还原型谷胱甘肽对尿毒症维持性血液透析患者微炎症状态的影响

柳永兵*（宜昌市第二人民医院/三峡大学第二人民医院肾内科，湖北 宜昌 443000）

中图分类号 R692 **文献标志码** A **文章编号** 1001-0408（2015）12-1637-03
DOI 10.6039/j.issn.1001-0408.2015.12.20

摘 要 目的：观察还原型谷胱甘肽对尿毒症维持性血液透析患者微炎症状态的影响。方法：60例维持性血液透析患者随机分为对照组（25例）和观察组（35例）。所有患者均使用4008B血液透析机，每周透析3次，每次4 h。与此同时，对照组患者给予低盐低脂优质蛋白饮食；血红蛋白未达标者给予重组人促红细胞生成素10 000 U/周，皮下注射；合并高血压者给予降压治疗。观察组患者在对照组治疗的基础上给予还原型谷胱甘肽片400 mg，口服，tid。两组患者疗程均为12周。观察两组患者治疗前后C反应蛋白（CRP）、白细胞介素6（IL-6）、肿瘤坏死因子α（TNF-α）、血清白蛋白（ALB）、前白蛋白（PA）、血清转铁蛋白（SF）、血清肌酐（Scr）、血尿素氮（BUN）及不良反应发生情况。结果：治疗后，对照组患者上述指标与治疗前比较差异均无统计学意义（$P>0.05$）。观察组患者ALB、PA、SF均显著高于同组治疗前，且高于对照组；CRP、IL-6、TNF-α均显著低于同组治疗前，且低于对照组，差异均有统计学差异（$P<0.05$）；Scr、BUN比较差异无统计学意义（$P>0.05$）。两组患者治疗期间均未见严重不良反应发生。结论：还原型谷胱甘肽可改善尿毒症维持性血液透析患者的微炎症状态及营养状况，安全性较好。

关键词 还原型谷胱甘肽；尿毒症；维持性血液透析；微炎症状态

Effect of Reduced Glutathione on the Micro-inflammatory State of Patients with Uremia Maintenance Hemodialysis

LIU Yong-bing（Dept. of Nephrology, the Second People's Hospital of Yichang City/Second People's Hospital of China Three Gorges University, Hubei Yichang 443000, China）

ABSTRACT OBJECTIVE: To investigate the effects of reduced glutathione on the micro-inflammatory state of patients with uremia maintenance hemodialysis. METHODS: 60 cases of maintenance hemodialysis patients were randomly divided into control group (25 cases) and observation group (35 cases). All the patients were dialyzed by hemodialysis machine, 3 times a week, 4 h for each time. Meanwhile, patients in control group were given low-salt low-fat high-protein diet; the patients who did not meet the hemoglobin were given recombinant human erythropoietin 10 000 U/week, sc; the patients with hypertension were given antihypertensive treatment. Patients in observation group were orally given Reduced glutathione tablets 400 mg based on the treatment of control group, tid. The course of both was 12 weeks. The clinic data was observed, including CRP, IL-6, TNF-α, ALB, PA, SF, Scr, BUN and ADR incidence before and after treatment. RESULTS: There were no significant differences in control group before and after treatment ($P>0.05$). The ALB, PA and SF in observation group were significantly higher than before and control group; CRP, IL-6 and TNF-α were significantly lower than before and control group ($P<0.05$); there was no significant difference between Scr and BUN ($P>0.05$). There was no serious ADR in 2 groups during treatment. CONCLUSIONS: Reduced glutathione can improve the micro-inflammatony state of patients with uremia maintenance hemodialysis with good safety.

KEYWORDS Reduced glutathione; Uremia; Maintenance hemodialysis; Micro-inflammatory state

随着血液净化技术的普及和不断发展，尿毒症维持性血液透析患者的生存率得到了极大的提高，但其远期并发症和病死率仍高于正常人群[1]。心血管疾病被认为是终末期肾病（ESRD）患者最常见的并发症和最主要的死亡原因[2]。Schöming M等[3]首先提出了尿毒症患者存在“微炎症状态”，认为炎症标记物可用于预测血液透析患者未来血管事件的发生。还原型谷胱甘肽是人类细胞自然合成的一种肽，在肾脏中丰富存在，可参与体内抗氧化、清除自由基及解毒等多种生化反应，药理作用广泛。目前，已尝试将该药用于肾病的治疗并取得了较好疗效，但该药对尿毒症维持性血液透析患者微炎症状态的影响鲜有报道。为此，在本研究中笔者观察了还原型谷胱甘肽对尿毒症维持性血液透析患者微炎症状态的影响，以为临床治疗提供参考。

*副主任医师。研究方向：肾病内科学。电话：0717-6211030。E-mail：891281180@qq.com.

