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芪红汤联合美托洛尔对冠心病心绞痛气虚血瘀型患者血浆 ET、hs-CRP、NT-proBNP 水平的影响 *

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摘要 目的:探讨芪红汤联合美托洛尔对冠心病心绞痛气虚血瘀型患者血浆内皮素(ET)、超敏 C 反应蛋白(hs-CRP)、氨基末端 B 型脑利钠肽原(NT-proBNP)水平的影响。**方法:**选择我院 2014 年 6 月~2016 年 6 月收治的 98 例冠心病心绞痛气虚血瘀型患者,按治疗方式分为对照组与研究组,每组 49 例。对照组选用美托洛尔治疗,研究组在美托洛尔基础上联合芪红汤治疗,两组均持续治疗 1 个月。观察和比较两组的临床疗效,治疗前后症状积分、血浆 ET、hs-CRP、NT-proBNP、左室射血分数(LVEF)、6 min 步行试验、心绞痛持续时间、发作频率及心脏不良事件的发生情况。**结果:**治疗后,研究组总有效率显著高于对照组($P<0.05$),两组症状积分、ET、hs-CRP、NT-proBNP、心绞痛持续时间、发作频率均较治疗前显著降低($P<0.05$),且研究组以上指标均显著低于对照组($P<0.05$);两组 LVEF、6-WMT 均较治疗前上升($P<0.05$),且研究组以上指标均明显高于对照组($P<0.05$)。研究组心脏不良事件发生率显著低于对照组($P<0.05$)。**结论:**芪红汤联合美托洛尔治疗冠心病心绞痛气虚血瘀型患者的临床效果肯定,能够有效降低患者血浆 ET、hs-CRP、NT-proBNP 水平。

关键词:冠心病心绞痛;气虚血瘀型;芪红汤;美托洛尔;内皮素;超敏 C 反应蛋白;氨基末端 B 型脑利钠肽原

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Influence of Qihong Tang Combined with Metoprolol on the Plasma ET, hs-CRP, NT-ProBNP Levels of Patients with Coronary Heart Disease Angina Pectoris Qi Deficiency and Blood Stasis Type*

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ABSTRACT Objective: To research the influence of Qihong Tang combined with metoprolol on the plasma endothelin (ET), hypersensitive c-reactive protein (hs-CRP) and amino terminal b-type brain natriuretic peptide (NT-proBNP) levels of patients with coronary heart disease angina pectoris qi deficiency and blood stasis type. **Methods:** 98 cases of patients with coronary heart disease angina pectoris Qi deficiency and blood stasis type from June 2014 to June 2016 were selected and divided into the control group and the research group according to the treatment mode with 49 cases in each group. The control group was treated with metoprolol, while the research group was treated with qihong tang based on metoprolol, both groups were treated for 1 month. The clinical curative effect, symptom score, plasma ET, hs-CRP, NT-proBNP levels, left ventricular ejection fraction (LVEF), 6 min walk test, angina, duration, attack frequency before and after the treatment and the incidence of cardiac adverse events were observed and compared between two groups. **Results:** After treatment, the total effective rate of research group was significantly higher than that of the control group ($P<0.05$). The symptom score, plasma ET, hs CRP, NT-proBNP levels, LVEF, symptom integral, 6 min walk test, duration of angina pectoris, seizure frequency of both groups were all significantly reduced than those before treatment, and the above indicators of research group were significantly lower than those of the control group ($P<0.05$); the LVEF, 6-WMT of both group were risen, and the above indicators of research group were significantly higher than those of the control group ($P<0.05$). The incidence of cardiac adverse events of research group was significantly lower than that of the control group ($P<0.05$). **Conclusion:** Qihong Tang combined metoprolol was effective in the treatment of patients with Coronary heart disease angina pectoris Qi deficiency and blood stasis type, Qihong Tang combined metoprolol, the effect of winding, sure, which could effectively reduce the plasma levels of ET, HHS - CRP, NT-proBNP of patients.

