

大黄麻黄方对 COPD 缓解期患者肺功能及血压节律的影响

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DOI: 10.3969/j.issn.1008-9691.2018.01.007

【摘要】 目的 探讨大黄麻黄方对慢性阻塞性肺疾病 (COPD) 缓解期患者肺功能及血压节律的影响。**方法** 选择 2014 年 3 月至 2016 年 12 月哈励逊国际和平医院收治的 COPD 缓解期患者 152 例, 按随机数字表法分为西医对照组 72 例和大黄麻黄组 80 例。西医对照组给予常规治疗, 大黄麻黄组在西医常规治疗基础上加用大黄麻黄方 (大黄 6 g、麻黄 5 g、仙鹤草 15 g、甘草 15 g), 水煎服, 每日 2 次口服, 疗程为 3 个月。于治疗前和治疗 1、2、3 个月后检测两组患者的血气分析指标、肺功能、6 min 步行距离 (6MWD), 并观察两组改良医学研究委员会 (mMRC) 呼吸困难问卷评分、动态血压水平的变化及临床疗效。**结果** 与治疗前比较, 两组治疗后血气指标动脉血氧分压 (PaO_2)、动脉血氧饱和度 (SaO_2) 和肺功能指标 1 秒用力呼气容积 (FEV1) 占预计值的百分比 (FEV1%)、FEV1 与用力肺活量的比值 (FEV1/FVC) 以及 6MWD 均持续升高, 动脉血二氧化碳分压 (PaCO_2) 和 mMRC 评分均持续降低, 西医对照组治疗 2 个月时与治疗前比较出现统计学差异, 大黄麻黄组治疗 1 个月时就出现统计学差异。治疗 3 个月后, 大黄麻黄组 PaO_2 、 SaO_2 、FEV1%、FEV1/FVC、6MWD 明显高于西医对照组 [PaO_2 (1 mmHg=0.133 kPa): 95.42 ± 14.88 比 88.28 ± 13.38 , SaO_2 : 0.97 ± 0.02 比 0.96 ± 0.02 , FEV1%: 77.35 ± 11.57 比 72.63 ± 10.66 , FEV1/FVC (%): 71.01 ± 9.47 比 69.28 ± 10.04 , 6MWD (m): 318.0 ± 40.1 比 306.6 ± 35.7], PaCO_2 、mMRC 明显低于西医对照组 [PaCO_2 (mmHg): 40.35 ± 7.58 比 43.57 ± 7.85 , mMRC 评分 (分): 1.09 ± 0.65 比 1.23 ± 0.69], 两组各指标比较差异均有统计学意义 (均 $P < 0.05$)。治疗 3 个月后, 西医对照组血压异常节律型患者降为 44.4% (32/72), 大黄麻黄组降为 32.5% (26/72), 大黄麻黄组治疗后降幅大于西医对照组, 但两组比较差异无统计学意义 ($P > 0.05$)。大黄麻黄组出现血压晨峰值的患者比例明显低于西医对照组 [23.8% (19/80) 比 73.6% (53/72), $P < 0.05$], 大黄麻黄组总有效率明显高于西医对照组 [92.5% (74/80) 比 73.6% (53/72), $P < 0.05$]。**结论** 大黄麻黄方对 COPD 缓解期患者血气分析、肺功能和血压节律有明显的改善作用, 且疗效显著。

【关键词】 大黄麻黄方; 慢性阻塞性肺疾病; 血气分析; 肺功能; 血压节律

基金项目: 河北省中医药管理局中医药类科研计划项目 (2014320)

Effects of Chinese rhubarb and ephedra prescription on pulmonary function and blood pressure rhythm in patients with chronic obstructive pulmonary disease in remission stage Yu Lijie, Li Fengdan, Xiao Hemei, Lei Xinfeng, Li Bingmao

