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基于 L- 丙氨酰谷氨酰胺的肠外营养在 ICU 重症颅脑损伤的应用 *

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摘要 目的：探讨基于 L- 丙氨酰谷氨酰胺的肠外营养在重症监护病房(Intensive Care Unit，ICU)重症颅脑损伤的应用价值。**方法：**2018 年 6 月到 2020 年 6 月选择在本院 ICU 诊治的重症颅脑损伤患者 540 例，根据随机数字表法把患者分为研究组与对照组各 270 例。对照组给予标准肠外营养支持方法，研究组在对照组治疗的基础上给予 L- 丙氨酰谷氨酰胺辅助治疗，两组都治疗观察 14 d。**结果：**研究组治疗第 7 d 与 14 d 的营养不足发生率分别为 4.8 %和 6.7 %，显著低于对照组的 13.0 %和 17.0 %(P<0.05)。两组治疗后的血清总蛋白与白蛋白含量高于治疗前，研究组高于对照组，对比差异都有统计学意义(P<0.05)。研究组治疗期间的肺部感染、尿路感染、消化道反应、压疮等并发症发生率为 4.8 %，显著低于对照组的 15.6 %(P<0.05)。两组治疗后的血清降钙素原(Procalcitonin，PCT)值低于治疗前，研究组低于对照组，对比差异都有统计学意义(P<0.05)。**结论：**基于 L- 丙氨酰谷氨酰胺的肠外营养在 ICU 重症颅脑损伤的应用能降低患者营养不足与并发症发生率，促进恢复机体的营养状况，抑制 PCT 的释放。

关键词：L- 丙氨酰谷氨酰胺；肠外营养；ICU；重症颅脑损伤；降钙素原

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Application of L-alanylglutamine-based Parenteral Nutrition in ICU with Severe Head Injury*

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ABSTRACT Objective: To explore the application values of L-alanylglutamine-based parenteral nutrition in the Intensive Care Unit (ICU) of severe head injury. **Methods:** A total of 540 patients with severe head injury, who were diagnosed and treated in the ICU of First Affiliated Hospital of Xinjiang Medical University from June 2018 to June 2020, were selected and were randomly divided into study group(n=270) and control group(n=270). The control group was given standard parenteral nutrition support, and the study group was given L-alanylglutamine adjuvant therapy based on the treatment of the control group. Both groups were treated and observed for 14 days. **Results:** The incidence(4.8 % and 6.7 %) of undernutrition on the 7th and 14th day of treatment in the study group was significantly lower than that (13.0 % and 17.0 %) in the control group (P<0.05). The serum total protein and albumin content of the two groups after treatment were higher than that before treatment, and the study group was higher than that of the control group, and the differences were statistically significant (P<0.05). The incidence of complications such as lung infection, urinary tract infection, digestive tract reaction, pressure ulcers, etc. during treatment in the study group was 4.8 %, which were significantly lower than that (15.6 %) in the control group (P<0.05). The serum procalcitonin (PCT) value of the two groups after treatment was lower than that before treatment, and the study group was lower than that of the control group, the difference was statistically significant (P<0.05). **Conclusion:** The application of parenteral nutrition based on L-alanylglutamine in ICU with severe head injury can reduce the incidence of undernutrition and complications, promote the restoration of the body's nutritional status, and inhibit the release of PCT.

Key words: L-alanylglutamine; Parenteral nutrition; ICU; Severe head injury; Procalcitonin

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前言

颅脑损伤当前在临床上比较常见，其中重症颅脑损伤患者具有很高的死亡率，多需要在重症监护病房(Intensive Care Unit，ICU)进行急救[1]。并且该病患者在发病后可导致全身处于应激状态，极易造成感染及脓毒血症，使得机体出现营养不良，