1 资料与方法

1.1 资料来源

选取我院2013年1月－2014年3月尿毒症维持性血液透析患者60例。纳入标准：①维持性血液透析＞3个月；②观察前4周均无感染病史；③无风湿、类风湿性关节炎病史，未使用糖皮质激素及其他免疫抑制剂；④无肿瘤，或无肿瘤术后肿瘤复发；⑤预计1年内不行肾移植术。将所有患者按随机数字表法分为对照组（25例）和观察组（35例）。两组患者性别、年龄等基本资料比较，差异均无统计学意义（$P>0.05$），具有可比性，详见表1。本研究方案经我院医学伦理委员会批准，所有患者均签署了知情同意书。

表1　两组患者基本资料比较(例)

Tab 1　Comparison of general information between 2 groups (case)

组别	n	男性/女性	年龄,岁	慢性肾小球肾炎	糖尿病肾病	多囊肾	高血压肾病
观察组	35	21/14	54.3±12.7	15	8	3	9
对照组	25	15/10	56.2±15.6	12	6	3	4

1.2　治疗方法

所有患者均使用4008B血液透析机,聚砜膜F7透析器碳酸氢盐透析液透析,血流量200～250 ml/min,透析液流量500 ml/min,每周透析3次,每次4 h。与此同时,对照组患者给予低盐低脂优质蛋白饮食;血红蛋白未达标者给予重组人促红细胞生成素10 000 U/周,皮下注射;合并高血压者给予降压治疗。观察组患者在对照组治疗的基础上给予还原型谷胱甘肽片(重庆药友制药有限责任公司,规格:100 mg/片)400 mg,口服,tid。两组患者疗程均为12周。

1.3　观察指标

观察两组患者治疗前后C反应蛋白(CRP)、白细胞介素6(IL-6)、肿瘤坏死因子α(TNF-α)、血清白蛋白(ALB)、前白蛋白(PA)、血清转铁蛋白(SF)、血清肌酐(Scr)、血尿素氮(BUN)及不良反应发生情况。

1.4　统计学方法

采用SPSS 17.0统计软件对数据进行分析。计量资料以$\bar{x}\pm s$表示,采用t检验;计数资料以率表示,采用χ^2检验。$P<0.05$为差异有统计学意义。

2　结果

2.1　两组患者治疗前后ALB、PA、SF、Scr、BUN比较

治疗前,两组患者ALB、PA、SF、Scr、BUN比较,差异均无统计学意义($P>0.05$)。治疗后,对照组患者上述各项指标与治疗前比较,差异均无统计学意义($P>0.05$);观察组患者ALB、PA、SF均显著高于同组治疗前,且显著高于对照组,差异均有统计学差异($P<0.05$),而Scr、BUN比较差异无统计学意义($P>0.05$),详见表2。

表2　两组患者治疗前后ALB、PA、SF、Scr、BUN比较($\bar{x}\pm s$)

Tab 2　Comparison of ALB, PA, SF, Scr and BUN between 2 groups before and after treatment($\bar{x}\pm s$)

组别	n	时间	ALB,g/L	PA,mg/L	SF,g/L	Scr,μmol/L	BUN,mmol/L
对照组	25	治疗前	30.2±9.1	251.6±32.8	1.44±0.30	625.0±32.0	12.7±0.4
		治疗后	30.6±11.0	256.3±28.6	1.49±0.33	639.8±32.5	13.6±0.6
观察组	35	治疗前	30.9±10.8	260.5±34.3	1.41±0.36	635.0±30.0	13.1±0.6
		治疗后	37.7±9.4$^{*\#}$	287.6±32.4$^{*\#}$	1.67±0.43$^{*\#}$	639.0±36.0	11.7±1.8

注:与治疗前比较,$^{*}P<0.05$;与对照组比较,$^{\#}P<0.05$

Note: vs. before treatment, $^{*}P<0.05$; vs. control group, $^{\#}P<0.05$

2.2　两组患者治疗前后CRP、IL-6、TNF-α比较

治疗前,两组患者CRP、IL-6、TNF-α比较,差异均无统计学意义($P>0.05$)。治疗后,对照组患者上述指标与治疗前比较,差异均无统计学意义($P>0.05$);观察组患者CRP、IL-6、TNF-α均显著低于同组治疗前,且显著低于对照组,差异均有统计学差异($P<0.05$),详见表3。