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【Abstract】 Objective To investigate the effect of Chinese rhubarb and ephedra prescription on the pulmonary function and blood pressure rhythm in patients with chronic obstructive pulmonary disease (COPD) in remission stage. **Methods** One hundred and fifty-two patients with COPD were admitted to Harrison International Peace Hospital from March 2014 to December 2016, and they were divided into a western medicine control group (72 cases) and a rhubarb and ephedra prescription group (80 cases) by random number table method, the conventional therapy was given to both groups, and in the rhubarb and ephedra group, additionally Chinese rhubarb and ephedra prescription (rhubarb 6 g, ephedra 5 g, agrimony 15 g, licorice 15 g) was applied, one dose orally taken daily, once 1/2 dose, 2 times a day, the therapeutic course being 3 months. The blood gas analysis, pulmonary function, 6-minute walking distance (6MWD) were detected, and modify medical research committee (mMRC) questionnaire for dyspnea score, the change of ambulatory blood pressure level monitoring and clinical effect were observed before and after treatment for 1, 2, 3 months. **Results** Compared with those before treatment, the blood gas indexes, the arterial partial pressure of oxygen (PaO_2), arterial blood oxygen saturation (SaO_2), and pulmonary function indexes, the percentage of one second forced expiratory volume (FEV1) in predictive value (FEV1%), the ratio of FEV1/forced vital capacity (FEV1/FVC) and 6MWD levels in both groups were continuously increased after treatment, while the arterial partial pressure of carbon dioxide (PaCO_2) and mMRC score were persistently decreased after treatment in the two groups. After treatment for 2 months, compared with before treatment, the statistical differences appeared in the western medicine control group, while in the rhubarb and ephedra group, the statistical differences turned up after 1 month of treatment. After 3 months of treatment,

the PaO_2 , SaO_2 , FEV1%, FEV1/FVC and 6MWD in the rhubarb and ephedra group were significantly higher than those in the western medicine control group [PaO_2 (mmHg, 1 mmHg = 0.133 kPa): 95.42 ± 14.88 vs. 88.28 ± 13.38 , SaO_2 : 0.97 ± 0.02 vs. 0.96 ± 0.02 , FEV1%: 77.35 ± 11.57 vs. 72.63 ± 10.66 , FEV1/FVC (%): 71.01 ± 9.47 vs. 69.28 ± 10.04 , 6MWD (m): 318.0 ± 40.1 vs. 306.6 ± 35.7], PaCO_2 and mMRC were obviously lower in the rhubarb and ephedra group than those in the western medicine control group [PaCO_2 (mmHg): 40.35 ± 7.58 vs. 43.57 ± 7.85 , mMRC score: 1.09 ± 0.65 vs. 1.23 ± 0.69], the differences of the two groups were statistically significant (all $P < 0.05$). After 3 months of treatment, in the western medicine control group, the percentage of patients with abnormal blood pressure rhythm was reduced to 44.4% (32/72), while in the rhubarb and ephedra group, was decreased to 32.5% (26/72), and the decrease amplitude of the rhubarb and ephedra group was greater than that of the western medicine control group ($P > 0.05$). The ratio of blood pressure morning peak in the rhubarb and ephedra group was significantly lower than that in the western medicine control group [23.8% (19/80) vs. 31.9% (23/72), $P < 0.05$], and the total effective rate in rhubarb and ephedra group was significantly higher than that in the western medicine control group [92.5% (74/80) vs. 73.6% (53/72), $P < 0.05$].

Conclusion Chinese rhubarb and ephedra prescription can improve indexes of blood gas analysis, pulmonary function and blood pressure rhythm in COPD patients in remission phase, and its clinical efficacy is significant.

