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桉柠蒎对慢性阻塞性肺疾病急性加重期患者肺功能及氧化应激的影响*

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摘要 目的:探讨桉柠蒎对慢性阻塞性肺疾病急性加重期(AECOPD)患者肺功能及氧化应激的影响。方法:选取2010年9月-2017年6月在我院进行治疗的AECOPD患者126例,采用乱数表法将所有患者分为对照组和研究组各63例。对照组给予盐酸氨溴索口服溶液治疗,研究组给予桉柠蒎肠溶软胶囊治疗,比较两组患者的临床疗效及治疗前后的用力肺活量(FVC)、第1秒用力呼气容积(FEV1)以及第1秒用力呼气容积占预计值百分比(FEV%)、丙二醛(MDA)、8-异构前列腺素(8-isoprostane)水平,观察两组患者治疗过程中不良反应发生率。结果:研究组患者的总有效率为95.24%,高于对照组的82.54%($P<0.05$)。两组患者治疗前的FVC、FEV1、FEV%比较无统计学差异($P>0.05$),治疗28d后两组患者的FVC、FEV1、FEV%均明显上升,且研究组的FVC、FEV1、FEV%高于对照组($P<0.05$)。两组患者治疗前的MDA、8-isoprostane比较无统计学差异($P>0.05$),治疗28d后两组患者的MDA、8-isoprostane明显下降($P<0.05$),治疗28d后研究组的MDA、8-isoprostane低于对照组($P<0.05$)。对照组不良反应发生率为7.94%(5/63),与研究组的6.35%(4/63)相比,差异无统计学意义($P>0.05$)。结论:桉柠蒎可明显改善AECOPD患者的肺功能和氧化应激,具有较好的临床疗效,且不良反应率低,值得临床推广应用。

关键词:慢性阻塞性肺疾病;桉柠蒎;肺功能;氧化应激;疗效

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Effect of Eucalyptus on Pulmonary Function and Oxidative Stress in Patients with Acute Exacerbation of Pulmonary Chronic Obstructive Pulmonary Disease*

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ABSTRACT Objective: To investigate the effect of eucalyptus on pulmonary function and oxidative stress in patients with acute exacerbation of pulmonary chronic obstructive pulmonary disease (AECOPD). **Methods:** A total of 126 patients with AECOPD, who were treated in Anhui NO.2 Provincial People's Hospital from September 2010 to June 2017, were selected and randomly divided into control group ($n=63$) and study group ($n=63$). The control group was treated with Ambroxol Hydrochloride Oral Solution, the study group was given eucalyptol linonene pinene enteric soft capsule. The clinical efficacy and the forced vital capacity (FVC), forced expiratory volume in 1 second (FEV1), the forced expiratory volume in one second (FEV%), the malondialdehyde (MDA) and the 8- heterogeneous prostaglandin (8-isoprostane) level before and after treatment were compared between the two groups. The incidence of adverse reactions during the treatment of the two groups was observed. **Results:** The total effective rate (95.24%) of the study group was higher than that (82.54%) of the control group ($P<0.05$). There were no significant differences in FVC, FEV1 and FEV% in the two groups before treatment ($P>0.05$), the FVC, FEV1 and FEV% of the two groups were significantly increased after the treatment of 28d, and the FVC, FEV1 and FEV% of the study group were higher than those of the control group ($P<0.05$). There were no significant differences in MDA and 8-isoprostane between the two groups before treatment ($P>0.05$). The MDA and 8-isoprostane decreased significantly in the two groups after the treatment of 28d ($P<0.05$), the MDA and 8-isoprostane of the study group were lower than those of the control group after the treatment of 28 d ($P<0.05$). The incidence of adverse reactions in the control group was 7.94% (5/63), and the difference was not statistically significant compared with the 6.35% (4/63) of the study group ($P>0.05$). **Conclusion:** Eucalyptus can significantly improve the pulmonary function and oxidative stress in patients with AECOPD, with good clinical effect and low adverse reaction rate, which is worthy of clinical application.