Key words: Coronary heart disease angina pectoris; Breath deficiency and blood stasis; Qihong decoction; Metoprolol; Endothelin; Hypersensitive c-reactive protein; Amino terminal b-type brain natriuretic peptide

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前言

冠心病是临床常见的心血管疾病,由于冠状动脉粥样硬化或者痉挛造成官腔狭窄导致血流受阻,引起心肌的供血不足所致,遗传、肥胖、吸烟、高血压是其常见诱因^[1]。心绞痛为冠心病的一种急性心脏事件,以不稳定型心绞痛较为常见,可出现呕吐、恶心、乏力、气短、胸闷等临床表现,病情较为隐匿,且进展快速,未能及时就诊者可进展至急性心肌梗死^[2]。药物是不稳定型心绞痛的重要治疗手段,美托洛尔是其常用药物,能够透过血脑屏障,使心输出量减少,减慢心率,减轻心脏的后负荷,但有研究显示冠心病心绞痛患者单用美托洛尔的临床效果并不理想^[3,4]。研究表明冠心病心绞痛常见类型为气虚血瘀,芪红汤是气虚血瘀型心衰的代表方剂,但临床鲜有关于冠心病心绞痛的应用报道^[5,6]。冠心病心绞痛能够诱导多种相关血清因子的表达,其中氨基末端 B 型脑利钠肽原(NT-proBNP)、血浆内皮素(ET)、超敏 C 反应蛋白(hs-CRP)表现较为明显,通过测定其浓度能够有助于疗效评估^[7,8]。本研究主要探讨了芪红汤联合美托洛尔治疗冠心病心绞痛气虚血瘀型患者的临床疗效及对患者心功能的影响。

1 资料与方法

1.1 一般资料

将 98 例冠心病心绞痛患者纳入研究,纳入标准:均与不稳定型心绞痛相关诊断标准相符^[9],并经临床确诊;属中医气虚血瘀型^[10](乏力、心悸气短、胸闷胸痛、舌紫淡、脉弱、面色紫黯);无外科治疗指征;近期无急性创伤或者感染;未见药物或者酒精依赖史。将血液、免疫系统严重病变;肝肾功能显著不全;伴风湿性心脏病、先天性心脏病等;急性心肌梗死;左室射血分数在 30%以下者排除。对照组 26 例男,23 例女;年龄在 47~72 岁,平均(63.28±2.56)岁。研究组 28 例男,21 例女;年龄在 45~73 岁,平均(64.51±2.79)岁。两组一般临床特征比较差异均无统计学意义($P>0.05$),具有可比性。

1.2 治疗方法

两组均予以基础治疗,对照组选用美托洛尔治疗,口服 25 mg 美托洛尔(国药准字 H20060054, 50 mg/片, 140521, 河北国泰医药有限公司),bid。研究组在美托洛尔基础上联合芪红汤治疗,黄芪 30 g,桂枝 6 g,红景天 9 g,川芎 9 g,泽泻 12 g,葶苈子 9 g 等,每天 1 剂,共 200 mL,bid。两组均连续服用 30 天,于服用结束时对疗效进行评估,并统计患者心绞痛发作情况,于治疗 6 个月时统计心脏不良事件的发生率。

1.3 观察指标

1.3.1 临床疗效及症状积分观察 临床体征及症状均显著减轻,症状积分下降在 70%以上为显效;临床体征及症状均有一定减轻,症状积分下降在 30%以上为有效;临床体征及症状均未见缓解,症状积分下降在 30%以下为无效;临床体征及症状均可见加剧,症状积分未见下降为加重。显效与好转均判定为总有效。症状积分包含乏力、心悸气短、胸闷胸痛、舌紫淡、脉弱、面色紫黯 6 个方面,单项评分为 0~5 分^[11]。

1.3.2 指标观察 于治疗前及治疗结束时抽取 2 mL 患者晨起静脉血,常规处理标本并于低温中保存。测定选用酶联免疫法 ET、hs-CRP、NT-proBNP 进行。左室射血分数(LVEF)采取超声进行。6 min 步行试验:于 30 m 直走廊两端与中间各放置一凳子,指导患者于 30 m 走廊里尽最可能的往返步行,且排除外界干扰,记录患者 6 min 中内的最远距离。

1.4 统计学分析

数据处理选用 SPSS18.0 进行,用($\bar{x} \pm s$)表示计量资料,组间比较选用 t 检验进行,用[(例)%]表示计数资料,比较用 χ^2 检验, $P<0.05$ 为差异有统计学意义。

2 结果

2.1 两组临床疗效的比较

研究组总有效率为 89.79%,明显高于对照组(71.42%, $P<0.05$),见表 1。

表 1 两组临床疗效的比较[(例)%]

Table 1 Comparison the clinical curative effect between two groups[(n)%]

Groups	n	Effective	Improved	Invalid	Aggravated	Total effective rate
Control group	49	5(10.20)	30(61.22)	13(26.53)	1(2.04)	35(71.42)
Research group	49	10(20.41)	34(69.38)	4(8.16)	1(2.04)	44(89.79) ^a

Note: Compared with control group $P<0.05$.

