doi: 10.13241/j.cnki.pmb.2015.15.029

左卡尼汀联合蔗糖铁对血液透析患者肾性贫血及氧化应激的影响

陈熙军[1] 胡开洪[1] 鲁 毅[1] 毛晓琴[1] 杨 岳[2]

(1 四川省射洪中医院肾内科 四川 遂宁 629200;2 四川省南充市中心医院肾内科 四川 南充 637000)

摘要 目的:探讨左卡尼汀联合蔗糖铁对血透患者肾性贫血及氧化应激的影响。方法:抽选我院 2010 年 3 月 -2013 年 5 月行维持血透治疗的肾性贫血患者 79 例,采用数字表法分为对照组(39 例)和观察组(40 例),对照组采用促红细胞生成素(EPO)、单用蔗糖铁及常规对症治疗,观察组在对照组基础上联用左卡尼汀治疗。比较两组患者治疗前、治疗 6 个月后血红蛋白(Hb)、血细胞比容(Hct)、血浆铁蛋白(SF)、转铁蛋白饱和度(TSAT)、晚期蛋白质氧化产物(AOPP)及血丙二醛(MDA)水平,并对两组治疗开始时、治疗 3、6 个月时 EPO 使用剂量进行比较。结果:治疗 6 个月后,观察组患者 Hb、Hct、SF、TSAT 明显高于对照组(P<0.05),AOPP、MDA 明显低于对照组(P<0.05);对照组从治疗开始到治疗 6 个月时一直维持较高的 EPO 使用剂量,而观察组 EPO 用量依次递减,至治疗 6 个月时 EPO 用量显著低于对照组(P<0.05)。结论:左卡尼汀能联合蔗糖铁治疗肾性贫血的疗效显著,能有效缓解氧化应激反应,降低 EPO 用量,值得临床推广。

关键词:氧化应激;肾性贫血;蔗糖铁;左卡尼汀

中图分类号:R459.5 **文献标识码**:A **文章编号**:1673-6273(2015)15-2907-03

Effect of L-carnitine and Iron Sucrose on Renal Anemia and Oxidative Stress in Hemodialysis Patients

CHEN Xi-jun[1], HU Kai-hong[1], LU Yi[1], MAO Xiao-qin[1], YANG Yue[2]

(1 Department of nephrology, Shehong traditional Chinese Medicine Hospital of Sichuan Province, Suining, Sichuan, 629200, China; 2 Department of nephrology, Nanchong Central Hospital of Sichuan Province, Nanchong, Sichuan, 637000, China)

ABSTRACT Objective: To explore the impact of L-carnitine and iron sucrose on renal anemia and oxidative stress in hemodialysis patients. Methods: 79 cases of patients with renal anemia who treated in our hospital and underwent maintenance hemodialysis treatment from March 2010 to May 2013 were selected, they were randomly divided into control group (39 cases) who used erythropoietin (EPO), single iron sucrose and conventional symptomatic treatment and observation group (40 cases) who added with L-carnitine treatment on the basis of the control group. Compared the hemoglobin (Hb), hematocrit (Hct), plasma ferritin (SF), transferrin saturation (TSAT), advanced oxidation protein products (AOPP) and serum malondialdehyde (MDA) level of two groups before treatment and after 6 months treatment, and compared the use of EPO dose at the beginning of treatment and after treatment for 3, 6 months. Results: After 6 months treatment, Hb, Hct, SF, TSAT of observation group were significantly higher than those in control group (P<0.05); AOPP, MDA was significantly lower than that of the control group (P<0.05). The control group maintained a high dose of EPO from the beginning of treatment and after treatment for 6 months, and the treatment group was reduced, it was significantly lower than that of control group after treatment for 6 months (P<0.05). Conclusion: L-carnitine combined with iron sucrose in treatment of renal anemia has significantly effect, can effectively alleviate the oxidative stress reaction, reduce the use of EPO dose, which is worthy of clinical application.

