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复方α酮酸联合常规营养干预对维持性血液透析患者炎症反应及氧化应激反应的影响

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[摘要] **目的**:探讨复方α酮酸联合常规营养干预对维持性血液透析患者炎症反应及氧化应激反应的影响。**方法**:收集在本院接受维持性血液透析治疗的尿毒症患者78例,按照随机数表法分为对照组、观察组各39例。对照组接受常规营养干预,观察组接受复方α酮酸联合常规营养干预。透析前及透析后6个月,检测两组患者血清中炎症因子、氧化应激指标的含量。**结果**:透析前,两组血清中炎症因子、氧化应激指标含量比较,差异无统计学意义($P>0.05$)。透析后,两组血清中CRP、IL-6、TNF-α、MDA、AOPP的含量均高于透析前,SOD、GSHPx的含量均低于透析前($P<0.05$),且观察组透析后血清中CRP、IL-6、TNF-α、MDA、AOPP的含量低于对照组,SOD、GSHPx的含量高于对照组($P<0.05$)。**结论**:维持性血液透析患者接受复方α酮酸联合常规营养干预能够有效降低全身微炎症状态、抑制氧化应激反应。

[关键词] 维持性血液透析;复方α酮酸;炎症反应;氧化应激
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Effect of compound α-ketoacid combined with routine nutritional intervention on inflammatory response and oxidative stress response in patients with maintenance hemodialysis

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View from specialist: It is creative, and of certain scientific and educational value.

[ABSTRACT] Objective: To study the effect of compound α-ketoacid combined with routine nutritional intervention on the inflammatory response and oxidative stress response in patients with maintenance hemodialysis. Methods: A total of 78 patients with uremia who received maintenance hemodialysis in Dangyang Changbanpo Hospital were collected and divided into control group and observation group according to the random number table method, 39 cases in each group. The control group received routine nutritional intervention, and the observation group underwent compound α-ketoacid combined with routine nutritional intervention. The serum levels of inflammatory factors and oxidative stress indicators in two groups of patients were detected before dialysis and 6 months after dialysis. Results: Before dialysis, differences in serum levels of inflammatory factors and oxidative stress indexes were not statistically significant between two groups of patients ($P>0.05$). After dialysis, serum CRP, IL-6, TNF-α, MDA and AOPP levels of both groups of patients were higher than those before dialysis while SOD and GSHPx levels were lower than those before dialysis ($P<0.05$) and serum CRP, IL-6, TNF-α, MDA and AOPP levels of observation group after dialysis were lower than those of control group while SOD and GSHPx levels were higher than those of control

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group ($P<0.05$). **Conclusions**: Compound α-ketoacid combined with routine nutritional intervention can effectively reduce the systemic microinflammatory state and inhibit the oxidative stress response in patients with maintenance hemodialysis.

[KEY WORDS] Maintenance hemodialysis; Compound α-ketoacid; Inflammatory response; Oxidative stress

维持性血液透析是延长尿毒症患者生存时间、提高其生活质量的过渡方法，但该方法非完全的肾脏替代方法、无法彻底清除患者体内代谢毒素，随透析时间延长患者可出现一系列内环境紊乱甚至并发症[1,2]。营养不良是影响维持性血液透析患者预后的重要因素，目前发生率约为23%～76%，需早期采取积极的干预措施。合理饮食尤其是低蛋白饮食，可优化机体磷的摄入，但无法彻底逆转钙磷代谢紊乱。复方α酮酸是由多种氨基酸组成的复方制剂，既往多用于慢性肾功能不全患者的治疗，有助于尿毒症毒性产物的蓄积[3,4]。本次研究在营养干预的基础上将复方α酮酸用于维持性血液透析患者的治疗，以期明确其在维持患者内环境稳态方面的作用。

1 资料与方法

1.1 一般资料

2014年2月～2016年11月间在当阳长坂坡医院接受维持性血液透析治疗的尿毒症患者78例，患者家属签署知情同意书。按照随机数表法，将入组患者分为对照组、观察组各39例。对照组中男性21例，女性18例，年龄45～77岁；观察组中男性20例，女性19例，年龄43～74岁。两组患者的性别、年龄分布无显著差异($P>0.05$)，伦理委员会批准此研究实施。

