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尼可地尔联合盐酸曲美他嗪治疗微血管性心绞痛的 临床效果和安全性分析*

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摘要 目的:分析尼可地尔联合盐酸曲美他嗪治疗微血管性心绞痛的临床效果和安全性。**方法:**选择陕西省人民医院 2013 年 1 月-2017 年 1 月收治的微血管性心绞痛患者 518 例为研究对象,根据入院顺序经随机数字表法分为对照组和研究组,对照组 260 例患者采用盐酸曲美他嗪进行治疗,研究组 258 例在对照组基础上联合尼可地尔进行治疗,对比两组患者的临床总有效率、内皮血管功能和不良反应发生率。**结果:**治疗后,研究组的总有效率[88.76%(229/258)]显著高于对照组[62.69%(163/260)]($P<0.05$);治疗前,两组患者的一氧化氮(NO)、内皮素(ET-1)和 C-反应蛋白(CRP)水平均无差异($P>0.05$);治疗后,两组患者的 CRP、ET-1 水平均低于治疗前,且研究组低于对照组($P<0.05$);NO 水平均高于治疗前,且研究组高于对照组($P<0.05$);对照组患者在治疗后的总不良反应发生率为 9.23%(24/260),与研究组[10.85%(28/258)]相比差异无统计学意义($P>0.05$)。**结论:**尼可地尔联合盐酸曲美他嗪较单用盐酸曲美他嗪治疗微血管性心绞痛的效果更好,其可显著改善患者内皮血管功能,且安全性与单用盐酸曲美他嗪相当。

关键词:尼可地尔;盐酸曲美他嗪;微血管性心绞痛

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Analysis of the Efficacy and Safety of Nicorandil Combined with Trimetazidine Hydrochloride in the Treatment of Microvascular Angina*

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ABSTRACT Objective: To analyze the efficacy and safety of nicorandil combined with trimetazidine hydrochloride in the treatment of microvascular angina. **Methods:** 518 cases of patients with microvascular angina pectoris from January 2013 to January 2017 in Shaanxi Provincial People's Hospital were selected as the study subjects. According to the admission sequence, they were divided into the control group and the study group by a random number table method, 260 patients in the control group were treated with trimetazidine hydrochloride, and 258 patients in the study group were treated with nicorandil on the basis of control group. The total clinical efficacy, endothelial vascular function and incidence of adverse reactions were compared between the two groups of patients. **Results:** After treatment, the total effective rate of study group was 88.76% (229/258), it was higher than that of the control group [62.69% (163/260)] ($P<0.05$); no significant difference was found in the Nitric oxide (NO), endothelin (ET-1), and C-reactive protein (CRP) levels were before treatment between the two groups ($P>0.05$); after treatment, the CRP and ET-1 levels of both groups of patients were lower than those before treatment, they were lower in the study group than those of the control group ($P<0.05$); the NO levels of both groups of patients were higher than those before treatment, and it was higher in the study group than that of the control group ($P<0.05$); the incidence of total adverse reactions in the control group after treatment was 9.23% (24/260), and no difference was found in comparison to that of the study group [10.85%(28/258)] ($P>0.05$). **Conclusion:** Nicorandil combined with trimetazidine hydrochloride had better efficacy in the treatment of microvascular angina pectoris, it can significantly improve the endothelial vascular function of patients with equal safety to trimetazidine hydrochloride alone.

Key words: Nicorandil; Trimetazidine hydrochloride; Microvascular angina

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前言

微血管性心绞痛又称 X 综合征,是指具有典型的心绞痛症状且存在缺血证据,但冠脉造影的结果显示正常的一类综合

征^[1-3]。目前,关于微血管性心绞痛的发病机制尚未研究清楚,研究认为可能与内皮功能障碍、冠状动脉血流下降、雌激素缺乏、胰岛素抵抗、精神神经功能异常等原因有关,临床上主要通过钙拮抗剂、他汀类、ACE 抑制剂、 β 受体阻滞剂、阿司匹林等

