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呋塞米联合硝普钠注射液治疗顽固性心力衰竭的临床效果研究 *

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摘要 目的：探讨呋塞米与硝普钠注射液联合治疗顽固性心力衰竭的临床效果及安全性。**方法：**选择 2016 年 5 月至 2018 年 5 月在我院进行治疗的 90 例顽固性心力衰竭患者，按照随机数字表法分为观察组和对照组。对照组给予基础治疗，观察组以对照组为基础加用呋塞米联合硝普钠注射液治疗。治疗后，观察和比较两组的临床疗效、治疗前后血清 B 型脑钠肽(BNP)、C- 反应蛋白(CRP)水平及心功能[左室射血分数(LVEF)、左室舒张末容积指数(LVEDVI)、左室收缩末容积指数(LVESVI)、左室舒张早期与晚期充盈速度比值(E/A)]的变化。**结果：**治疗后，观察组总有效率(91.1%)明显高于对照组(66.7%)(P<0.05)。与治疗前相比，两组患者治疗后的血清 BNP、CRP、LVEDVI、LVESVI 水平均明显低于治疗前，LVEF、E/A 明显高于治疗前(P<0.05)；与对照组相比，观察组治疗后血清 BNP、CRP、LVEDVI、LVESVI 水平均明显降低，LVEF、E/A 显著升高(P<0.05)。两组治疗期间均未发生严重不良反应。**结论：**与常规治疗相比，呋塞米联合硝普钠注射液治疗顽固性心力衰竭患者可更有效改善其心功能，提高其临床疗效，且安全性高。

关键词：呋塞米；硝普钠注射液；顽固性心力衰竭

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Clinical Effect of Furosemide Combined with Sodium Nitroprusside Injection on the Refractory Heart Failure*

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ABSTRACT Objective: To study the curative efficacy and security of furosemide combined with sodium nitroprusside in the treatment of refractory heart failure. **Methods:** 90 patients with refractory heart failure who were treated from May 2016 to May 2018 in our hospital were selected as the research objects and divided into the observation group and the control group according to different treatment. The control group was given basic treatment, while the observation group was given furosemide combined with sodium nitroprusside on the basis of control group. The clinical curative effect, changes of serum b-type brain natriuretic peptide (BNP), C-reactive protein (CRP) levels and heart function [left ventricular ejection fraction (LVEF), left ventricular end-diastolic volume index (LVEDVI), left ventricular contraction at the end of the volume index (LVESVI), left ventricular diastolic early and late filling speed ratio (E/A)] before and after treatment were compared between two groups. **Results:** After treatment, the total effective rate of observation group(91.1%) was obviously higher than that of control group (66.7%) (P<0.05). Compared with before treatment, the serum BNP and CRP levels, LVEDVI and LVESVI of both groups were significantly lower than those before the treatment, the LVEF, E/A were significantly higher than those before treatment (P<0.05). Compared with the control group, the serum BNP and CRP, and LVEDVI and LVESVI levels were significantly reduced, LVEF, E/A significantly higher of observation group after treatment (P<0.05). No serious adverse reaction was found between two groups during treatment. **Conclusion:** Compared with the conventional treatment, Furosemide combined with sodium nitroprusside could more effectively improve the cardiac function of patients with heart failure, enhance the clinical curative effect with high safety.

Key words: Furosemide; Sodium Nitroprusside; Refractory heart failure

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前言

心力衰竭是由于机体心脏排血量不足,致静脉出现淤血的进行性加重临床综合征。多数心力衰竭患者病程较长,经过各种治疗后仍不见好转,可能发展为顽固性心力衰竭[1-3]。对于一般心力衰竭患者而言,休息、利尿剂、强心剂、吸氧、低钠饮食、心电监测等常规治疗方式治疗通常有效,但对于顽固性心力衰竭而言,上述常规治疗疗效并不理想,且患者易复发,病死率也相对较高[3,4]。

研究表明治疗心力衰竭可从改善体循环方面入手。呋塞米为高效利尿剂,作用于髓袢升支粗段髓质部以及皮质部,具有强大的利尿作用;而硝普钠可作用于多巴胺受体,增加机体排尿量,二者均可减轻心脏前负荷、减少心肌耗氧量[5-7]。呋塞米与硝普钠在治疗顽固性心力衰竭均有一定临床疗效[8],但二者联用的报道较为罕见。本研究旨在探讨呋塞米联合硝普钠注射液治疗顽固性心力衰竭的临床疗效及安全性。