入组标准：(1)符合尿毒症诊断标准；(2)规律接受维持性血液透析≥6月；(3)配合临床干预及相关检查。排除标准：(1)合并其他组织脏器严重感染性疾病；(2)合并基础性营养不良；(3)合并恶性肿瘤性疾病。

1.2 干预方法

对照组患者在维持性血液透析过程中采取常规营养干预，具体如下：低蛋白饮食，单日蛋白摄入量以0.6 g/kg为宜，且易牛奶、瘦肉、鸡蛋等优质蛋白为主，保持总热量摄入在30～35 kcal/(kg·d)之间。观察组患者在维持性血液透析过程中接受复方α酮酸联合常规营养干预，具体如下：复方α酮酸(北京费森尤斯卡比医药有限公司，国药准字H20041442)，0.63 g/片，12片/d，连续治疗6月。营养干预方法同对照组患者。

1.3 炎症反应

维持性血液透析前后，均抽取两组患者的空腹肘静脉血3.0 mL，抗凝后低速离心取上层血清，采用酶联免疫吸附法(ELISA)检测血清中炎症因子的含量，包括C反应蛋白(CRP)、白介素-6(IL-6)、肿瘤坏死因子α(TNF-α)。

1.4 氧化应激

维持性血液透析前后，以相同方式获取两组患者的外周血血清，采用ELISA检测其中氧化应激指标的含量，包括超氧化物歧化酶(SOD)、谷胱甘肽过氧化物酶(GSHPx)、丙二醛(MDA)、晚期氧化蛋白产物(AOPP)。

1.5 统计学处理

所有数据采用SPSS24.0统计软件对数据进行分析处理，炎症因子、氧化应激指标等计量资料以均数±标准差($\bar{x}\pm s$)表示，组内透析前后比较采用配对t检验，两组间透析前、透析后分别比较采用成组t检验，$P<0.05$为差异有统计学意义。

2 结果

2.1 炎症反应

透析前，两组血清中CRP、IL-6、TNF-α含量的差异无统计学意义($P>0.05$)。透析后，两组血清中CRP、IL-6、TNF-α的含量均高于透析前，而观察组血清中CRP、IL-6、TNF-α的含量低于对照组，差异均有统计学意义($P<0.05$)。见表1。

表1 两组维持性血液透析前后血清中炎症因子含量的比较($n=39,\bar{x}\pm s$)

组别	CRP(mg/L)		IL-6(pg/mL)		TNF-α(pg/mL)	
	透析前	透析后	透析前	透析后	透析前	透析后
对照组	7.27±0.85	11.83±1.79	8.09±0.95	17.25±2.19	20.17±2.68	43.28±5.79
观察组	7.19±0.83	8.62±0.94	8.13±0.92	10.84±1.73	20.09±2.59	24.71±3.09
t	0.136	9.173	0.209	12.476	0.251	19.184
P	>0.05	<0.05	>0.05	<0.05	>0.05	<0.05

2.2 氧化应激

透析前，两组患者血清中SOD、GSHPx、MDA、AOPP含量的差异无统计学意义($P>0.05$)。透析后，两组血清中SOD、GSHPx的含量低于透析前，MDA、AOPP的含量高于透析前，而观察组血清中SOD、GSHPx的含量高于对照组，MDA、AOPP的含量低于对照组，差异均有统计学意义($P<0.05$)。见表2。

表 2　两组维持性血液透析前后血清中氧化应激指标含量的比较($n=39$,$\bar{x}\pm s$)

组别	SOD(μU/L)		GSHPx(U/L)		MDA(μmol/L)		AOPP(μmol/L)	
	透析前	透析后	透析前	透析后	透析前	透析后	透析前	透析后
对照组	56.28±6.19	41.72±5.16	70.58±8.25	57.49±6.21	9.34±1.52	14.28±1.76	53.28±6.11	79.54±8.63
观察组	56.19±5.87	50.88±6.15	70.47±8.19	64.72±7.09	9.27±1.49	11.54±1.39	52.76±6.08	60.17±7.42
t	0.173	13.294	0.209	11.583	0.153	9.738	0.218	15.827
P	>0.05	<0.05	>0.05	<0.05	>0.05	<0.05	>0.05	<0.05