Key words: Pulmonary chronic obstructive pulmonary disease; Eucalyptus; Pulmonary function; Oxidative stress; Curative effect

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前言

慢性阻塞性肺疾病(chronic obstructive pulmonary disease, COPD)是呼吸内科最为常见的慢性疾病,以持续性气流受限为主要特征,患者表现为咳嗽、咳痰、呼吸困难、胸闷等症状^[1,2]。近年来,随着吸烟人数的增多和日益严重的环境污染,COPD的发病率呈逐年增长的趋势,相关研究显示^[3],我国≥40岁人群COPD患病率为9.9%(95%CI:8.8%-11.0%),而≥70岁人群COPD患病率高达20.3%(95%CI:18.2%-22.4%),由此可见,COPD对人们的健康构成巨大的威胁,已成为我国主要的公共卫生问题。慢性阻塞性肺疾病急性加重期(acute chronic obstructive pulmonary, AECOPD)是COPD较为严重的类型,AECOPD是一个急性的起病过程,患者的呼吸系统出现急性加重现象,如气喘、痰量增多且变脓,可导致患者肺功能进一步恶化^[4,5]。桉柠蒎是一种粘液溶解性祛痰药,临床上常用于治疗急性慢性支气管炎、肺炎、COPD等呼吸道疾病,具有较好的临床疗效^[6,7]。有研究显示^[8,9],氧化应激可加重COPD患者的气道炎症反应,导致气道平滑肌功能异常,在COPD的发生及发展中起到重要的作用。本研究旨在探讨桉柠蒎对AECOPD患者肺功能及氧化应激的影响,以为AECOPD的治疗提供参考。

1 资料与方法

1.1 一般资料

选取2010年9月-2017年6月在我院进行治疗的AECOPD患者126例,纳入标准:(1)所有患者均存在明显的致病因素且表现出AECOPD的典型临床症状,即气促加重、喘息、胸闷、咳嗽加剧、痰量增加、痰液颜色和/或黏度改变以及发热等,诊断标准参考《慢性阻塞性肺疾病急性加重(AECOPD)诊治中国专家共识(2014年修订版)》^[10];(2)年龄在18-80岁之间;(3)病历资料完整者;(4)患者及其家属对本研究知情同意。排除标准:(1)对本研究药物过敏者;(2)GOLD肺功能分级为IV级者^[9];(3)存在心、肝、肾等重要脏器严重病变者;(4)合并恶性肿瘤者、其他严重的肺部疾病者;(5)具有支气管镜禁忌症者;(6)依从性不高者。采用乱数表法将所有患者分为对照组和研究组,两组均为63例。其中对照组男性36例,女性27例,年龄46-78岁,平均年龄(57.86±9.43)岁,GOLD肺功能分级:II级30例,III级33例。研究组男性38例,女性25例,年龄43-79岁,平均年龄(58.31±9.62)岁,GOLD肺功能分级:II级28例,III级35例。两组的一般资料比较无统计学差异($P>0.05$),可行组间比较。本研究符合我院伦理委员会制定的相关标准,并已审批通过。

1.2 治疗方法

两组患者在入院后均采用Venturi面罩进行氧疗,氧疗30 min后复查动脉血气,以确认氧合满意,并根据患者的实际情况给予镇咳、祛痰、抗炎等常规治疗。对照组患者给予盐酸氨溴索口服溶液(江苏恒瑞医药股份有限公司,国药准字:H20064090,规格:100 mL:0.6 g)治疗,10 mL/次,3次/d,共治疗28 d。研究组患者给予桉柠蒎肠溶软胶囊(北京九和药业有限公司,国药准字:H20052401,规格:0.3 g/粒)治疗,1粒/次,3次/d,共治疗28 d。在治疗期间叮嘱患者戒烟、戒酒、饮食清淡。

1.3 观察指标

1.3.1 疗效评估 两组患者在治疗28 d后进行疗效评估,若患者的临床症状较治疗前得到明显改善,且肺部啰音基本消失,则判定为显效;若患者的临床症状较治疗前有所改善,且肺部啰音减少,则判定为有效;若患者的临床症状及体征较治疗前无明显改变或者加重,则判定为无效。总有效率=显效率+有效率。

