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早期肠内营养对胃癌根治术患者术后恢复和免疫功能的影响*

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摘要 目的:评价早期肠内营养(EEN)对胃癌根治术患者术后恢复和免疫功能的影响。**方法:**选入 2011 年 6 月~2014 年 1 月在我院行胃癌根治术治疗的患者 60 例,根据术后营养方式不同分为 EEN 组和全肠外营养支持(TPN)组,每组 30 例。比较两组患者机体恢复及免疫功能情况。术后随访 3 年,观察并记录两组无进展生存率和总生存率。**结果:**EEN 组术后排气时间[(2.46±0.78)d vs (3.85±1.03)d]、排便时间[(4.03±1.17)d vs (5.67±1.23)d]、进流质时间[(5.88±1.30)d vs (7.26±1.59)d]、进半流食时间[(7.94±1.85)d vs (11.01±2.36)d]和住院天数[(14.87±2.56)d vs (17.54±3.30)d]均显著短于 TPN 组,差异均有统计学意义($P<0.05$)。术后第 1d,两组各项体液免疫指标(IgA、IgG、IgM 浓度)和细胞免疫指标(CD3⁺、CD4⁺和 CD4⁺/CD8⁺水平)均显著下降($P<0.05$),营养支持后逐渐恢复,而 EEN 组恢复幅度较 TPN 组大,差异具有统计学意义($P<0.05$)。EEN 组术后并发症总发生率显著低于 TPN 组(13.33% vs 36.67%, $P<0.05$)。EEN 组患者 1 年、2 年和 3 年无进展生存率和总生存率均稍高于 TPN 组,但差异无统计学意义($P>0.05$)。**结论:**EEN 可有效促进胃癌根治术患者的肠功能恢复,缩短住院时间,提高机体免疫功能,降低并发症的发生,值得在临床推广应用。

关键词:胃癌根治术;早期肠内营养;全肠外营养支持;机体恢复;免疫功能;并发症

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Effect of Early Enteral Nutrition on Postoperative Recovery and Immune Function in Patients Undergoing Radical Gastrectomy for Gastric Cancer*

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ABSTRACT Objective: To evaluate the effect of early enteral nutrition (EEN) on postoperative recovery and immune function in patients undergoing radical gastrectomy for gastric cancer. **Methods:** 60 patients with gastric cancer underwent radical gastrectomy in our hospital from June 2011 to January 2014 were divided into EEN group and total parenteral nutrition (TPN) group according to the postoperative nutrition, 30 cases in each group. The recovery and immune function of the two groups were compared. All patients were followed up for 3 years. The progression free survival rate and overall survival rate of the two groups were observed and recorded. **Results:** The postoperative exhaust time [(2.46±0.78)d vs. (3.85±1.03)d], defecation time [(4.03±1.17)d vs. (5.67±1.23)d], liquid diet time [(5.88±1.30)d vs. (7.26±1.59)d], semi liquid diet time [(7.94±1.85)d vs. (11.01±2.36)d] and length of stay [(14.87±2.56)d vs. (17.54±3.30)d] in EEN group were significantly shorter than those in TPN group, the differences were statistically significant ($P<0.05$). At postoperative 1d, the humoral immune indices (IgA, IgG, IgM) and cellular immunity indices (CD3⁺, CD4⁺ and CD4⁺/CD8⁺) of two groups were significantly decreased ($P<0.05$), which gradually recovered after nutrition support, and the recovery of EEN group was larger than that of TPN group, the difference was statistically significant ($P<0.05$). The incidence of postoperative complications in EEN group was significantly lower than that in TPN group (13.33% vs. 36.67%, $P<0.05$). The 1 year, 2 year and 3 year progression free survival rate and overall survival rate of patients in EEN group were higher than those in TPN group, but the differences were not statistically significant ($P>0.05$). **Conclusion:** EEN can effectively promote the recovery of intestinal function in patients undergoing radical gastrectomy for gastric cancer, shorten the length of stay, improve the immune function and reduce the incidence of complications, it is worthy of recommendation in clinical practice.