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药物来缓解患者的临床症状,改善其生活质量^[4-6]。

盐酸曲美他嗪是一种具有口服吸收快、起效快、半衰期长等优点的新型的哌嗪类衍生物,其通过优化心肌的能量代谢改善心肌缺血及左心室功能,进而达到缓解心绞痛的目的^[7-9]。尼可地尔是临床上常用的抗心绞痛的药物之一,具有生物利用度高、口服吸收完全、半衰期长等优点^[10-12]。本研究主要分析了尼可地尔联合盐酸曲美他嗪治疗微血管性心绞痛的临床效果和安全性,旨在为临床治疗微血管性心绞痛提供新的新的线索,现将具体结果报道如下:

1 材料与方法

1.1 一般资料

选择我院 2013 年 1 月 -2017 年 1 月收治的微血管性心绞痛患者 518 例,根据入院顺序经随机数字表法分为对照组和研究组,对照组 260 例,男 142 例、女 118 例,年龄 40-81 岁,平均年龄为 55.6 ± 3.4 岁,病程 3 个月 -4 年,平均病程为 2.3 ± 0.5 年;研究组 258 例,男 138 例、女 120 例,年龄 42-80 岁,平均年龄为 56.1 ± 3.1 岁,病程 2 个月 -4 年,平均病程为 2.4 ± 0.6 年;统计学软件对比两组基础资料差异无统计学意义($P > 0.05$),具有可比性。

1.2 纳入及排除标准

纳入标准:①符合微血管性心绞痛的诊断标准(存在劳心性心绞痛症状、ST 段缺血性压低 > 0.1 mV、左室功能正常、冠状动脉造影正常)者;②同意并支持本次研究者。

排除标准:①合并有冠脉痉挛、心脏病、感染性疾病者;②对本次研究所用药物过敏者;③存在严重精神障碍疾病者;④正参与其它临床研究者。

1.3 研究方法

对照组:采用盐酸曲美他嗪(施维雅(天津)制药有限公司,国药准字 H20055465,20 mg× 30 片)进行治疗,口服,每次 1 片,每天 2-3 次。

研究组:在对照组基础上,联合尼可地尔(Nipro Pharma Corporation Kagamiishi Plant,H20150023,5 mg× 100 s)进行治疗,每次 1 片,每天 3 次。

两组患者均治疗 3 个月。

1.4 观察指标

1.4.1 疗效对比 治疗后,患者的心绞痛症状基本消失,且发作次数减少在 75%以上者即为显效;患者心绞痛发作次数减少在 50%-75%之间者即为有效;未达到上述标准者即为无效。

1.4.2 血管内皮功能对比 空腹取静脉血 5 mL,离心得到血清,分别经硝酸还原酶法、酶联吸附法、免疫比浊法检测其一氧化氮(NO)、内皮素(ET-1)和 C-反应蛋白(CRP)水平。

1.4.3 安全性对比 随访三个月,统计两组患者的不良反应的发生情况。

1.5 统计学分析

采用 SPSS20.0 统计学软件进行数据分析,计量资料(均数±标准差)组间比较采用 t 检验;计数资料(百分比)组间比较采用卡方分析,以 $P < 0.05$ 时表示差异存在统计学意义。

2 结果

2.1 两组临床疗效的对比

治疗后,研究组的总有效率[88.76%(229/258)]显著高于对照组[62.69%(163/260)]($P < 0.05$),见表 1。

表 1 两组临床疗效的对比[例(%)]

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

Group	n	Excellent	Effective	Invalid	Total
Research group	258	132(51.16)	97(37.60)	29(11.24)	229(88.76)*
Control group	260	89(34.23)	74(28.46)	97(37.31)	163(62.69)

Note: compared with the Control group, * $P < 0.05$.