[Key words] Chinese rhubarb and ephedra prescription; Chronic obstructive pulmonary disease; Blood gas analysis; Pulmonary function; Blood pressure rhythm

Fund program: Traditional Chinese Medicine Science Planning Project of Hebei Province Administration of Traditional Chinese Medicine (2014320)

慢性阻塞性肺疾病(COPD)是一种以持续气流受限为特征可以预防和治疗的疾病,其气流受限多呈进行性发展趋势,不仅累及呼吸系统,也可引起全身不良效应,严重影响患者生活质量^[1]。尤其在环境问题越来越严重的今天,其高病死率问题已引起人们的广泛关注。COPD患者不仅肺功能下降,常并发电解质紊乱、血流动力学变化,而且还常伴有心血管疾病(CVD)^[2-3],而血压节律异常与CVD发生发展有密切联系^[4]。中医药治疗COPD也取得一定疗效。现代中药理论研究认为,大黄、麻黄有改善肺通气、保护心血管等作用^[5]。本研究旨在探讨大黄麻黄方对COPD缓解期患者肺功能及血压节律的影响。

1 资料与方法

1.1 一般资料:选取2014年3月至2016年12月本院门诊就诊的COPD缓解期患者152例,其中男性91例,女性61例;年龄46~79岁,平均(60.2 ± 6.8)岁;病程4~13年,平均(8.24 ± 4.71)年。诊断均符合2013年中华医学会呼吸病学分会制定的COPD标准^[6];排除严重心、脑、肝、肾、造血系统损害,以及肿瘤、精神疾病、妊娠期、哺乳期、精神心理疾病患者。

1.2 研究分组:将患者按随机数字表法分为西医对照组(72例)和大黄麻黄组(80例)。两组性别、年龄、病程、疾病严重程度等一般情况比较差异均无

统计学意义(均 $P > 0.05$;表1),说明两组资料均衡,有可比性。

1.3 伦理学:本研究符合医学伦理学标准,并经本院医学伦理委员会批准,所有治疗和检测方法均取得患者或家属知情同意,并积极配合治疗。

1.4 治疗方法

1.4.1 西医对照组:给予沙美特罗替米松气雾剂(商品名:舒利迭,50/250 μg),每次1吸,每日2次;茶碱缓释片0.2 g口服,每日2次;羧甲司坦100 mg口服,每日3次。同时给予定期宣教,指导肺康复锻炼^[7]。

1.4.2 大黄麻黄组:在西医常规治疗基础上给予大黄麻黄方,药物组成:大黄6 g、麻黄5 g、仙鹤草15 g、甘草15 g,水煎服,每日1剂分2次口服。疗程为3个月。

1.5 观察指标及方法

1.5.1 血气分析:于治疗前和治疗后1、2、3个月采用USA GEMPremier3000血气分析仪测定两组患者血气功能状态,包括动脉血氧分压(PaO_2)、动脉血二氧化碳分压(PaCO_2)、动脉血氧饱和度(SaO_2)。

1.5.2 肺功能:治疗前后采用Master Screen Diffusion高级组合式肺功能仪(德国耶格公司生产)测定两组患者肺功能状态,主要观察指标:1秒用力呼气容积(FEV1)占预计值的百分比(FEV1%)、FEV1与用力肺活量的比值(FEV1/FVC)。

表1 两组患者一般资料

组别	例数 (例)	性别(例)		年龄 (岁, $\bar{x} \pm s$)	病程 (年, $\bar{x} \pm s$)	病情严重程度(例)		
		男性	女性			I级	II级	III级
西医对照组	72	45	27	60.39 ± 6.87	9.16 ± 5.72	11	49	12
大黄麻黄组	80	51	29	59.74 ± 7.41	8.81 ± 5.49	13	54	13

1.5.3 呼吸困难程度评分:以改良的英国医学研究委员会(mMRC)呼吸困难问卷评分标准^[8]评价患者的呼吸功能。

1.5.4 6 min 步行距离(6MWD)测定:在一条标有刻度的病房走廊上测定患者 6 min 内用最快速度行走的最远距离,评价患者的运动耐力,重复 2 次,取最大值。