Key words: Radical gastrectomy; EEN; TPN; Body recovery; Immune function; Complication

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前言

胃癌是最常见的胃肠道恶性肿瘤之一,具有较高的发病率和死亡率,严重威胁着人民的生命健康^[1-3]。胃癌患者由于食欲不佳和肿瘤本身的消耗,术前伴随着不同程度营养不良,而手术创伤和应激使患者处于高代谢紊乱状态,加重了营养不良^[4-6]。营养不良不仅增加手术治疗的风险,同时降低了机体的免疫功能,增加术后感染、肺功能障碍等并发症的发生率及死亡率^[7-9]。因此,对胃癌患者采取有效的营养支持是必要的,也是至关重要的。全胃肠外营养(total parenteral nutrition, TPN)是胃癌根治术患者选择营养支持治疗的“金标准”,但长期使用可引起多种功能和代谢性并发症^[10-12]。早期肠内营养(early enteral nutrition, EEN)在术后能够有效降低并发症并促进患者康复,逐渐得到越来越多临床医生的重视和应用^[13-15],但 EEN 对于患者术后免疫功能的影响尚无统一认识,本研究旨在评价 EEN 对胃癌根治术患者术后恢复和免疫功能的影响,为临床应用提供参考,现报告如下。

1 资料和方法

1.1 一般资料

选入 2011 年 6 月~2014 年 1 月在我院行胃癌根治术治疗的患者 60 例,纳入标准:(1)术前亦明确诊断,术后病理学确诊为胃癌,并行胃癌根治术(全胃切除术、远端胃切除术、近端胃切除术)治疗;(2)近期无白蛋白和/或免疫增强剂服用史以及放化疗史;(3)术前肠功能正常;(4)知情同意。排除标准:(1)术前合并肝肾功能异常、凝血功能障碍、免疫缺陷以及内分泌疾病等;(2)术前肠内或肠外营养治疗,伴有严重胃肠功能障碍;(3)肿瘤出现远处转移及广泛转移;(4)已知对营养液某成分过敏;(5)近期应用免疫抑制剂或化疗药物。将本组患者根据术后营养方式不同分为 EEN 组和 TPN 组,每组 30 例。其中 EEN 组,男 18 例,女 12 例,年龄 43~77 岁,平均年龄(60.81±8.42)岁;术前体重 51~79kg,平均(64.35±5.62)kg;肿瘤 TNM 分期:II 期 10 例,III 期 20 例。TPN 组中,男 16 例,女 14 例,年龄 44~78 岁,平均年龄(61.13±8.50)岁;术前体重 49~81kg,平均(65.09±5.74)kg;TNM 分期:II 期 9 例,III 期 21 例。两组一般资料差异无统计学意义($P>0.05$),临床资料具均衡可比性。

1.2 方法

EEN 组:胃癌患者通过术中放置鼻肠管至空肠吻合口以下 30~40 cm 处,于术后 12~24h 输注 0.9% NaCl 溶液 0.5 L,术后 24h 开始输注肠内营养乳剂(TP)——瑞素,热量为 30 mL (30kcal)/(kg·d),营养成分包括蛋白质(3.8%)、脂肪(3.4%)、饱和脂肪酸(1.6%)、不饱和脂肪酸(1.3%)、中链甘油三酯(1.2%)、碳水化合物(13.8%)及糖(0.5%)等,连续输注 7d,依据先慢后快、先稀后浓的原则,并根据患者的耐受情况逐步调节用量及输注速度,从半量逐步过渡至全量;可经口饮食后,逐渐减少 EEN 输入量,并适当补充电解质、维生素及微量元素等,营养液温度控制在 39℃左右,以免冷刺激引起肠痉挛,导致腹痛、腹泻。TPN 组:术后 24h 开始应用与 EEN 组等氮等热量的全肠外营养支持,肠外制剂选用卡文(脂肪乳氨基酸葡萄糖注射液),首选外周静脉输入,患者无法耐受时改为经外周静脉置入中心静脉导管(peripherally inserted central catheter, PICC)输入,每日输入时间为 18~20 h,并根据患者情况补充电解质、维生素以及微量元素。连续治疗 7d,可经口饮食后,逐渐减少 TPN 输入量。

1.3 观察指标

(1)记录患者术后第 1 次排气时间、排便时间、进流质时间、进半流质时间和住院天数;(2)免疫指标:分别于术前 1d、术第 1d、第 8d 晨起静脉采血,采用免疫透射比浊法测定体液免疫指标免疫球蛋白 IgA、IgG、IgM 浓度,采用流式细胞仪技术检测细胞免疫指标 T 淋巴细胞亚群 CD3⁺、CD4⁺ 和 CD4⁺/CD8⁺ 水平;(3)统计并发症情况;(4)术后随访 3 年,记录两组患者无进展生存率和总生存率。