Key words: Oxidative stress; Renal anemia; Iron sucrose; L-carnitine

Chinese Library Classification(CLC): R459.5 Document code: A

Article ID:1673-6273(2015)15-2907-03

前言

慢性肾功能衰竭终末期会引起贫血现象,而红细胞生成素(erythropoietin,EPO)能改善慢性肾衰患者的贫血症状[1]。但仍有许多行血透治疗的肾性贫血患者对 EPO 治疗无反应或疗效差,其主要是受铁缺乏、慢性感染及营养不良等因素的影响[2,3]。因此,临床中多辅以蔗糖铁补铁治疗。然后大量研究证明,蔗糖铁在治疗过程中会引起患者体内氧化应激反应的增加,引发心脑血管等事件发生[4,5]。左卡泥丁在改善营养不良和抗氧化作用方面效果显著,也可减少血透贫血患者 EPO 用量,从而减轻患者治疗经济压力[6,7]。笔者举措展开研究,旨在探讨蔗糖铁联合左卡泥丁治疗血透肾性贫血患者的效果及氧化应激的影响,现报道如下。

1 资料和方法

1.1 临床资料

抽选我院 2010 年 3 月 -2013 年 5 月行维持血透治疗的患

作者简介:陈熙军(1976-),男,本科,主治医师,从事血液透析方面的研究,E-mail:58954612@qq.com

(收稿日期:2014-11-23 接受日期:2014-12-18)

者 79 例，均存在肾性贫血。纳入标准[8]：病情稳定日期 >1 个月，每周透析 2-3 次；血红蛋白(Hb) ≤ 90g/L，血浆铁蛋白(SF) ≤ 200 ng/mL，转铁蛋白饱和度(TSAT) ≤ 20%；近 4 周未口服或静脉输注铁剂、无输血。排除铁剂过敏、失血、感染者。采用数字表法将患者分为对照组 (39 例) 和观察组 (40 例)，其中观察组男 20 例，女 20 例，年龄 34-66 岁，平均(49.46± 10.13)岁，透析时间 17.6-43.3 个月；对照组男 20 例，女 19 例，年龄 35-67 岁，平均(49.57± 9.97)岁，透析时间 18.2-43.6 个月。两组年龄、性别比及透析年限差异无显著性 (P＞0.05)，均衡可比。

1.2 方法

对照组患者在血透治疗后行 EPO 皮下注射，每周 80-120 U/kg，采用 100 mg 的蔗糖铁在每次透析后回血时注入透析管路静脉壶中，每月 100 mg 维持，并给予血压控制、叶酸及维生素 B12 补充等对症治疗，治疗 6 个月。观察组在对照组组的基础上采用 1.0 g 的左卡尼汀 (国药准字 H20050443，长春海悦药业有限公司)，在血透结束后加入 20 mL 的生理盐水中静脉注射，每周 2-3 次，治疗 6 个月。

1.3 观察指标

比较两组患者治疗前、治疗 6 个月后 Hb、血细胞比容 (Hct)、SF、TSAT、和晚期蛋白质氧化产物(AOPP)、血丙二醛 (MDA)水平，记录两组治疗开始时、治疗 3、6 个月时 EPO 维持剂量。

1.4 统计学方法

采用 SPSS17.0 软件进行统计分析，计量资料以 ($\bar{x}\pm s$) 表示，采用 t 值检验，P<0.05 表示差异有统计学意义。

2 结果

2.1 两组血液学指标和氧化应激指标比较

两组患者治疗前 Hb、Hct、SF、TSAT、AOPP 及 MDA 水平差异均无统计学意义 (P>0.05)。治疗 6 个月后，观察组 Hb、Hct、SF、TSAT 明显高于对照组 (P<0.05)；AOPP、MDA 明显低于对照组 (P<0.05)，详见表 1。

表 1 两组血液学指标和氧化应激指标比较 ($\bar{x}\pm s$)

Table 1 Comparison of hematological indexes and oxidative stress indices between the two groups ($\bar{x}\pm s$)

指标 Indexes	时间 Time	对照组 (n=39) Control group	观察组 (n=40) Observation group	T	P
Hb(g/l)	治疗前 Before treatment	74.89± 14.32	75.31± 14.87	0.128	0.899
	治疗后 After treatment	92.73± 12.52	114.38± 12.26	7.766	0.000
Hct(× 10^{-2})	治疗前 Before treatment	21.91± 4.30	21.43± 4.51	0.484	0.629
	治疗后 After treatment	34.73± 5.88	40.21± 5.76	4.185	0.000
SF(ng/ml)	治疗前 Before treatment	118.36± 58.36	120.45± 60.13	0.157	0.876
	治疗后 After treatment	245.63± 81.37	345.09± 85.91	5.280	0.000
TSAT(× 10^{-2})	治疗前 Before treatment	17.23± 3.90	17.31± 3.92	0.091	0.928
	治疗后 After treatment	24.36± 5.33	29.78± 5.42	4.480	0.000
AOPP(nmol/l)	治疗前 Before treatment	82.63± 22.46	81.79± 20.53	0.174	0.863
	治疗后 After treatment	121.79± 31.67	89.67± 30.55	4.588	0.000
MDA(nmol/l)	治疗前 Before treatment	4.23± 1.53	4.25± 1.54	0.058	0.954
	治疗后 After treatment	9.56± 2.62	4.83± 2.59	8.069	0.000