1.5.5 临床疗效:观察两组治疗后临床疗效的变化。

1.5.6 动态血压测定:于治疗前及治疗 1、2、3 个月采用德国 Mobil 公司生产的 Mobil-O-Graph 动态血压仪监测血压,白天每 15 min 测量 1 次,夜间每 30 min 测量 1 次。分别计算昼、夜平均收缩压和舒张压。根据血压昼夜差值百分比将血压的昼夜节律分为杓型、非杓型、超杓型、反杓型 4 种,将非杓型、超杓型、反杓型统称为异常节律型^[9]。06:00~08:00 收缩压的平均值与最低收缩压(等于夜间最低收缩压及其前后共 3 个有效读数的平均值)的差值 ≥ 23.6 mmHg(1 mmHg=0.133 kPa)即为血压晨峰值^[10]。

1.6 疗效判定标准^[6]:治疗 3 个月后判断疗效。评价标准:①临床控制:呼吸系统症状消失或基本消失,症状积分减少 $\geq 95\%$;②显效:呼吸系统症状明显减轻,症状积分减少 $\geq 70\%$;③有效:呼吸系统症状有好转,症状积分减少 $\geq 30\%$;④无效:呼吸系统症状无明显改善,症状积分减少不足 30%。总有效率=(临床控制+显效+有效)/总例数 $\times 100\%$ 。

1.7 统计学方法:使用 SPSS 16.0 统计软件对数据进行分析,符合正态分布的计量资料以均数 $\pm$ 标准差($\bar{x}\pm s$)表示,采用 *t* 检验,计数资料用例(率)表示,采用 χ^2 检验; $P<0.05$ 为差异有统计学意义。

2 结果

2.1 两组患者治疗前后血气分析指标比较(表 2):

与治疗前比较,两组治疗后 PaO₂、SaO₂ 持续升高, PaCO₂ 持续降低。治疗 1 个月起,大黄麻黄组 PaO₂ 均明显高于西医对照组, PaCO₂ 显著低于西医对照组,持续到治疗 3 个月后(均 $P<0.05$);治疗 3 个月后,大黄麻黄组 SaO₂ 明显高于西医对照组($P<0.05$)。

2.2 两组患者治疗前后肺功能指标比较(表 2):与治疗前比较,两组患者治疗后 FEV1%、FEV1/FVC、6MWD 均持续升高, mMRC 持续降低,且以大黄麻黄组患者治疗 3 个月后上述指标的变化更显著(均 $P<0.05$)。

2.3 两组治疗后临床疗效比较(表 3):治疗 3 个月后,大黄麻黄组总有效率明显高于西医对照组($P<0.05$)。

表 3 两组 COPD 缓解期患者临床疗效比较

组别	例数 (例)	临床疗效[例(%)]				总有效率 [例(%)]
		临床控制	显效	有效	无效	
西医对照组	72	34(47.2)	10(13.9)	9(12.5)	19(26.4)	73.6(53)
大黄麻黄组	80	50(62.5)	16(20.0)	8(10.0)	6(7.5)	92.5(74) ^a

注:与西医对照组比较,^a $P<0.05$

2.4 动态血压比较

2.4.1 两组血压节律比例比较(表 4):治疗前,西医对照组和大黄麻黄组均有患者出现血压异常节律型;治疗 3 个月后,两组血压异常节律型患者比例均明显降低,且大黄麻黄组治疗后的降低程度较西医对照组更显著,但两组治疗后比较差异无统计学意义($P>0.05$)。

表 4 两组 COPD 缓解期患者治疗前后血压节律比例比较

组别	时间	例数 (例)	杓型 [% (例)]	异常节律型 [% (例)]	χ^2 值	<i>P</i> 值
西医对照组	治疗前	72	36.1(26)	63.9(46)	4.727	0.030
	治疗 3 个月	72	55.6(40)	44.4(32) ^a		
大黄麻黄组	治疗前	80	37.5(30)	62.5(50)	13.258	0.000
	治疗 3 个月	80	67.5(54)	32.5(26) ^a		