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导致病情急剧恶化并形成多器官功能衰竭，是重型颅脑损伤患者致死的重要原因之一[2,3]。不过很多患者因为意识功能丧失、胃肠功能障碍、吞咽困难等原因，可导致机体出现神经 - 内分泌轴受损，导致患者进食困难[4,5]。有研究显示，营养不足可使得颅脑损伤患者的健康状况的进一步恶化，增加医疗费用支出，延长住院时间延长[6]。并且营养不足可造成机体免疫系统损害，从而降低身体抵御感染的能力，增加并发症的发生[7,8]。营养支持能保持机体肠道的完整性，能减少细菌易位，促进维持机体氮平衡，提高机体免疫力，还能改善患者心理及生理功能[9,10]。L-丙氨酰谷氨酰胺是人体的重要营养支持氨基酸，主要含丙氨酸和谷氨酰胺等两种成分，其中谷氨酰胺是人体最重要、功能最多、含量最高的游离氨基酸，能有效促进机体蛋白合成，具有影响免疫系统识别、吞噬和杀菌等功能[11,12]。本文具体探讨了基于 L- 丙氨酰谷氨酰胺的肠外营养在 ICU 重症颅脑损伤的应用价值，以明确 L- 丙氨酰谷氨酰胺的作用效果与机制。现总结报道如下。

1 资料与方法

1.1 研究对象

2018 年 6 月到 2020 年 6 月选择在本院 ICU 诊治的重症颅脑损伤患者 540 例，纳入标准：符合重症颅脑损伤的诊断标准，在 ICU 急诊治疗，预计生存期≥ 1 个月；年龄 30~70 岁；具有肠外营养支持的指征；医院伦理委员会批准了此次研究；患者或者患者家属知情同意本研究。排除标准：有自身免疫性疾病史或过去 6 个月内服用免疫抑制剂的患者；临床资料缺乏者；妊娠与哺乳期妇女；在研究期间死亡的患者；入院时即存在肺炎或其他感染性疾病的患者；既往有消化道出血等严重器官功能障碍者。

根据随机数字表法把患者分为研究组与对照组各 270 例，两组患者的 APACHEⅡ评分、性别、年龄、病因、GCS 评分、体重指数等对比差异无统计学意义(P>0.05)，见表 1。

表 1 两组一般资料对比

Table 1 Comparison of general data between two groups

Groups	n	APACHEⅡ score (score)	Gender (M/F)	Age (years)	Etiology (cerebral contusion / intracerebral hematoma / subdural hematoma / epidural hematoma)	GCS score (score)	BMI (kg/m^2)
Study group	270	13.26± 1.92	143/127	49.22± 2.17	58/67/52/93	8.42± 1.44	22.76± 1.42
Control group	270	13.33± 2.22	144/126	49.76± 1.73	55/70/55/90	8.49± 1.22	22.19± 2.09

1.2 营养支持方法

对照组：给予标准肠外营养支持方法，采用 10 %脂肪乳、50 %葡萄糖双能源，使用 1.5 %复合氨基酸供氮(非蛋白热卡：氮为 130：1)，加入微量元素、电解质、胰岛素，配成全营养混合液，在 24 h 内采用深静脉输入。

研究组：在对照组治疗的基础上给予 L- 丙氨酰谷氨酰胺辅助治疗，静脉注射 20 % L- 丙氨酰谷氨酰胺注射液，0.40 g/kg，1 次 /d。

两组都治疗观察 14 d。

1.3 观察指标

(1) 所有患者在治疗第 7 d 与 14 d 采用营养风险量表(NRS-2002) 进行筛查，NRS-2002 评分≥ 3 分表示为营养不足。(2)记录所有患者在治疗前后抽取患者的空腹静脉血，低温离心后分离上层血清，采用全自动生化分析仪检测血清总蛋白与白蛋白含量。(3)记录两组患者在治疗过程中出现的肺部感染、尿路感染、消化道反应、压疮等并发症情况。(4)取上述的血清学样本，采用全自动免疫检测系统检测降钙素原(Procalcitonin，PCT)含量。

1.4 统计方法

选择 SPSS18.00 软件对本研究的所有数据进行分析，计数资料采用百分比(%)描述(对比为卡方分析)，计量数据采用(均数± 标准差)、或中位数(M)和四分位数间距(Q)表示(对比为 t 检验)，检验水准为α=0.05。