1.3.2 肺功能指标检测 在治疗前和治疗28 d后采用肺功能检测仪(德国Jaeger MS-DIFFUSION)检测两组患者的肺功能,检测指标包括用力肺活量(forced vital capacity, FVC)、第1秒用力呼气容积(forced expiratory volume in one second, FEV₁)以及第1秒用力呼气容积占预计值百分比(percent of forced expiratory volume in one second, FEV₁%)。

1.3.3 氧化应激指标检测 两组患者在治疗前和治疗28 d后采用电子显微支气管镜(奥林巴斯BF-260)进行肺泡灌洗,每次采用60-100 mL的生理盐水进行灌洗,收集50 mL回收液,采用3000 r/min的离心速度进行20 min的离心运动,收集上清液,置于-20℃的环境下保存。采用酶联免疫吸附法检测肺泡灌洗液中的丙二醛(malondialdehyde, MDA)、8-异前列腺素(8-isoprostane),由我院经验丰富的检验医师完成检测,MDA、8-isoprostane检验试剂盒均购于上海江莱生物科技有限公司,具体的检验步骤均严格遵循试剂盒中的操作指南进行。

1.3.4 不良反应 观察并记录两组患者在治疗过程中出现的不良反应。

1.4 统计学方法

应用SPSS22.0进行数据处理。以均数±标准差($\bar{x} \pm s$)表示肺功能指标、氧化应激指标等计量资料,采用t检验,以率的形式表示总有效率、不良反应发生率等计数资料,采用 χ^2 检验,将 $\alpha=0.05$ 作为检验标准。

2 结果

2.1 两组患者的治疗效果比较

研究组患者的总有效率为95.24%,高于对照组的82.54% ($P<0.05$),见表1。

表1 两组患者的治疗效果比较[n(%)]

Table 1 Comparison of therapeutic effects of two groups[n(%)]

Groups	n	Excellence	Effective	Invalid	Total effective rate
Control group	63	28(44.44)	24(38.10)	11(17.46)	52(82.54)
Study Group	63	39(61.90)	21(33.33)	3(4.76)	60(95.24)
χ^2					5.143
P					0.023

2.2 两组患者治疗前后肺功能指标比较

两组患者治疗前的 FVC、FEV1、FEV% 比较无统计学差异 ($P>0.05$), 治疗 28 d 后两组患者的 FVC、FEV1、FEV% 均明显

上升, 且研究组的 FVC、FEV1、FEV% 高于对照组 ($P<0.05$), 见表 2。

表 2 两组患者治疗前后肺功能指标比较 ($\bar{x} \pm s$)

Table 2 Comparison of pulmonary function indexes before and after treatment in two groups ($\bar{x} \pm s$)

Groups	n	Time	FVC(L)	FEV1(L)	FEV%(%)
Control group	63	Before treatment	1.68± 0.52	1.34± 0.18	55.47± 2.64
		After the treatment of 28 d	1.90± 0.61*	1.57± 0.19*	67.42± 4.33*
Study Group	63	Before treatment	1.66± 0.57	1.36± 0.16	55.82± 2.73
		After the treatment of 28 d	2.21± 0.63**	1.89± 0.21**	71.65± 5.02**

Note: compared with before treatment, * $P<0.05$; compared with the control group, ** $P<0.05$.

2.3 两组患者治疗前后氧化应激指标比较

两组患者治疗前的 MDA、8-isoprostane 比较无统计学差异 ($P>0.05$), 治疗 28 d 后两组患者的 MDA、8-isoprostane 明显下

降 ($P<0.05$), 治疗 28 d 后研究组的 MDA、8-isoprostane 低于对照组 ($P<0.05$), 见表 3。

表 3 两组患者治疗前后氧化应激指标比较 ($\bar{x} \pm s$)

Table 3 Comparison of oxidative stress indicators before and after treatment in two groups ($\bar{x} \pm s$)

Groups	n	Time	MDA (mmol/mL)	8-isoprostane (pg/mL)
Control group	63	Before treatment	15.48± 2.53	123.71± 6.47
		After the treatment of 28 d	11.22± 4.19*	107.33± 5.73*
Study Group	63	Before treatment	15.46± 2.54	122.52± 6.63
		After the treatment of 28 d	9.39± 4.22**	99.56± 5.42**

Note: compared with before treatment, * $P<0.05$; compared with the control group, ** $P<0.05$.