2.3　不良反应

两组患者治疗期间均未见严重不良反应发生。

3　讨论

临床研究表明,尿毒症维持性血液透析患者普遍存在微炎症状态,引起微炎症状态的原因是多方面的[4]:(1)尿毒症及肾功能减退可减少机体对促炎症细胞因子的消除;(2)心力衰竭和容量负荷过度,可引起血浆内毒素水平、炎性细胞因子浓度升高,导致炎症状态;(3)氧化应激反应可导致内皮细胞功能受损;(4)透析膜的生物不相容性可导致外周血单核细胞(PBMC)的激活,并分泌一系列炎症因子;(5)透析液污染可激发免疫反应;(6)血管通路感染。目前,用于检测微炎症状态的因子有CRP、TNF-α、IL-6、PA、血清淀粉样蛋白A以及脂蛋白[5]。Shlipak MG等[6]指出,CRP可以作为透析患者慢性炎症状态的标记物。本研究亦发现,维持性血液透析患者的CRP水平在治疗前已经升高,表明维持性血液透析患者存在微炎症状态。

表3　两组患者治疗前后CRP、IL-6、TNF-α比较($\bar{x}\pm s$)

Tab 3　Comparison of CRP, IL-6 and TNF-α between 2 groups before and after treatment($\bar{x}\pm s$)

组别	n	时间	CRP,mg/L	IL-6,ng/ml	TNF-α,pg/ml
对照组	25	治疗前	8.39±2.13	16.71±0.93	151.25±31.36
		治疗后	7.85±2.15	15.69±5.13	147.66±33.68
观察组	35	治疗前	8.35±2.63	16.22±3.89	154.16±33.68
		治疗后	5.12±1.22$^{*\#}$	10.31±4.33$^{*\#}$	108.03±23.03$^{*\#}$

注:与治疗前比较,$^{*}P<0.05$;与对照组比较,$^{\#}P<0.05$

Note: vs. before treatment, $^{*}P<0.05$; vs. control group, $^{\#}P<0.05$

谷胱甘肽由谷氨酸、半胱氨酸和甘氨酸组成,可参与人体内三羧酸循环及糖代谢,使人体获得高能量,可激活多种酶,如体内的巯基酶等,从而促使糖类、脂肪及蛋白质代谢,影响细胞的代谢过程[7]。谷胱甘肽的活性成分为还原型谷胱甘肽,其对抗氧化剂对巯基的破坏,可保护细胞膜中含巯基的蛋白质和含巯基酶不被破坏,同时还可对抗自由基对重要脏器的损害[8]。焦桂萍等[9]通过动物实验初步证实了还原型谷胱甘肽可有效抑制TNF-α的释放;武方奇等[10]报道了还原型谷胱甘肽可使急性冠状动脉综合征患者CRP显著下降,提示该药具有抗炎作用。

本研究结果显示,治疗后观察组患者CRP、IL-6、TNF-α显著低于对照组及同组治疗前,提示还原型谷胱甘肽具有改善微炎症状态的作用;观察组患者ALB、PA、SF显著高于对照组及同组治疗前,提示患者营养状态得到改善,表明还原型谷胱甘肽可促进患者糖类、脂肪及蛋白质代谢,使人体获得高能量。有研究表明,还原型谷胱甘肽具有肾脏保护作用,能延缓慢性肾功能不全进程[11]。但对于尿毒症维持性血液透析患者来说,药物干预并不能逆转肾组织的损伤,临床治疗仍以血液透析为主。

综上所述,还原型谷胱甘肽可改善尿毒症维持性血液透析患者的微炎症状态及营养状况,安全性较好。由于本研究纳入的样本量较小,此结论有待大样本、多中心研究进一步证实。

参考文献

[1] 陈明喆,张莹雯.大黄联合辛伐他汀对维持性血液透析患者微炎症状态的影响[J].武汉大学学报:医学版,2009,30(4):473.

[2] Zoccali C, Mallamaci F, Tripepi G. Novel cardiovascular risk factors in end-stage renal disease. [J]. *J Am Soc Nephrol*,2004,15:S77.

[3] Schömig M, Eisenhardt A, Ritz E.The microinflammatory state of uremia[J]. *Blood Purif*,2000,18(4):327.

[4] 陈江华,何强,徐莹.维持性血液透析患者微炎症状态的认识与防治[J].中华肾脏病杂志,2005,21(2):117.

盐酸氨溴索联合肾上腺素治疗小儿急性喉炎的临床观察

何成川*(绵阳市妇幼保健院,四川 绵阳 621000)

中图分类号 R767.11 **文献标志码** A **文章编号** 1001-0408(2015)12-1639-03
DOI 10.6039/j.issn.1001-0408.2015.12.21