1.4 统计学方法

通过 SPSS 21.0 软件进行数据统计分析,其中计量资料以($\bar{x} \pm s$)的形式表示,计数资料以率(n/%)的形式表示,分别进行 t 检验和 χ^2 检验, $P<0.05$ 表示差异有统计学意义。

2 结果

2.1 两组术后恢复情况比较

EEN 组术后排气时间、排便时间、进流质时间、进半流食时间和住院天数均显著短于 TPN 组,差异均有统计学意义($P<0.05$),见表 1。

表 1 两组术后恢复情况比较($\bar{x} \pm s$)

Table 1 Comparison of postoperative recovery between two groups($\bar{x} \pm s$)

Groups	n	Postoperative exhaust time(d)	Defecation time(d)	Liquid diet time(d)	Semi liquid diet time(d)	Length of stay(d)
EEN group	30	2.46±0.78	4.03±1.17	5.88±1.30	7.94±1.85	14.87±2.56
TPN group	30	3.85±1.03	5.67±1.23	7.26±1.59	11.01±2.36	17.54±3.30
T value		5.893	5.291	3.680	5.607	3.501
P value		0.000	0.000	0.000	0.000	0.000

2.2 两组免疫指标比较

术后第 1d,两组各项体液免疫指标(IgA、IgG、IgM 浓度)和细胞免疫指标(CD3⁺、CD4⁺ 和 CD4⁺/CD8⁺ 水平)均显著下降($P<0.05$);营养支持后逐渐恢复,而 EEN 组恢复幅度较 TPN 组

大,差异具有统计学意义($P<0.05$),见表 2。

2.3 两组并发症情况比较

EEN 组术后并发症总发生率 13.33%,显著低于 TPN 组的 36.67%,差异具有统计学意义($P<0.05$),见表 3。

表 2 两组各项免疫指标结果比较($\bar{x} \pm s$)Table 2 Comparison of immune indexes between two groups($\bar{x} \pm s$)

Groups	Time	Humoral immunity indices			Cellular immune indices		
		IgA(g/L)	IgG(g/L)	IgM(g/L)	CD3 ⁺ (%)	CD4 ⁺ (%)	CD4 ⁺ /CD8 ⁺
EEN group	Preoperative	1.90± 0.54	11.53± 2.77	1.17± 0.41	58.97± 4.85	36.42± 4.43	1.44± 0.36
	Postoperative 1d	1.36± 0.47 ^a	8.34± 1.85 ^a	0.77± 0.31 ^a	45.07± 5.63 ^a	26.97± 3.86 ^a	0.91± 0.28 ^a
	Postoperative 8d	2.01± 0.72b*	11.80± 3.12b*	1.25± 0.37b*	59.18± 6.27b*	37.66± 4.64b*	1.47± 0.39b*
	F value	10.566	16.002	14.839	62.256	54.889	24.801
	P value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
TPN group	Preoperative	1.88± 0.57	11.48± 2.81	1.22± 0.43	58.54± 4.52	36.55± 4.51	1.42± 0.34
	Postoperative 1d	1.30± 0.44 ^a	7.99± 1.96 ^a	0.75± 0.30 ^a	44.14± 5.40 ^a	25.88± 3.90 ^a	0.85± 0.27 ^a
	Postoperative 8d	1.65± 0.51 ^b	10.13± 2.86 ^b	0.95± 0.29 ^{ab}	55.79± 6.12 ^b	32.96± 4.38 ^{ab}	1.18± 0.30 ^{ab}
	F value	9.86	13.995	13.947	60.425	48.469	26.467
	P value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

Note: Compared with preoperative, ^a $P<0.05$; Compared with postoperative 1d, ^b $P<0.05$; Compared with TPN group at the same time, * $P<0.05$.