2.4 两组患者治疗过程中不良反应比较

两组患者在治疗过程中均未出现严重的不良反应。对照组出现 3 例腹泻, 2 例腹胀, 不良反应发生率为 7.94% (5/63); 研究组出现 2 例腹泻, 2 例腹胀, 不良反应发生率为 6.35% (4/63), 两组患者的不良反应率无统计学差异 ($\chi^2=0.100$, $P=0.752$)。

3 讨论

COPD 是导致人类死亡的重要原因, 据全球疾病负担研究预测^[1], 在 2020 年 COPD 将排在全球死亡原因中的第 3 位, 因此探究治疗 COPD 的方法具有重要的临床意义。AECOPD 患者由于气道炎症反应产生大量的氧化自由基和炎性因子, 导致粘液分泌腺增大, 引发气流受限, 另外炎性反应降低黏膜纤毛清除功能和肺泡巨噬细胞吞噬功能, 并导致肺泡活性物质散失, 进而降低气道黏液清除能力、增加黏液黏度, 加重气道堵塞, 导致肺功能下降^[12-14]。氧化应激是指体内的氧化 - 抗氧化失衡, 气道炎症因子中的白介素 -1, 肿瘤坏死因子 - α 、干扰素 γ 可刺激气道平滑肌细胞, 导致细胞内线粒体产生大量的活性氧簇, 提高氧化能力, 另一方面, AECOPD 患者转录因子叉头框蛋白和转化生长因子 - β 表达异常, 导致抗氧化酶超氧化物歧化酶、过氧化氢酶表达下降, 进而引起氧化 - 抗氧化失衡^[15,16]。氧化应激可造成组织器官的氧化性损伤, 同时可促进中性粒细胞聚集, 放大炎症反应, 进而加重 AECOPD 患者的病情^[17-19]。

在本次研究中, 研究组患者的总有效率为 95.24%, 高于对照组的 82.54% ($P<0.05$), 治疗后两组患者的 FVC、FEV1、

FEV% 均明显上升, 且研究组的 FVC、FEV1、FEV% 高于对照组 ($P<0.05$), 说明采用桉柠蒎治疗 AECOPD 患者有较好的临床疗效, 可有效改善患者的肺功能。桉柠蒎主要由桉油精、柠檬烯和 α - 蒎烯组成, 其中桉油精具有抗炎、消菌、解热、镇痛、平喘的作用, 而柠檬烯具有祛痰、镇咳、缓解支气管平滑肌痉挛的作用, α - 蒎烯有镇咳、抗真菌、祛痰的作用^[20-22]。另外, 桉柠蒎为脂溶性挥发油, 可碱化分泌物, 改善黏液的 pH 值和黏滞度, 同时桉柠蒎还可以刺激纤毛摆动, 进而加强纤毛的清除能力, 改善气道堵塞情况^[23,24]。MDA、8-isoprostane 是重要氧化应激产物, 其水平可反映机体氧化应激的程度^[25-27]。本研究结果还显示, 治疗后两组患者的 MDA、8-isoprostane 明显下降, 且研究组的 MDA、8-isoprostane 低于对照组 ($P<0.05$), 说明桉柠蒎可有效降低 AECOPD 患者的氧化应激, 改善氧化 - 抗氧化失衡现象。这可能是由于桉柠蒎可改善气道环境, 减轻气道炎症反应, 进而减少由炎症应激促进产生的活性氧簇水平, 从而改善氧化 - 抗氧化失衡现象^[28-30]。在不良反应方面, 两组患者均未出现严重不良反应, 且两组的不良反应率无统计学差异 ($P>0.05$), 说明桉柠蒎安全性较好, 无明显的副作用。

综上所述, 桉柠蒎治疗 AECOPD 患者具有较好的临床疗效, 可明显提升患者的肺功能, 改善氧化应激状态, 且安全性较好, 值得临床推广应用。

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