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低剂量多巴胺对急性心衰合并肾功能不全患者的影响*

韦 宏 贾 静 李光男 杨庆辉 陈延军[△]

(哈尔滨医科大学附属第四医院 黑龙江 哈尔滨 150001)

摘要 目的:探讨低剂量多巴胺能否通过利尿作用改善急性左心衰患者的充血症状以及肾功能。**方法:**将 2013 年 9 月至 2013 年 12 月我院收治的 80 例急性心衰合并肾功能不全的患者随机分为对照组和治疗组,每组各 40 例。对照组给予常规治疗,治疗组在常规治疗的基础上加用小剂量多巴胺静脉泵入 48 小时。观察和比较两组患者 48 小时内的总尿量及血清胱抑素 C 的变化、充血症状、肾功能及临床疗效的差异。**结果:**与对照组相比,治疗组 48 小时总尿量、血清胱抑素 C 的变化、体重变化、BNP 变化、肌酐变化、进展性心衰发生率、死亡率、治疗失败患者比例均无明显差异($P>0.05$)。**结论:**低剂量多巴胺不能在利尿治疗基础上减轻急性心力衰竭并发肾功能不全患者的充血症状或改善肾功能。

关键词:多巴胺;急性心力衰竭;肾功能不全

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Effect of Low-Dose Dopamine on the Patients of Acute Heart Failure with Renal Dysfunction*

WEI Hong, JIA Jing, LI Guang-nan, YANG Qing-hui, CHEN Yan-jun[△]

(The Fourth Affiliated Hospital of Harbin Medical University, Harbin, Heilongjiang, 150001, China)

ABSTRACT Objective: To investigate the effect of low-dose dopamine on the decongestion symptoms and renal function of patients with acute heart failure. **Methods:** 80 patients with acute heart failure and renal dysfunction admitted in our hospital from September 2013 to December 2013 were randomized into the treatment group and control group. The control group accepted the conventional treatment, while the treatment group was administered with the same treatment addition of low-dose dopamine. The 48-hour cumulative urine volume, change of serum cystatin C levels, decongestion symptoms, renal function and clinical efficacy were observed and compared. **Results:** Compared with the control group, low-dose dopamine had no significant effect on the 48-hour cumulative urine volume, change of serum cystatin C level, weight, BNP, creatinine, incidence rate of advanced heart failure, mortality and ratio of failed patients ($P>0.05$). **Conclusion:** Low-dose dopamine couldn't relieve the decongestion symptoms or improve the renal function of patients with acute heart failure and acute renal insufficiency on the basis of diuretic treatment.

Key words: Dopamine; Acute Heart Failure; Renal Dysfunction

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前言

急性心力衰竭的主要治疗目标为减轻充血症状同时避免肾功能不全和其他副作用的发生^[1,2]。急性心力衰竭时,若并发中度或重度的肾功能不全,会使充血症状加重且肾功能恶化,均会造成临床不良的预后^[3]。在治疗急性心力衰竭期间,肾辅助治疗对于减轻充血和保护肾功能十分必要^[4]。多巴胺是内源性儿茶酚胺类物质,低剂量($\leq 3 \mu\text{g/kg/min}$)即可选择性地激活多巴胺受体并促进肾血管舒张^[5,6]。既往的研究表明,在利尿剂治疗急性心力衰竭的过程中,加用低剂量多巴胺能增强利尿效果,减轻充血症状并保护肾功能。然而,既往研究多为小样本研究,且多巴胺剂量及用法不一^[7]。本研究旨在证实低剂量多巴胺能否通过利尿作用改善急性左心衰患者的充血症状以及肾

功能。

1 对象和方法

1.1 研究对象

选择 2013 年 9 月至 2013 年 12 月在我院治疗的急性心衰合并肾功能不全患者共 80 例,其中男性 53 例,女性 27 例。入选患者均为 NYHA 心功能 III-IV 级。肾功能不全的评价指标:肾小球滤过率为 $15-60 \text{ mL/min/1.73 m}^2$ 。急性心力衰竭的诊断是基于至少 1 个症状(呼吸困难、端坐呼吸或水肿)和 1 个心脏衰竭体征(啰音、水肿、腹水),左室射血分数 $< 50\%$ 。将所有患者随机分为对照组和治疗组,两组间基础资料比较无统计学差异($P>0.05$),具有可比性。见表 1。