表 3 两组术后并发症情况比较[n(%)]

Table 3 Comparison of postoperative complications between two groups[n(%)]

Groups	n	Digestive tract reaction	Pulmonary infection	Anastomotic fistula	Incisional infection	Intestinal obstruction	Total incidence rate(%)
EEN group	30	2(6.67)	1(3.33)	0(0.00)	1(3.33)	0(0.00)	13.33
TPN group	30	1(3.33)	3(10.00)	3(10.00)	3(10.00)	1(3.33)	36.67
χ^2 value							4.356
P value							0.037

2.4 两组患者生存情况比较

稍高于 TPN 组,但差异无统计学意义($P>0.05$),见表 4。

EEN 组患者 1 年、2 年和 3 年无进展生存率和总生存率均

表 4 两组患者无进展生存率和总生存率比较[n(%)]

Table 4 Comparison of progression free survival rate and overall survival rate in two groups of patients

Groups	n	Progression free survival rate			Overall survival rate		
		1 year	2 year	3 year	1 year	2 year	3 year
EEN group	30	22(73.33)	15(50.00)	11(36.67)	26(86.67)	22(73.33)	18(60.00)
TPN group	30	18(60.00)	10(33.33)	6(20.00)	22(73.33)	17(56.67)	14(46.67)
χ^2 Value		1.200	1.714	2.052	1.667	1.831	1.701
P Value		0.273	0.190	0.152	0.197	0.176	0.301

3 讨论

胃癌患者由于肿瘤影响、厌食、味觉异常、恶心呕吐、消化吸收障碍以及肿瘤大量消耗等原因,常伴有营养不良,而较大范围的根治性切除术带来的创伤、机体应激反应、高代谢状态以及术后长时间禁食,又会加重营养不良^[16-18]。临床报道证实,营养不良可导致机体免疫功能低下,增加感染、器官功能障碍等多种并发症的发生风险,影响预后^[19-21]。近年来,应用于肿瘤患者营养支持的肠内、肠外营养剂发展很快,营养支持的概念逐渐受到人们的重视,其在促进患者免疫功能恢复、改善预后方面的价值也逐渐被认可。

TPN 是胃癌根治术患者的重要营养途径之一,提供包括热量、氨基酸、脂肪、电解质、微量元素等在内的相关营养素,可使机体在不能进食的情况下仍能维持良好的营养状态与相关正氮平衡,减少体重丢失,促进伤口愈合,且使用方便、安全^[22-24]。但在调节免疫功能、改善应激反应方面疗效欠佳,长期使用还会导致肠饥饿综合征,继而引发肠道细菌易位、肠粘膜损害、肝内淤胆以及免疫相对抑制等并发症,严重可导致毒血症的发生,且价格比较昂贵^[25,26]。随着对胃癌根治术后肠道功能的深入研究认识到,肠内营养支持的营养物质经小肠吸收,由肠系膜静脉回流入肝门静脉,更符合生理,有利于肝脏的蛋白质合成,同时维持肠道的生理功能,降低肠源性感染的发生^[27,28]。而传统

观点认为,只有胃肠道功能恢复,即肛门排气/排便后才可进行肠内营养支持。现代胃肠动力学研究表明,术后胃肠道麻痹仅限于胃和结肠,小肠蠕动与吸收功能在术后数小时便可恢复正常。已有报道证实^[29],EEN可促进肠道功能恢复,维持肠黏膜的屏障作用;另外,EEN可促进机体的蛋白质代谢,纠正营养不良,提高机体的免疫力。本研究中,EEN组术后排气时间、排便时间、进流质时间、进半流食时间和住院天数均显著短于TPN组($P<0.05$);术后第1d,两组各项体液免疫指标(IgA、IgG、IgM浓度)和细胞免疫指标(CD3⁺、CD4⁺和CD4⁺/CD8⁺水平)均显著下降($P<0.05$);营养支持后逐渐恢复,而EEN组恢复幅度较TPN组大,差异具有统计学意义($P<0.05$);EEN组术后并发症总发生率显著低于TPN组(13.33% vs. 36.67%, $P<0.05$)。鲁力等^[30]研究了早期肠内营养对老年胃癌患者术后免疫功能及营养状态的影响,结果表明,早期肠内营养组患者术后第1d白蛋白、前白蛋白、转铁蛋白、CD4⁺、CD8⁺和CD4⁺/CD8⁺水平下降程度均显著低于未进行早期肠内营养支持的患者,术后8d时早期肠内营养组患者上述各指标均恢复正常,而未进行早期肠内营养支持的患者上述指标仍低于正常范围。

综上所述,EEN可有效促进胃癌根治术患者的肠功能恢复,缩短住院时间,提高机体免疫功能,降低并发症的发生,值得临床推荐。

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