3　讨论

维持性血液透析患者随透析时间延长，可出现毒素蓄积尤其是钙磷代谢紊乱，可导致肾性骨营养不良及血管钙化[5]。既往研究指出，营养不良的维持性血液透析患者预后多不佳，可直接增加心血管疾病死亡率，故纠正维持性血液透析患者的钙磷代谢紊乱及营养不良是此类患者临床干预的重点。磷的摄入与蛋白质摄入基本平衡，故低蛋白饮食是避免磷过度摄入的主要方法，但单纯低蛋白饮食可能加剧机体本身存在的微炎症状态，而持续的微炎症状态又可进一步加剧患者的营养不良，由此形成恶性循环，如何改变维持性血液透析患者的这一困境是目前临床研究的重点。复方 α 酮酸作为氨基酸复方制剂，含有 4 种酮代氨基酸钙、1 种羟代氨基酸钙、5 种氨基酸，在提供人体必需氨基酸的同时可利用非必需氨基酸的氨转化为氨基酸，由此减少尿素合成及毒性产物蓄积[6]。复方 α 酮酸分子量较小，不会引起残存肾单位的高滤过，有助于改善肾性高磷血症及肾性骨营养不良。本次研究在低蛋白饮食的基础上，将复方 α 酮酸作作为辅助干预方式用于维持性血液透析患者的治疗，从机体微炎症状态、氧化应激状态两方面对其作用进行阐述。

众多研究已经证实，维持性血液透析患者存在微炎症状态。微炎症是指非病原微生物感染引起的循环血中炎性蛋白、炎性因子含量升高，可引发患者各种非显性炎症状态[7,8]。微炎症状态的出现一方面与基础性慢性肾功能不全相关，另一方面与维持性血液透析过程中各种毒素蓄积相关，故若不加以针对性干预，随透析时间延长患者微炎症状态加剧[9,10]。CRP 是炎症因子含量升高的标志，可促进 IL-6、TNF-α 等炎症因子分泌，并诱导中性粒细胞聚集，检测其含量可客观、量化反映机体微炎症状态[11]。本次研究发现，两组患者透析后血清中 CRP、IL-6、TNF-α 的含量均高于透析前，证实透析过程中毒素蓄积可加剧机体微炎症状态；进一步与对照组比较，观察组患者血清中 CRP、IL-6、TNF-α 的含量较低，说明复方 α 酮酸联合常规营养干预有助于减轻微炎症状态的加重，可能与其减少磷及尿毒等代谢产物蓄积直接相关。

在微炎症及持续性毒素蓄积的状态下，维持性血液透析患者还存在氧化应激反应，当机体清除氧自由基功能下降时大量氧化代谢产物蓄积，进一步引起组织脏器损伤，降低血液透析效果[12,13]。SOD、GSHPx 均是具有抗氧化作用的物质，可与氧自由基结合并降低其氧化型损伤作用，故在强烈氧化应激状态下 SOD、GSHPx 消耗增多，血清含量下降[14,15]。MDA、AOPP 是脂质过氧化终产物，可引起蛋白质、核酸等大分子物质交联聚合，具有细胞毒性，是氧化应激状态存在的标志物[16]。本次研究对比两组患者透析前后血清中上述氧化应激标志物含量的差异，发现：与透析前比较，两组患者透析后血清中 SOD、GSHPx 含量较低，MDA、AOPP 含量较高，说明维持性血液透析可加剧患者全身氧化应激状态；进一步与对照组比较，观察组患者透析后血清中 SOD、GSHPx 含量较高，MDA、AOPP 含量较低，证实复方 α 酮酸联合常规营养干预可有效减轻机体氧化应激状态，这与上文中其抑制微炎症状态的作用密切相关。

综上所述，维持性血液透析患者接受复方 α 酮酸联合常规营养干预，可有效抑制机体微炎症及氧化应激反应，有望改善治疗预后。

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