1.2 处理方法

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作者简介:韦宏(1982-)男,医师,E-mail:wei_hong007@163.com

[△]通讯作者:陈延军,男,主任医师,研究方向:心力衰竭 E-mail:chenyanjunhyd@163.com

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患者进行基线评估,其中包括病史和体格检查和充血性症状,记录心血管药物、生命体征、生物标志物(血浆肌酐、血浆胱抑素 C、血浆 BNP),完成病人的整体健康评估和呼吸困难评估。两组均给予地高辛、速尿、螺内酯等治疗,治疗组加用小剂

量多巴胺 $2\mu\text{g/kg/min}$ 静脉持续泵入 48 小时。所有患者按照美国心衰协会 2010 年心力衰竭实践指南的要求,接受每日 <2000 毫克的钠饮食及 <2000 毫升液体摄入^[1]。

表 1 两组患者基础资料的比较

Table 1 Comparison of the baseline characteristics between two groups

Characteristic	Control group	Treatment group
Age(year)	67.8± 4.2	66.4± 3.6
Male sex,(male:female)	25:15	28:12
BMI	25.5± 2.2	25.0± 1.8
Systolic blood pressure, mmHg	114± 10	117± 8
Ejection fraction %	42.0± 2.5	41.2± 2.4
Diabetes mellitus, No	30	32
Hospitalization for acute HF in previous y, NO	35	37
Plasma cystatin C, mg/L	1.71± 0.37	1.68± 0.40
Creatinine, mg/dL	1.60± 0.40	1.62± 0.36
eGFR, mL/min/1.73 m ²	45.5± 10.2	45.0± 9.8
Blood urea nitrogen, mg/dL	35± 10	37± 9
BNP, pg/mL	3760± 424	3620± 486

1.3 观察指标

主要终点事件:以 48 小时累积尿量作为减轻充血功效的标准,48 小时后光抑素 C 变化作为肾功能改善的指标,48 小时胱抑素 C 变化 $>0.3\text{ mg/L}$ 具有临床意义^[9]。次要终点事件:充血症状减轻,肾功能改善,临床疗效改善的相关指标。治疗失败定义为随机化后 48 小时内以下任一项的发生:1 型心肾综合征、恶化或持续性心脏衰竭;定义为需要抢救治疗(额外的静脉注射血管活性药物,超滤,或机械或呼吸支持)需要停用药物的显著低血压;或需要停用药物的显著心动过速。

1.4 统计学方法

所有数据均采用 SPSS13.0 软件进行统计学分析,计量资

料数据以均数± 标准差($\bar{x}\pm s$)表示,采用 t 检验,计数资料两组间采用 χ^2 检验,以 $P<0.05$ 为差异具有统计学意义。

2 结果

2.1 两组主要终点事件的比较

经强心、利尿等对症治疗后,患者的临床症状缓解。研究期间,两组患者接受常规药物的剂量、48 小时的累积尿量均无显著差异(治疗组:4740± 320 mL;对照组:4820± 300 mL, $P=0.59$),48 小时内胱抑素 C 水平无明显变化(治疗组:0.12± 0.06 mg/L,对照组:0.11± 0.05 mg/L, $P=0.72$),见表 2。

表 2 两组主要终点事件的比较

Table 2 Comparison of the primary end point events between two groups

Primary End Point events	Control group	Treatment group	P Value
Cumulative urine volume from randomization to 48 h, mL	4820± 300	4740± 320	0.59
Change in cystatin C level from randomization to 48 h, mg/L	0.11 ± 0.05	0.12 ± 0.06	0.72

2.2 两组次要终点事件的比较

两组间次要终点指标(48 小时内体重变化、BNP 变化、肌

酐变化、进展性心衰发生率、死亡率、治疗失败患者比例)比较均无统计学意义($P>0.05$),见表 3。

表 3 两组次要终点事件的比较

Table 3 Comparison of the secondary end point events between two groups

Secondary End Point events	Control group	Treatment group	P Value
Change in weight fro randomization to 48 h(kg)	0.92± 0.18	1.0± 0.2	$P>0.05$
Change in BNP level to 48 h, pg/mL	1450± 420	1520± 500	$P>0.05$
Change in creatinine level to 48 h, mg/dL	0.32± 0.01	0.028 ± 0.03	$P>0.05$
Persistent or worsening HF within 48 h	4	3	$P>0.05$
Death from any cause within 48h, No	0	0	NA
Treatment failure within 48 h, No	2	3	$P>0.05$