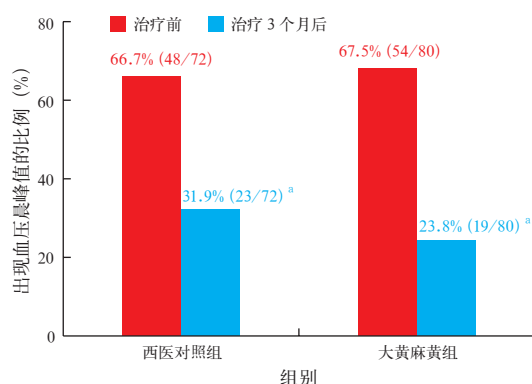
注:与治疗前比较,^a $P<0.05$

表 2 两组 COPD 缓解期患者治疗前后血气分析及肺功能指标比较($\bar{x}\pm s$)

组别	时间	例数 (例)	PaO ₂ (mmHg)	PaCO ₂ (mmHg)	SaO ₂	FEV1 (%)	FEV1/FVC (%)	mMRC 评分 (分)	6MWD (m)
西医对照组	治疗前	72	77.38 $\pm$ 11.10	51.35 $\pm$ 9.14	0.95 $\pm$ 0.01	55.24 $\pm$ 9.23	62.14 $\pm$ 11.26	1.523 $\pm$ 0.732	268.4 $\pm$ 37.1
	治疗 1 个月	72	80.27 $\pm$ 10.91	48.86 $\pm$ 8.61	0.95 $\pm$ 0.02	58.52 $\pm$ 10.15 ^a	63.08 $\pm$ 9.54	1.447 $\pm$ 0.729	277.5 $\pm$ 34.9
	治疗 2 个月	72	85.11 $\pm$ 12.57 ^a	45.19 $\pm$ 8.15 ^a	0.96 $\pm$ 0.01 ^a	65.32 $\pm$ 8.22 ^a	66.29 $\pm$ 12.16 ^a	1.347 $\pm$ 0.821	291.9 $\pm$ 41.5 ^a
	治疗 3 个月	72	88.28 $\pm$ 13.38 ^b	43.57 $\pm$ 7.85 ^b	0.96 $\pm$ 0.02 ^a	72.63 $\pm$ 10.66 ^b	69.28 $\pm$ 10.04 ^a	1.232 $\pm$ 0.690 ^b	306.6 $\pm$ 35.7 ^b
大黄麻黄组	治疗前	80	75.17 $\pm$ 9.76	52.07 $\pm$ 8.05	0.95 $\pm$ 0.01	54.59 $\pm$ 10.31	62.52 $\pm$ 10.61	1.542 $\pm$ 0.718	265.4 $\pm$ 42.5
	治疗 1 个月	80	82.15 $\pm$ 10.17 ^a	46.04 $\pm$ 9.91 ^{bc}	0.96 $\pm$ 0.02	60.13 $\pm$ 9.62 ^a	65.02 $\pm$ 12.44 ^a	1.401 $\pm$ 0.655	281.2 $\pm$ 39.2 ^a
	治疗 2 个月	80	93.91 $\pm$ 13.87 ^{bc}	42.67 $\pm$ 8.49 ^{bc}	0.96 $\pm$ 0.02 ^a	68.89 $\pm$ 9.54 ^b	78.45 $\pm$ 10.29 ^b	1.257 $\pm$ 0.877 ^a	299.0 $\pm$ 42.8 ^b
	治疗 3 个月	80	95.42 $\pm$ 14.88 ^{bc}	40.35 $\pm$ 7.58 ^{bc}	0.97 $\pm$ 0.02 ^{ac}	77.35 $\pm$ 11.57 ^{bc}	71.01 $\pm$ 9.47 ^{bc}	1.088 $\pm$ 0.649 ^{bc}	318.0 $\pm$ 40.1 ^{bc}

注:与本组治疗前比较,^a $P<0.05$,^b $P<0.01$;与西医对照组比较,^c $P<0.05$

2.4.2 两组出现血压晨峰值的患者比例比较(图1):治疗前,西医对照组和大黄麻黄组患者出现血压晨峰值的比例均达到 60% 以上;治疗 3 个月后两组出现血压晨峰值的比例均较治疗前明显降低,差异有统计学意义(均 $P < 0.05$)。



