%
Control group	78	20.5%
P		<0.05

3 讨论

MOJ 是指因肝胆胰恶性肿瘤生长、浸润或其他器官恶性肿瘤的转移、压迫、浸润导致肝内外胆管梗阻所引起的一种临床症状^[9],胆道内支架置入术已成为目前晚期恶性梗阻性黄疸姑息性减黄治疗的主要治疗方法^[10]。MOJ 患者在接受治疗之后的疾病症状减轻,但是也能可发生一些并发症,给患者手的预后情况带来一些负面影响,如胆道内支架置入术的术后并发症如感染、出血、漏胆、诱发胰腺炎等较为常见,特别是术后感染最为常见,发生率可高达 30-50%^[11]。MOJ 造成的机体免疫力的低下、肠粘膜屏障的破坏导致肠道细菌移位以及胆道支架植入术后逆行感染等原因,最终导致肠源性内毒素入血,从而造成术后严重的脓毒症和 MODS, 严重者往往导致患者围手术期死亡^[12,13]。

ω-3 鱼油脂肪酸(ω-3PUFAs)的主要成分为二十碳五烯酸(eicosapentaenoic acid,EPA) 和 二十二碳六烯酸(docosahexaenoic acid,DHA),机体自身只能极少量合成。EPA 和 DHA 可增加细胞膜磷脂(I)-3 脂肪酸成分,在减少炎性二十烷类产生的同时增加非炎性二十烷类产生,以竞争花生四烯酸至二十烷类合成途径,从而调节机体内一系列细胞因子的水平,增强机体免疫功能^[14]。谷氨酰胺(glutamine,Gln)是一种条件必需氨基酸,作为肝内糖异生的重要底物是肠粘膜上皮细胞的主要能源燃料,同时可促进粘膜上皮细胞的再生和修复,对维持小肠粘膜屏障形态和功能完整性具有重要作用^[15]。研究表明在各种肠内或肠外营养中,添加 Gln 能逆转肠粘膜萎缩、修复肠粘膜、增强肠道免疫功能、防止肠道细菌移位^[16]。本研究结果显示观察组术后感染发生率为 5.1%,明显低于对照组 (20.5%),表明免疫营养素可降低胆道支架植入术后的感染的发生率,促进患者的康复。

恶性梗阻性黄疸术后过度的促炎反应是造成全身炎症反应综合征和多器官功能障碍综合征的重要原因,过度促炎反应

后继发的抗炎反应可造成免疫功能抑制,成为患者预后不良的重要原因。因此,营养支持目标是需要调整炎症反应平衡、调节免疫功能紊乱及预防菌群移位^[17,18]。ω-3 鱼油脂肪酸和谷氨酰胺等在发挥营养支持作用之外,还能够增强免疫细胞应答能力,调控细胞因子的产生和释放,减轻有害或过度的炎性反应,维持肠粘膜屏障的结构和功能^[19,20]。本研究结果显示所有患者术后 15 d 的 CD4⁺ 值都明显高于术后 1 d,血清 IL-6 和 TNF-α 值都明显低于术后 1 d,同时观察组术后 15 d 的 CD4⁺ 值明显高于对照组,血清 IL-6 和 TNF-α 值明显低于对照组(P<0.05)。这表明梗阻性黄疸患者术后给予肠内营养制剂中添加 ω-3 鱼油脂肪酸和谷氨酰胺能阻断恶性梗阻性黄疸患者的过度炎症反应,保护免疫功能。

总之,术前应用免疫营养素可改善胆道支架植入术患者的免疫功能,抑制炎症因子的释放,从而减少感染的发生率,促进患者的康复,其是一种安全、有效的营养支持方式。

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