2 结果

2.1 营养不足发生率对比

研究组治疗第 7 d 与 14 d 的营养不足发生率分别为 4.8 %和 6.7 %，显著低于对照组的 13.0 %和 17.0 %(P<0.05)，见表 2。

表 2 两组营养不足发生率对比(例，%)

Table 2 Comparison of incidence of undernutrition between two groups (n, %)

Groups	n	Treatment on the 7th day	Treatment on the 14th day
Study group	270	13(4.8)*	18(6.7)*
Control group	270	35(13.0)	46(17.0)

Note: a compared with the control group, *P<0.05.

2.2 血清总蛋白与白蛋白含量变化对比

两组治疗后的血清总蛋白与白蛋白含量高于治疗前，研究组高于对照组，对比差异都有统计学意义(P<0.05)。见表 3。

2.3 并发症情况对比

研究组治疗期间的肺部感染、尿路感染、消化道反应、压疮等并发症发生率为 4.8 %，显著低于对照组的 15.6 %(P<0.05)，见表 4。

表 3 两组治疗前后血清总蛋白与白蛋白含量变化对比(g/L,$\bar{x}\pm s$)

Table 3 Comparison of serum total protein and albumin content between two groups before and after treatment (g/L, $\bar{x}\pm s$)

Groups	n	Total protein		Album	
		Pre-treatment	After treatment	Pre-treatment	After treatment
Study group	270	34.10± 6.38	52.28± 4.58#*	6.51± 0.28	12.30± 0.88#*
Control group	270	34.20± 7.35	40.00± 5.14#	6.50± 0.14	8.44± 0.68#

Note: a compared with the control group, *P<0.05, a compared with the pre-treatment, #P<0.05.

表 4 两组治疗后并发症情况对比(例,%)

Table 4 Comparison of complications after treatment between two groups (n, %)

Groups	n	Pulmonary infection	Urinary tract infections	Digestive tract reaction	Pressure sore	Total
Study group	270	1	2	6	4	13(4.8)*
Control group	270	5	7	21	9	42(15.6)

2.4 血清 PCT 变化对比

两组治疗后的血清 PCT 值低于治疗前，研究组低于对照组,对比差异都有统计学意义(P<0.05),见表 5。

表 5 两组治疗前后血清 PCT 变化对比(μg/L,$\bar{x}\pm s$)

Table 5 Comparison of serum PCT changes before and after treatment between two groups (μg/L, $\bar{x}\pm s$)

Groups	n	Pre-treatment	After treatment
Study group	270	7.82± 0.15	0.98± 0.11#*
Control group	270	7.88± 0.13	3.10± 0.18#

3 讨论

重型颅脑损伤患者多处于应激状态，主要表现为高血糖、胃肠功能低下、尿氮排出增加、能量消耗增加、分解代谢增高等,将促使机体诱发出现各种并发症,加重脑水肿、降低机体免疫功能,是导致患者死亡的重要原因之一[13,14]。营养支持可以有效地改善患者的营养状况,轻胃肠道的消化负担,维持胃肠道正常的功能,帮助患者尽快恢复神经功能与改善预后[15]。