3 讨论

急性心力衰竭时,若并发中度或重度的肾功能不全,会造成不良的临床预后^[9]。目前,没有特异性疗法可以在减轻充血症状的同时,维持急性心脏衰竭患者的肾功能^[2]。本研究结果表明,低剂量多巴胺不能通过加强利尿作用改善急性心衰患者充血症状以及肾功能。

本研究参与者事件的发生率与其他研究相似,表明该类患者能够代表急性心衰合并肾功能不全的患者^[9-11]。目前的研究结果不同于既往的小规模研究,既往研究显示小剂量的多巴胺在急性心衰的治疗中是有益的,但大多数研究没有针对肾功能不全的患者,只包括射血分数低于 40% 的患者,使用较高剂量的多巴胺同时静脉泵入多巴胺时间是多变的^[12,13]。本研究中多巴胺的持续时间明显长于大多数既往研究达到 48 小时持续作用。研究结果均不支持使用小剂量多巴胺可以作为肾脏辅助治疗急性心脏衰竭和肾功能不全。

既往研究中,多巴胺和安慰剂组分别使用不同剂量的利尿剂,利尿剂剂量未根据门诊患者的利尿需求进行调整^[12,13]。本研究中所用的多巴胺剂量是最常用的 " 肾特异性 " 剂量,同时此剂量可减少 α - 和 β - 肾上腺素能介导性肌力和致心律失常作用^[9]。然而,在该剂量时,较低的低血压发生率以及较高的心动过速发生率,表明不完全的肾功能特异性。小剂量多巴胺可使肾血流量及肾小球滤过率均增加,促进尿量及尿钠排泄量增加,而对心率无明显影响。通过加用小量多巴胺配合静脉利尿剂的作用,改善利尿剂抵抗作用,对心肾功能减退患者有更明显的作用^[14]。

急性心脏衰竭的管理指南说明,在利尿剂治疗期间小剂量多巴胺 " 或许应该考虑 ", 小剂量多巴胺增强利尿效果、保持肾功能,但缺乏数据支持^[2]。目前的研究结果也并不支持这一结论。既往研究表明在剂量相同条件下,连续静脉泵入速尿效果优于一次性推注^[15],但本研究中速尿为团注推注,对多巴胺效果有无影响未知。本研究中选取脱氧素 C 作为主要观察终点指标,其特异性、敏感性均高于肌酐变化,是比较新的反映肾功能变化的特异性指标^[16-18]。本研究中患者经对症治疗呼吸后呼吸困难、临床症状缓解,但两组间主要终点、次要终点指标比较均无临床意义。

肾功能不全患者面临着充血症状减轻不理想、肾功能恶化的风险。研究结果表明,急性心衰患者中很大一部分患者使用了多巴胺,但同时上述药物的应用与更长的住院时间,更高的治疗成本,更高的死亡率相关^[19]。这些数据表明,多巴胺要么是有利的,要么就是治疗高危患者时优先使用。本研究中测试了多巴胺的推荐剂量,并没有发现任何肾特异性或临床益处的证据。在本试验中,根据射血分数或血压水平,有不同的治疗效果。具有较高的射血分数或基线血压偏高者低剂量多巴胺 48 小时累积尿量数值更低。低剂量的多巴胺可降低心衰患者肾血管、全身血管阻力,同时降低射血分数。

本研究中存在一定的局限性。根据最新指南分类^[20],心衰分为射血分数保留的心衰、射血分数降低的心衰。本研究中入选的患者射血分数均低于 50%, 属于射血分数降低心衰范畴。对于射血分数保留的心衰患者,多巴胺的疗效未知,需要进一

步的研究。总之,本研究结果表明治疗具有中度或严重的潜在肾功能障碍的急性失代偿性心脏衰竭患者时,低剂量的多巴胺不能减轻充血症状或改善肾功能。

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患者病情进展,改善临床症状,减轻美多巴带来的不良反应,以提高 PD 病患生活质量。实验表明,联合应用依达拉奉和葛根素治疗帕金森病拥有更好的疗效和安全性,抗氧化剂联用具有较好的临床应用前景。而关于两种抗氧化剂协同作用于 PD 治疗的机制,还有待进一步研究证实。

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