摘 要 目的:观察盐酸氨溴索联合肾上腺素治疗小儿急性喉炎的临床疗效和安全性。方法:180例小儿急性喉炎患儿随机均分为研究组和对照组。两组患儿均给予常规治疗。在此基础上,对照组Ⅰ度喉梗阻患儿给予地塞米松5 mg,加入0.9%氯化钠注射液5 ml中超声雾化吸入,每日2次,每次15 min;Ⅱ度喉梗阻患儿给予地塞米松5~10 mg,静脉注射,每日2次。研究组≥1岁的Ⅰ度喉梗阻患儿给予氨溴索7.5 mg+肾上腺素1 mg超声雾化吸入,每日2次,每次15 min;<1岁的Ⅰ度喉梗阻患儿给予氨溴索7.5 mg+肾上腺素0.5 mg,超声雾化吸入,每日2次,每次15 min;Ⅱ度喉梗阻患儿用法用量同研究组Ⅰ度喉梗阻患儿,只需每日增加雾化吸入1~2次。两组患儿疗程均为72 h。观察两组患儿的临床疗效、治疗前后临床症状评分、临床症状消失时间及不良反应发生情况。结果:研究组患儿总有效率显著高于对照组,各临床症状消失时间均短于对照组,差异均有统计学意义($P<0.05$)。治疗后两组患儿各临床症状评分均显著低于同组治疗前,且研究组低于对照组($P<0.05$)。两组患儿不良反应发生率比较差异无统计学意义($P>0.05$)。结论:盐酸氨溴索联合肾上腺素治疗小儿急性喉炎的疗效显著,安全性较好。

关键词 急性喉炎;氨溴索;肾上腺素;雾化;疗效;安全性

Clinical Observation of Ambroxol Hydrochloride Combined with Epinephrine in Treatment of Children with Acute Laryngitis

HE Cheng-chuan(Mianyang Maternal and Child Health Hospital, Sichuan Mianyang 621000, China)

ABSTRACT OBJECTIVE: To observe the clinical efficacy and safety of ambroxol hydrochloride and epinephrine in treatment of children with acute laryngitis (AL). METHODS: 180 children with AL were randomly divided into research group and control group. They were all given routine treatment. Based on it, children with Ⅰ degree laryngeal obstruction in control group were given dexamethasone 5 mg with atomization inhalation, twice a day, 15 min each time; children with Ⅱ degree laryngeal obstruction were given dexamethasone 5-10 mg, iv, twice a day. Children with Ⅰ degree laryngeal obstruction and older than 1 year in research group were given ambroxol 7.5 mg and epinephrine 1 mg with atomization inhalation; children with Ⅰ degree laryngeal obstruction and younger than 1 year were given ambroxol 7.5 mg and epinephrine 1 mg with atomization inhalation, twice a day, 15 min each time; children with Ⅱ degree laryngeal obstruction were given the same usage and dosage as the Ⅰ degree laryngeal obstruction in research group and increased atomization inhalation once or twice a day. The course of both was 72 h. The clinic data was observed, including the efficacy, scores of clinical symptoms before and after treatment, disappearance time of clinical symptoms and incidence of adverse reactions. RESULTS: The total effective rate in research group was significantly higher than control group, and the disappearance time of clinical symptoms were shorter than control group, with significant difference ($P<0.05$). After treatment, the scores of clinical symptoms in 2 groups were significantly lower than before, and research group was significantly lower than control group($P<0.05$). There was no significant difference in the incidence of adverse reactions($P>0.05$). CONCLUSIONS: Ambroxol hydrochloride combined with epinephrine have significant efficacy in the treatment of children with AL with good safety.

KEYWORDS Acute laryngitis; Ambroxol; Epinephrine; Atomization; Efficacy; Safety

[5] 李俊,李艳锋,韩晓铃.维持性血液透析患者微炎症状态及相关因子研究[J].医学综述,2008,14(4):493.
[6] Shlipak MG, Fried LF, Crump C, *et al*. Elevations of inflammatory and procoagulant biomarkers in elderly persons with renal insufficiency[J]. *Circulation*, 2003, 107(1):87.
[7] 陈新谦,金有豫,汤光.新编药物学[M].17版.北京:人民卫生出版社,2011:885.
[8] 袁平戈,张大志.还原型谷胱甘肽的作用机制及临床应用[J].药品评价,2006,3(5):385.
[9] 焦桂萍,赵兵,袁志柳,等.还原型谷胱甘肽对大鼠肺缺血-再灌注后黏附分子-1,肿瘤坏死因子α蛋白表达影响[J].中国现代医学杂志,2006,16(18):2 764.
[10] 武方奇,马巧平.还原型谷胱甘肽对急性冠脉综合征患者血浆C-反应蛋白的影响[J].中国心血管病研究杂志,2007,5(8):588.
[11] 柳永兵.还原型谷胱甘肽联合尿毒清颗粒治疗慢性肾功能衰竭的临床观察[J].中国药房,2011,22(36):3 428.

*主治医师。研究方向:儿童生长发育。E-mail:113665163@qq.com

(收稿日期:2014-09-17 修回日期:2015-02-16)
(编辑:陈 宏)