注:与治疗前比较,^a $P < 0.05$

图 1 两组 COPD 缓解期患者治疗前后出现血压晨峰值的比例

3 讨论

COPD 是一种常见的慢性呼吸系统疾病,患者多为老年人,近年来其发病率逐年升高,目前居全球死亡原因的第 4 位,直接影响患者生活质量。COPD 患者常经历急性加重,每一次发作将加重病情并促进疾病的发展^[11]。中医学并无 COPD 这一病名,根据临床症状将其归属于“咳嗽”“喘证”“痰饮”“肺胀”等范畴。由于 COPD 的病情复杂,治疗难度大,临床多主张采用综合疗法^[12-15],提高患者生活质量。COPD 发病机制复杂,不仅包括炎症反应,而且有研究发现,微小 RNA(miRNA)的异常表达也可能在 COPD 发病过程中有重要作用^[16]。综合疗法在临床上应用更为广泛,即在常规西医治疗基础上,结合中医中药以及康复训练,可起到延缓病情进展,提高患者生活质量的作用^[17]。现代药理学研究表明,大黄有调节免疫、清除氧自由基、抑菌抗炎、抗病毒、保肝利胆、保护心血管等作用,现代临床常用于急性肺损伤以改善患者肺通气功能^[5-6]。中医学认为麻黄是“肺经专药”^[18-19]。故本研究在常规西药治疗基础上给予大黄麻黄方治疗 COPD,同时定期宣教,指导肺康复锻炼。

随着病情进展, COPD 患者的气流受限不完全可逆,最终导致肺通气和换气功能障碍;同时患者肺功能持续下降,导致机体缺氧和二氧化碳潴留,进而引发低氧血症、高碳酸血症,使血液黏稠度增加^[20-22]。中度至极重度 COPD 患者睡眠低氧普遍存在^[23]。本研究表明,两组患者治疗后血气分析

指标 PaO_2 、 PaCO_2 、 SaO_2 均较治疗前明显改善,且大黄麻黄组的改善程度更明显;同时检测患者肺功能相关指标 FEV1% 和 FEV1/FVC、6MWD、mMRC 发现,虽然大黄麻黄组和西医对照组治疗后 1 个月开始,肺功能各项指标均明显改善,但大黄麻黄组治疗 3 个月后 FEV1%、FEV1/FVC、6MWD、mMRC 已与西医对照组比较差异有统计学意义,且治疗 3 个月后大黄麻黄组总有效率明显高于西医对照组。提示,大黄麻黄方对改善 COPD 患者血气分析和肺功能作用更显著。

异常的血压节律是心血管系统疾病发生发展的独立危险因素,也是独立于血压水平之外的预测因素,与靶器官损害密切相关^[24-26]。血压基本节律异常时发生心脑血管并发症的危险性显著增加^[4]。另一方面,清晨血压的陡增又是诱发恶性心脏事件的主要因素之一,致使该时段内恶性心脏事件的发生率明显高于同日其他时段^[10]。血压昼夜节律已成为判断高血压严重程度和预后的一个重要指标,恢复血压昼夜节律对靶器官损害的逆转和改善预后具有重要意义。有研究表明, COPD 急性加重期(AECOPD)异常血压节律者占多数^[27-28]。故在治疗 COPD 的同时,应加强对患者血压节律的监测,及时纠正其异常节律,减少对机体的损伤及心血管事件的发生。本研究还表明, COPD 缓解期患者中血压异常节律型占比高达 60%,这对预后有潜在危险。治疗 3 个月后,两组血压异常节律型患者比例及出现血压晨峰值的比例均明显降低。提示大黄麻黄方在一定程度上可改善 COPD 患者血压节律。

综上所述,大黄麻黄方可以通过改善 COPD 患者血气分析、延缓肺功能损害、纠正血压异常节律以减少继发损害、保护心肺功能,从而提高患者生活质量。

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(收稿日期: 2017-09-02)