2.2 两组治疗期间 EPO 使用剂量比较

对照组从治疗开始到治疗 6 个月时一直维持较高的 EPO 使用剂量，而观察组 EPO 用量依次递减，至治疗 6 个月后 EPO 用量显著低于对照组 (P<0.05)，详见表 2。

表 2 两组治疗期间 EPO 使用剂量比较[$\bar{x}\pm s$，U /(kg·w)]

Table 2 Comparison of the use of EPO dose between the two groups during treatment[$\bar{x}\pm s$，U /(kg·w)]

组别 Groups	n	治疗开始时 At the beginning of treatment	治疗 3 个月时 After treatment for 3 months	治疗 6 个月时 After treatment for 6 months
对照组 Control group	39	185.5± 14.8	179.1± 12.8	160.1± 12.1
观察组 Observation group	40	183.4± 15.6	163.2± 11.9	142.1± 12.5
T 值		0.614	5.720	6.501
P 值		0.541	0.000	0.000

3 讨论

肾性贫血主是因肾脏 EPO 产生不足引起，因此采用 EPO 治疗肾性贫血的疗效显著。但有临床调查发现，造血原料铁的缺乏对 EPO 的治疗疗效影响较大，有半数以上行 EPO 治疗的血透病人会因缺铁而疗效较差[9]。血液透析病人缺铁主要是因反复采血、透析器或管路中血液残留、促红素大剂量应用迅速消耗循环池中的铁，且不能及时释放出储存池中的铁，从而出现功能性缺铁以及微炎症状态，炎症又进一步降低了铁的利用[10-12]。因此，在血液透析肾性贫血病人中使用 EPO 治疗时通

常会常规给予铁剂。

而国内外亦有研究表明，蔗糖铁在带来肾性贫血治疗安全性和确切疗效的同时，还会导致患体内氧化应激反应的增加[13-15]。氧化应激是指当白细胞膜上还原型辅酶 II (NADPH) 被激活时，引起呼吸爆炸，使得大量氧自由基被释放出。左卡尼汀又称为左旋肉碱，是在机体组织内普遍存在的一种特殊氨基酸，是机体脂肪酸代谢所需。有文献报道，左卡尼汀能够促进清蛋白合成，使得红细胞膜稳定性明显提高，增加血细胞比容；同时，还能将长链脂肪酸运载入线粒体内而参与机体氧化反应[16,17]。维持性血透患者由于其自身左卡尼汀合成本来就少，在透析过程中又大量丢失，及应用 EPO 治疗时大量消耗等均会引起患者体内左卡尼汀的不足，导致严重代谢紊乱及增加正常红血细胞 (RBC) 脆性，缩短 RBC 寿命[18,19]。

本研究显示，两组患者在治疗前 AOPP 和 MDA 两种主要的氧化应激标志物均明显升高，表明血液透析肾性贫血病人体内本身存在氧化应激。经治疗 6 个月后，两组 AOPP，MDA 较治疗前均有明显上升。说明蔗糖铁诱发过氧化反应增加体内氧化应激(OS)，但是观察组患者 6 个月后 AOPP、MDA 上升幅度明显低于对照组 ($P<0.05$)，说明左卡尼汀抗氧化效果较好，能改善因蔗糖铁诱发的 OS。本研究还发现，观察组治疗 6 个月后患者的 Hb、Hct、SF、TSAT 明显高于对照组；并且观察组 EPO 用量依次递减，至治疗 6 个月后 EPO 用量显著低于对照组，提示左卡尼汀能提高 EPO 疗效，与 EPO 联合使用还能明显改善血透患者贫血症状，减少 EPO 用量，可能与左卡尼汀可作用于骨髓红系祖细胞的促进 EPO 吸收有关[20]。

综上所述，左卡尼汀能缓解氧化应激反应作用，联合蔗糖铁并可降低 EPO 用量，治疗肾性贫血的疗效显著，值得临床推广。

参 考 文 献 (References)

[1] Ryndina N, Kravchun P, Tytova G, et al. Cardiohemodynamic features and character of depressive disorders in patients with anemia varying grades of severity with chronic heart failure and chronic kidney disease[J].Georgian Med News, 2013,23(218):40-44

[2] 刘永泉,岳凌菊.维生素 C 与促红细胞生成素合用治疗尿毒症肾病贫血的疗效观察[J].辽宁医学院学报,2009,30(5):438-440
Liu Yong-quan, Yue Lin-ju. Efficacy observation of Vitamin C combined with erythropoietin in the treatment of uremic renal anemia[J]. Journal of Liaoning Medical University, 2009,30 (5): 438-440