有研究表明重型颅脑损伤的患者伴随有体内血浆丙氨酰谷氨酰胺表达水平下降,无法满足正常组织代谢。丙氨酰谷氨酰胺是人体的必需氨基酸，是胃肠黏膜细胞的主要能量来源,也为肠上皮细胞和免疫细胞提供主要氮源,是蛋白质、核酸等生化代谢的中间体,可促进蛋白合成[16,17]。研究表明 L- 丙氨酰谷氨酰胺具有维持肠黏膜组织结构,提高肠道黏膜免疫球蛋白水平,促进胃肠激素的分泌与改善肠黏膜通透性等作用[18]。本研究显示研究组治疗第 7 d 与 14 d 的营养不足发生率分别为 4.8 %和 6.7 %,显著低于对照组的 13.0 %和 17.0 %;两组治疗后的血清总蛋白与白蛋白含量高于治疗前，研究组高于对照组,与邓明[19]等学者的研究类似,该学者探讨丙氨酰谷氨酰胺对重型颅脑损伤患者肠黏膜通透性及血浆二胺氧化酶的影响,结果显示治疗后观察组血清总蛋白于白蛋白含量均显著高于对照组，表明基于 L- 丙氨酰谷氨酰胺的肠外营养在重症颅脑损伤的应用能降低营养不足发生率,纠正营养代谢障碍,改善患者营养状况,保护肠道黏膜屏障功能,提高总蛋白与白蛋白含量。特别是外源性 L- 丙氨酰谷氨酰胺是一种常用的人工合成的含谷氨酰胺二肽,性质稳定,纯度可达 100 %,加入到氨基酸中不影响体内谷氨酰胺的稳定性,应用安全性比较好[20,21]。

重型颅脑损伤发生后中枢神经受到严重损伤,丘脑、脑干、大脑皮层、下丘脑等功能出现紊乱,可导致患者出现食欲减退、进食障碍[22]。同时严重的应激反应可促使患者加速内脏蛋白的消耗,导致糖和脂肪代谢紊乱,使得体重显著下降。所以在这个时期要尽量减少机体蛋白质的消耗，通过提供适当的营养支持,满足机体高代谢的能量和其它营养素的需要[23,24]。本研究显示研究组治疗期间的肺部感染、尿路感染、消化道反应、压疮等并发症发生率为 4.8 %,显著低于对照组的 15.6 %,与马建华[25]等学者的研究探讨肠外营养添加丙胺酰谷氨酰胺和大剂量维生素 C 治疗急性重症创伤病人的应用价值，将 60 例急性重症创伤病人分为对照组(传统肠外营养治疗)和治疗组(传统肠外营养治疗添加丙氨酰谷氨酰胺和大剂量维生素 C),治疗后,治疗组感染发生率显著低于对照组，表明基于 L- 丙氨酰谷氨酰胺的肠外营养在重症颅脑损伤的应用能降低并发症的发生。从机制上分析,L- 丙氨酰谷氨酰胺可为肠黏膜提供能量，在肠道局部减轻炎症反应、维护肠屏障功能,可防止细菌移位和肠道毒素入血[26,27];并且能使药物能够辅助纠正患者的免疫紊乱状态,能有效促进机体蛋白合成、改善肠粘膜屏障,从而减少并发症的发生[28,29]。

重型颅脑损伤患者往往伴随有 PCT 的显著升高，其为一种无激素活性的糖蛋白,几乎不在健康人中表达,但在机体受到创伤、感染、应激等强烈刺激时 PCT 水平会显著升高,其升高程度可反映机体的病情状况[30,31]。本研究显示两组治疗后的

血清 PCT 值低于治疗前，研究组低于对照组，与明自强[32]等学者的研究类似，观察丙氨酰谷氨酰胺强化的营养支持对老年脓毒症患者的免疫和急性炎症反应的调理作用，丙氨酰谷氨酰胺组给予静滴丙氨酰谷氨酰胺联合常规治疗，对照组仅给予常规治疗(热量同前)，治疗后两组均 PCT 下降，且丙氨酰谷氨酰胺组显著低于对照组，表明基于 L- 丙氨酰谷氨酰胺的肠外营养在重症颅脑损伤的应用能抑制 PCT 的释放。不过也有研究表明，不合理使用肠外营养不仅会加重机体代谢的负担，而且还加重了生理功能的紊乱，为此在临床使用中要慎重使用[33,34]。且本研究也有一定的不足，没有进行长期随访，也没有进行肠内营养支持的对照分析，将在后续研究中深入分析。

总之，基于 L- 丙氨酰谷氨酰胺的肠外营养在 ICU 重症颅脑损伤的应用能降低患者营养不足与并发症发生率，促进恢复机体的营养状况，抑制 PCT 的释放。

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