2.2 两组治疗前后症状积分的比较

两组治疗前症状积分比较差异均无统计学意义($P>0.05$);两组治疗后乏力、心悸气短、胸闷胸痛、舌紫淡、脉弱、面色紫黯症状积分均较治疗前明显下降,且研究组以上指标明显低于对照组($P<0.05$),见表 2。

2.3 两组治疗前后血浆 ET、hs-CRP、NT-proBNP 水平的比较

两组治疗前血浆 ET、hs-CRP、NT-proBNP 水平比较差异无统计学意义($P>0.05$);两组治疗后血浆 ET、hs-CRP、NT-proBNP 水平均较治疗前明显下降,且研究组以上指标均显著低于对照组($P<0.05$),见表 3。

2.4 两组治疗前后心功能的比较

两组治疗前 6 min 步行试验、LVEF 比较差异无统计学意义($P>0.05$);两组治疗后 6 min 步行试验、LVEF 均显著上升,且研究组比较差异无统计学意义较对照组上升更明显($P<0.05$),见表 4。

2.5 两组治疗前后心绞痛发作情况的比较

两组治疗前心绞痛持续时间、发作频率比较差异无统计学意义($P>0.05$);两组治疗后心绞痛持续时间、发作频率均较治疗前明显下降,且研究组以上指标显著低于对照组($P<0.05$),见表 5。

表 2 两组治疗前后症状积分的比较($\bar{x}\pm s$)Table 2 Comparison of the symptom score between two groups before and after the treatment ($\bar{x}\pm s$)

Groups	n	Time	Fatigue	Palpitations and breathe hard	Chestache chest pain	Pale tongue	Weak pulse	Looking dark purple
Control group	49	Before treatment	4.72± 0.59	4.68± 0.56	4.78± 0.61	4.82± 0.60	4.83± 0.60	4.90± 0.63
		After treatment	3.11± 0.37 ^b	2.96± 0.35 ^b	2.89± 0.34 ^b	3.29± 0.41 ^{bb}	3.24± 0.43 ^b	3.31± 0.41 ^b
Research group	49	Before treatment	4.70± 0.62	4.63± 0.60	4.72± 0.63	4.87± 0.56	4.80± 0.63	4.86± 0.60
		After treatment	2.12± 0.29 ^{ab}	2.20± 0.25 ^{ab}	1.70± 0.21 ^{ab}	2.41± 0.31 ^{ab}	2.25± 0.29 ^{ab}	2.65± 0.32 ^{ab}

Note: Compared with control group ^aP<0.05; Compared with before treatment ^bP<0.05.

表 3 两组治疗前后血浆 ET、hs-CRP、NT-proBNP 水平的比较($\bar{x}\pm s$)Table 3 Comparison of the plasma ET,hs-CRP,NT-proBNP levels between two groups before and after the treatment ($\bar{x}\pm s$)

Groups	n	Time	ET(ng/L)	hs-CRP(mg/L)	NT-proBNP(μg/L)
Control group	49	Before treatment	129.65± 16.13	24.76± 3.21	642.09± 80.25
		After treatment	115.49± 14.34 ^b	19.02± 2.30 ^b	375.64± 46.88 ^b
Research group	49	Before treatment	132.21± 17.08	24.60± 3.90	643.11± 81.06
		After treatment	102.68± 12.76 ^{ab}	12.35± 1.56 ^{ab}	290.12± 35.84 ^{ab}

Note: Compared with control group ^aP<0.05; Compared with before treatment ^bP<0.05.

表 4 两组治疗前后心功能的比较($\bar{x}\pm s$)Table 4 Comparison of the cardiac function between two groups before and after the treatment ($\bar{x}\pm s$)

Groups	n	Time	6 min walk test(m)	LVEF(%)
Control group	49	Before treatment	178.34± 22.25	35.20± 4.05
		After treatment	274.12± 34.25 ^b	42.46± 5.32 ^b
Research group	49	Before treatment	179.25± 21.30	35.87± 4.98
		After treatment	325.87± 40.62 ^{ab}	48.12± 6.73 ^{ab}

Note: Compared with control group ^aP<0.05; Compared with before treatment ^bP<0.05.