1 材料与方法

1.1 一般资料

选择 2016 年 5 月至 2018 年 2 月在本院接受治疗的 90 例顽固性心力衰竭患者为研究对象。纳入标准:(1)临床诊断为顽固心力衰竭;(2)心力衰竭分级判定为 IV 级;(3)对本研究知情并同意。排除标准:(1)具有精神障碍;(2)伴有严重肝肾功能障碍。将入选患者根据治疗方案不同分为两组,观察组 36 例男性,19 例女性,年龄在 32~67 岁,平均年龄(49.48± 6.05)岁;病程 2.5~25 年,平均病程(13.32± 4.32)年;19 例冠心病,8 例充血性心肌病,10 例慢性肺炎性心脏病,8 例风湿性心脏病。观察组 34 例男,21 例女,年龄在 31~68 岁,平均年龄在(48.58± 6.11)岁;病程 3~25 年,平均病程(13.48± 4.06)年;17 例冠心病,10 例充血性心肌病,9 例慢性肺炎性心脏病,9 例风湿性心脏病。两组一般资料相比差异均无统计学意义(P>0.05),具有可比性。

1.2 治疗方法

对照组进行利尿剂、营养支持、洋地黄、吸氧等,观察组在此基础加用呋塞米(广东省丰鑫药业有限公司,2 mL:20 mg,国药准字 H42021912)联合硝普钠治疗,使用硝普钠(金华市明珠制药有限公司,50 mg,国药准字 H20054536)注射液 25 mg 与 0.9% 35 mL 生理盐 水混合静脉泵入,泵入剂量 2 mL/h,连续治疗 1 周,待患者症状有所缓解后使用呋塞米静脉推注治疗,1 次 40 mL,1 天 1 次,连续治疗 3 天。

1.3 观察指标

对两组临床疗效进行观察和比较,在治疗前后检测两组血清 BNP、CRP 水平及心功能[LVEF、LVEDVI、LVESVI、E/A],并对其进行比较。

在治疗前及治疗结束后,采集每位患者 3 mL 的空腹静脉血,采用胶体金法检测血清 BNP 水平,血清 CRP 水平检测使用电化学反光法,并使用超声显像仪检测 LVEF、LVEDVI、LVESVI、E/A。

临床疗效判定标准[9]:(1)显效:临床表现消失,同时心功能缓解 2 级;(2)有效:临床表现大致消失,同时心功能缓解 1 级;(3)无效:临床表现及心功能无明显变化,或加重。

1.4 统计学方法

本研究数据选择 SPSS18.0 进行统计,计量资料组间比较采用 t 检验,计数资料组间比较采用 x^2 检验,以 P<0.05 时表示差异具有统计学意义。

2 结果

2.1 两组临床疗效的比较

经治疗后,观察组总有效率为 91.1%,显著高于对照组(66.7%,P<0.05),详见表 1。

表 1 两组临床疗效的比较[例(%)]

Table 1 Comparison of the clinical efficacy between two groups[n(%)]

Groups	n	Excellent	Progressive	Stable	Total effective rate
Observation group	45	21(46.7)	20(44.4)	4(8.9)	41(91.1)[a]
Control group	45	13(28.9)	17(37.8)	15(33.3)	30(66.7)

Note: Compared with the control group, [a]P<0.05.

2.2 两组治疗前后血清 BNP、CRP 水平的比较

治疗前,两组血清 BNP、CRP 水平比较无显著差异(P>0.05);经治疗后,观察组血清 BNP、CRP 水平均明显低于对照组(P<0.05),详见表 2。

表 2 两组治疗前后血清 BNP、CRP 水平的比较($\bar{x}$± s)

Table 2 Comparison of the serum BNP, CRP levels between the two groups before and after treatment($\bar{x}$± s)

Groups	n	Time	BNP(pg/L)	CRP(mg/L)
Observation group	45	Before treatment	356.32± 48.32	4.94± 0.54
		After treatment	205.45± 25.86[ab]	2.05± 0.25[ab]
Control group	45	Before treatment	354.64± 40.42	4.87± 0.51
		After treatment	294.42± 33.35[b]	3.68± 0.43[b]

Note: Compared with the control group, [a]P<0.05; Compared with before treatment, [b]P<0.05.