2.2 两组治疗前后内皮血管功能指标的对比

治疗前,两组患者的血清 CRP、ET-1、NO 水平比较差异均无统计学意义($P > 0.05$);治疗后,两组的血清 CRP、ET-1 水平

均明显低于治疗前,且研究组以上指标显著低于对照组($P < 0.05$);两组血清 NO 水平均高于治疗前,且研究组明显高于对照组($P < 0.05$),见表 2。

表 2 两组治疗前后内皮血管功能对比($\bar{x} \pm s$)

Table 2 Comparison of the Endothelial Vascular Function before and after treatment between two groups($\bar{x} \pm s$)

Group	n	CRP(mg/L)		ET-1(μ mol/L)		NO(μ mol/L)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Research group	258	12.33± 2.51	6.58± 1.05**	143.12± 15.44	90.68± 10.30**	40.05± 5.67	79.69± 6.85**
Control group	260	12.27± 2.60	9.41± 1.32 [#]	142.63± 14.74	119.61± 12.342 [#]	39.48± 4.79	54.62± 6.592 [#]

Note: compared with the Control group, * $P < 0.05$; compared with the Before treatment, [#] $P < 0.05$.

2.3 两组安全性对比

随访结果显示对照组患者在治疗后有 11 例出现恶心呕吐

症状,13 例出现腹部不适症状,总不良反应发生率为 9.23%(24/260);研究组患者在治疗后有 6 例出现头晕头痛症状,12 例

出现恶心呕吐症状,5 例出现心悸多汗症状,5 例出现食欲不振症状,总不良反应发生率为 10.85%(28/258),两组之间对比差异无统计学意义($P>0.05$)。

3 讨论

微血管性心绞痛患者的主要临床症状有胸痛、胸闷,若得不到及时有效的治疗,患者易出现心肌梗死等不良后果,严重影响患者及其家属的生活质量^[13-15]。同时,心绞痛的反复发作常导致患者反复入院接受相关冠状动脉造影的检查,也间接导致了医疗资源的巨大消耗。因此,积极寻找有效的治疗手段是广大医务工作者共同关注的焦点之一^[16-18]。

目前,临床上多采用他汀类药物、 β 受体阻滞剂、阿司匹林、尼可地尔、盐酸曲美他嗪等治疗微血管性心绞痛患者^[19-21]。本研究结果显示尼可地尔联合盐酸曲美他嗪治疗微血管性心绞痛的效果优于单一盐酸曲美他嗪治疗组。分析其原因可能为尼可地尔为钾离子通道开放剂,具有扩张冠状动脉,增加冠状动脉血流量的作用,在一定程度上抑制了冠状动脉的痉挛;同时,盐酸曲美他嗪可有效维持缺氧、缺血状态下心肌细胞的正常能量代谢,保证透膜钠-钾流的正常运转,有利于内环境的稳定^[22-24],两者协同作用可有效调节微血管性心绞痛患者的血流黏度和流速,进而使其心电活动回复正常。据相关报道显示,微血管性心绞痛的发病原因可能与冠状动脉血流储备能力下降、内皮血管功能异常、精神心理障碍、雌激素水平异常、自主神经功能失调等有关^[25-27]。本文研究结果尼可地尔联合盐酸曲美他嗪可有效改善微血管性心绞痛患者的内皮血管功能,分析原因为 CRP 作为炎症反应的敏感指标,微血管内皮功能的紊乱与炎症反应损伤冠脉内皮细胞有关,尼可地尔联合盐酸曲美他嗪具有抑制炎症反应的作用,从而可改善内皮血管的功能^[28,29]。NO、ET-1 作为血管细胞的内源性平衡因子,分别与血管的舒张、收缩功能有关,尼可地尔为钾离子通道开放剂^[30,31],可协同盐酸曲美他嗪通过改善其在血清中的含量,从而改变内皮功能的紊乱状态。随访研究显示两者联合使用后微血管性心绞痛患者的不良反应发生率并未显著增加,安全性较好。

综上所述,尼可地尔联合盐酸曲美他嗪较单用盐酸曲美他嗪治疗微血管性心绞痛的效果更好,其可显著改善患者内皮血管功能,且安全性与单用盐酸曲美他嗪相当。

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