表 5 两组治疗前后心绞痛发作情况比较($\bar{x}\pm s$)Table 5 Comparison of the angina pectoris attack between two groups before and after the treatment ($\bar{x}\pm s$)

Groups	n	Time	Time of duration(min)	seizure frequency(Time/day)
Control group	49	Before treatment	7.21± 0.90	3.18± 0.39
		After treatment	4.06± 0.52 ^b	0.96± 0.12 ^b
Research group	49	Before treatment	7.19± 0.82	3.17± 0.42
		After treatment	2.54± 0.37 ^{ab}	0.39± 0.04 ^{ab}

Note: Compared with control group ^aP<0.05; Compared with before treatment ^bP<0.05.

2.6 两组心脏不良事件发生情况的比较

(16.32%, P<0.05), 见表 6。

研究组不良事件发生率为 4.08%，明显低于对照组

表 6 两组心脏不良事件发生情况的比较[(例)%]

Table 6 Comparison the incidence of cardiac adverse events between two groups[(n)%]

Groups	n	Sudden death	Acute myocardial infarction	Recurrence of angina pectoris	incidence of adverse events
Control group	49	1(2.04)	3(6.12)	4(8.16)	8(16.32)
Research group	49	0(0.00)	1(2.04)	1(2.04)	2(4.08) ^a

Note: Compared with control group ^aP<0.05.

3 讨论

冠心病心绞痛为急性冠状动脉综合征的主要类型,有稳定

型及不稳定型之分,临床多见于不稳定型,能够增加心脏不良事件的危险性^[12]。不稳定型心绞痛目前尚无特效疗法,药物是其重要手段,美托洛尔能够使 β 受体产生拮抗,口服后能够完

全、快速吸收,能够抑制交感神经造成的血管收缩,减小周围循环的阻力,且可减少心肌的耗氧量与血液粘稠度,利于心室的舒张功能改善^[13-14]。但国外研究报道,美托洛尔的负性肌力能够诱导心力衰竭,降低临床效果,本研究也发现单用,美托洛尔治疗者的疗效欠佳^[15]。

冠心病心绞痛主要病型为气虚血瘀,久病可引气虚,使血行不通,血脉瘀滞,水饮不化,致气短、心悸、胸痛、乏力、脉涩等,治应补气、利水、温阳^[16,17]。芪红汤以辩证论治之原则,选用黄芪为君药,可益气固本、补气升阳,起到气行瘀血则除之功效^[18,19]。桂枝可助阳化气、温通经络,二者可增强气行血运之功。红景天可活血祛瘀、补气生血;川芎可活血通络、养血益气,与红景天共用可气血同补^[20]。泽泻可利水渗湿,葶苈子可利水消肿,二者可祛邪标正,诸药共用可标本兼治,通补并施。药理最新报道,黄芪对缺氧缺血心肌可起到保护作用,避免心室重构,且可利于冠状动脉的扩张,使心脏后负荷下降;红景天能够使血氧含量增加,促进心功能的改善;桂枝、泽泻、葶苈子能够利于血液的循环,促进排尿、发汗,缓解体液瘀滞;川芎能够降低血压、促进心脏的排出量^[21]。临床研究显示芪红汤治疗冠心病心绞痛能够明显降低患者症状积分,提高临床疗效,本研究也证明此观点,但关于其作用机制仍不明确。

冠状动脉粥样硬化是冠心病不稳定型心绞痛的病变基础,但粥样硬化形成的机制尚未统一,考虑为多个因素综合所致。临床研究报道动脉粥样硬化的关键诱因为血管内皮功能障碍,ET作为一种活性生物多肽,能够诱导血管收缩,造成心率抑制^[22]。炎症反应能够参与内皮功能,hs-CRP能够加剧机体炎症反应,又能增加血管内皮细胞对ET的分泌,导致内皮细胞的相关酶活性下降,造成内皮细胞的功能产生不同程度的异常^[23]。冠心病心绞痛能够导致心肌细胞出现不同程度的损伤,机体能够激活神经激素系统,NT-proBNP更能客观反映心脏功能。本研究结果显示:两组血浆ET、hs-CRP、NT-proBNP水平均于治疗后降低,但联合芪红汤组下降幅度更大,说明两者联合治疗能够缓解内皮功能异常,减轻炎症反应,从而缓解动脉粥样硬化,利于心功能的改善。此外,联合芪红汤组6min步行试验、LVEF有明显上升,且心绞痛发作情况改善更为明显,提示两者联合治疗能够提高患者心功能,使临床症状显著减轻。此外,两组安全性均较高,但联合芪红汤组心脏不良事件的发生率明显较低,说明其对患者的预后能够起到良好的改善作用。

综上所述,芪红汤联合美托洛尔治疗冠心病心绞痛气虚血瘀型患者的临床效果肯定,优于单用美托洛尔治疗者,更有利于患者心功能的改善。

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