2.3 两组治疗前后心功能的比较

治疗前,两组患者 LVEF、E/A、LVEDVI、LVESVI 比较差异

均无统计学意义(P>0.05);治疗后,观察组 LVEF、E/A 高于对照组,LVEDVI、LVESVI 明显低于对照组(P<0.05),详见表 3。

表 3 两组只前后心功能指标的比较($\bar{x}\pm s$)

Table 3 Comparison of the cardiac function indexes between the two groups before and after treatment($\bar{x}\pm s$)

Groups	n	Time	LVEF(mL/m^2)	LVEDVI(mL/m^2)	LVESVI(mL/m^2)	E/A
Observation group	45	Before treatment	31.21± 3.28	53.01± 5.65	38.23± 4.29	0.92± 0.13
		After treatment	44.11± 4.85^{ab}	45.31± 4.78^{ab}	30.17± 3.22^{ab}	1.43± 0.19^{ab}
Control group	45	Before treatment	31.34± 3.52	52.75± 5.41	38.58± 4.15	0.97± 0.15
		After treatment	37.34± 4.06^{b}	49.53± 5.16^{b}	35.06± 3.76^{b}	1.13± 0.14^{b}

Note: Compared with the control group, ^{a}P<0.05; Compared with before treatment, ^{b}P<0.05.

2.4 两组不良反应发生情况的比较

治疗期间,两组均未发生严重不良反应。

3 讨论

对于常规心力衰竭而言,可通过利尿剂、强心剂、控制水钠摄入等常规治疗可达到较好疗效。但对于顽固心力衰竭而言,单纯使用上述基础治疗难以达到理想的疗效[10]。顽固性心力衰竭的血流动力学变化较为复杂,存在心脏负荷过重、心肌收缩功能较弱等不足[11,12]。因此,治疗上应遵循增加机体心肌收缩力,减轻心脏负荷等治疗方针。呋塞米为临床常用的一种强利尿剂,主要通过抑制对钠离子的重吸收,促进钠离子、钾离子等排出发挥强效的利尿作用,同时可降低血容量,从而减轻心室前负荷,改善患者心功能,从而达到治疗顽固性心力衰竭的目的[13]。此外,呋塞米对前列腺分解酶活性具有抑制作用,使前列腺素中 E2 水平增高[14,15]。

硝普钠为一种速效的血管扩张药物,当血管扩张后外周血管阻力会受到阻滞使其下降,从而发挥减压作用,同时减轻心室后负荷,增加心博量;缓解心室前负荷以及室壁张力,从而改善机体心功能[16-18],可有效治疗顽固性心力衰竭。但多项临床研究显示单纯使用呋塞米或硝普钠治疗顽固性心力衰竭其治疗效果虽然相比与常规治疗有所提高, 但并没有达到理想状态,其复发率仍较高。本研究中,患者经呋塞米联合硝普钠治疗后,心功能改善效果要明显优于常规治疗患者,与国外研究结论一致[19,20],提示呋塞米联合硝普钠可更有效治疗顽固性心力衰竭。

BNP 是一种多肽类神经激素,主要由心室分泌,在病理状态下,其水平会显著升高。据相关文献报道,心力衰竭患者其血清 BNP 水平明显高于健康者[21-23]。心力衰竭患者存在心室容量负荷,心室壁张力增加,此时心肌组织会大量合成及释放 BNP 进入血液,从而使其血清水平显著上升。心衰时,BNP 分泌性代偿性增加,在维持心脏代偿状态中具有重要作用。BNP 作为一种天然拮抗激素,可有效抑制促肾上腺皮质激素释放、交感神经的相关递质释放等,同时能够使血管松弛,利于利钠与利尿[24-26]。本研究显示患者治疗后血清 BNP 水平均有一定程度降低,且使用呋塞米联合硝普钠治疗减低效果更明显,可能是治疗后患者心室负荷的缓解抑制了 BNP 的合成与释放。

CRP 是一种机体对炎症、组织受损、感染等反应所产生的急性期反应蛋白,在应激状态下由肝脏合成[27]。心衰时,机体是处于应激状态,CRP 水平增加; 高水平 CRP 可促进细胞凋亡,抑制血管生成,促进左心室重构,使收缩功能受阻,致心功能恶化[28]。研究表明呋塞米可通过调节细胞凋亡改善 CRP 水平[29]。既往研究显示呋塞米、硝普钠可导致患者出现心律失常、恶心呕吐、皮疹等不良反应[30]。但本研究却未出现上述症状,分析其原因可能与纳入研究对象偏少或观察时间较短有关。

综上所述,与常规治疗相比,呋塞米联合硝普钠注射液治疗顽固性心力衰竭患者可更有效改善其心功能,提高其临床疗效,且安全性高。

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