[3] Malyszko J, Koc-Zorawska E, Malyszko JS, et al. GDF15 is related to anemia and hepcidin in kidney allograft recipients [J]. Nephron Clin Pract, 2013,123(1):112-117

[4] Pfenniger A, Schuller C, Christoph P, et al. Safety and efficacy of high-dose intravenous iron carboxymaltose vs iron sucrose for treatment of postpartum anemia[J]. J Perinat Med, 2012,40(4):397-402

[5] Beguin Y, Jaspers A. Iron sucrose - characteristics, efficacy and regulatory aspects of an established treatment of iron deficiency and iron-deficiency anemia in a broad range of therapeutic areas[J]. Expert Opin Pharmacother, 2014,15(14):2087-103

[6] Fischer M, Varady J, Hirche F, et al. Supplementation of L-carnitine in pigs: absorption of carnitine and effect on plasma and tissue carnitine concentrations[J]. Archives of Animal Nutrition, 2009,63(1):79-80

[7] 韦小红.左卡尼汀联合重组人促红细胞生成素治疗肾性贫血的疗效观察[J].广西医学,2013,(9):1218-1219,1234
Wei Xiao-hong. Observe the effect of levocarnitine combined withrecombinant human erythropoietin treatment of renal anemia [J]. Guangxi medicine, 2013,(9):1218-1219,1234

[8] Malaguarnera M, Vicari E, Calogero A, et al. Sexual dysfunction in chronic hepatitis C virus patients treated with interferon alpha and ribavirin[J]. J Interferon Cytokine Res, 2008,28(10):603-609

[9] Saluk-Juszczak J, Olas B, Wachowicz B, et al. L-carnitine modulates blood platelet oxidative stress[J]. Cell Biol Toxicol, 2010,26: 355-365

[10] Reuter SE, Faull RJ, Ranieri E, et al. Endogenous plasma carnitine pool composition and response to erythropoietin treatment in chronic haemodialysis patients [J]. Nephrol Dial Transplant, 2009,24 (3): 990-996

[11] Bonomini M, Sirolli V, Dottori S, et al. L-carnitine inhibits a subset of platelet activation responses in chronic uraemia [J]. Nephrol Dial Transplant, 2007,22(90):2623-2629

[12] Abdallah Y, Gligorievski D, Kasseckert SA, et al. The role of poly (ADP-ribose) polymerase (PARP) in the autonomous proliferative response of endothelial cells to hypoxia[J]. Cardiovasc Res, 2007,73(3): 568-574

[13] Wanic -Kossowska M, Kazmierski M. Combined therapy with L -carnitine and erythropoietin of anemia in chronic kidney failure patients undergoing hemodialysis [J]. Pol Arch Med Wewn, 2009,117 (1/2): 14-19

[14] Prats M, Font R, García C, et al. Oxidative stress markers in predicting response to treatment with ferric carboxymaltose in nondialysis chronic kidney disease patients[J]. Clin Nephrol, 2014,81(6):419-426

[15] El-Nakib GA, Mostafa TM, Abbas TM, et al. Role of alpha-lipoic acid in the management of anemia in patients with chronic renalfailure undergoing hemodialysis [J]. Int J Nephrol Renovasc Dis, 20136: 161-168

[16] Shema-Didi L, Kristal B, Ore L, et al. Shapiro G, Pomegranate juice intake attenuates the increase in oxidative stress induced by intravenous iron during hemodialysis[J]. Nutr Res, 2013,33(6):442-446

[17] Susantitaphong P, Riella C, Jaber BL. Effect of ultrapure dialysate on markers of inflammation, oxidative stress, nutrition and anemia parameters: a meta-analysis [J]. Nephrol Dial Transplant, 2013,28 (2): 438-446

[18] Dimitrijevic ZM, Cvetkovic TP, Djordjevic VM, et al. How the duration period of erythropoietin treatment influences the oxidative status ofhemodialysis patients[J]. Int J Med Sci, 2012,9(9):808-815

[19] Tonon J, Guarnier FA, Cecchini AL, et al. Anemia associated with extraerythrocytic oxidative stress damage mediated by neutrophil superoxide anion production in chronic renal failure patients undergoinghemodialysis[J]. Pathophysiology, 2012,19(4):261-268

[20] Yin L, Chen X, Chen J, et al. Multi-frequency low-dose intravenous iron on oxidative stress in maintenancehemodialysis patients[J]. Journal of Central South University (Medical Press), 2012,37(8):844-848