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在线全文

小青龙汤治疗表寒里饮证慢性阻塞性肺疾病急性加重期的临床观察*

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【摘要】 **目的** 分析小青龙汤联合基础西药治疗表寒里饮证慢性阻塞性肺疾病急性加重期（acute exacerbation of chronic obstructive pulmonary disease, AECOPD）的临床疗效，并评估其对患者短期预后的影响。 **方法** 将124例表寒里饮证AECOPD患者使用随机数字表法分为观察组（62例）与对照组（62例），对照组给予支气管舒张剂、糖皮质激素及抗菌药物等基础西药治疗，观察组在对照组治疗方案的基础上给予小青龙汤治疗，每日1剂，连续治疗10 d。主要结局指标为总有效率、治疗前及治疗10 d后主要中医证候积分。次要结局指标：治疗前、治疗10 d后感染及炎症指标〔白细胞计数（WBC）、降钙素原（PCT）、白细胞介素（IL）-6、C-反应蛋白（CRP）〕、动脉血气〔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）〕，治疗期间药物不良反应，出院后1个月随访呼吸困难程度〔改良英国医学研究委员会呼吸困难量表（mMRC）〕。 **结果** 与本组治疗前比较，治疗后两组各项主要中医证候积分及总分均降低（$P<0.05$）；治疗后与对照组比较，观察组患者咳嗽、恶寒、鼻塞、流涕证候积分及总积分降低（$P<0.05$）。观察组与对照组总有效率分别为94.91%、82.76%，观察组总有效率明显高于对照组（$P<0.05$）。与本组治疗前比较，两组患者治疗10 d后$PaCO_2$、WBC及PCT、IL-6、CRP水平均明显降低（$P<0.05$）；治疗后与对照组比较，观察组患者$PaCO_2$、WBC及PCT、IL-6、CRP水平降低（$P<0.05$）。与本组治疗前比较，两组患者治疗10 d后PaO_2、SaO_2明显升高（$P<0.05$）；治疗后与对照组比较，观察组患者PaO_2、SaO_2升高（$P<0.05$）。治疗期间两组患者均未出现肝肾功能异常等严重不良反应，也并未观察到与小青龙汤治疗相关的不良反应。两组患者出院后1个月随访时均无mMRC4级病例，与本组治疗前比较，出院后1个月两组患者mMRC分级均降低（$P<0.05$）；出院后1个月与对照组比较，观察组患者mMRC分级更低（$P<0.05$）。 **结论** 小青龙汤联合基础西药治疗表寒里饮证AECOPD患者临床疗效较好，可有效改善中医证候，缓解呼吸困难症状，减轻炎症反应，促进感染消退，延缓病情进展，改善短期预后，安全性良好。

【关键词】 慢性阻塞性肺疾病 急性加重期 小青龙汤 表寒里饮证 预后

Using Xiaoqinglong Decoction to Treat Acute Exacerbation of Chronic Obstructive Pulmonary Disease Presenting External Cold and Internal Fluid Retention Syndrome: Observation of the Clinical Efficacy

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[**Abstract**] **Objective** To study the clinical efficacy of Xiaoqinglong decoction combined with the conventional protocol of western medicine in the treatment of acute exacerbation of chronic obstructive pulmonary disease (AECOPD) presenting with exterior cold and interior fluid retention syndrome, and to evaluate its effect on the short-term prognosis of patients. **Methods** A total of 124 AECOPD patients presenting exterior cold and interior fluid retention syndrome were divided into an observation group (62 cases) and a control group (62 cases) using a random number table. Patients in the control and observation groups were managed with conventional western medicine treatment protocols consisting of bronchodilators, glucocorticoids, and antibacterial drugs. In addition, patients in the observation group were also given Xiaoqinglong decoction at one dose per day for 10 days in succession. The primary outcome indicators included the total effective treatment rate and the main traditional Chinese medicine (TCM) syndrome scores before treatment and after 10 days of Xiaoqinglong decoction treatment. The secondary outcome indicators included infection and inflammatory indicators, including white blood cell count (WBC), procalcitonin (PCT), interleukin (IL)-6, C-reactive protein (CRP), and arterial blood gas indicators, including arterial partial pressure of oxygen (PaO_2), arterial partial pressure of carbon dioxide ($PaCO_2$), and arterial oxygen saturation (SaO_2), measured before treatment and after 10 days of treatment, adverse

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drug reactions during treatment, and the severity of dyspnea assessed by the modified Medical Research Council (mMRC) dyspnea scale at the 1-month follow-up after discharge. **Results** Compared with baseline findings for the same group before treatment, the main TCM syndrome scores and the total score were reduced in both groups after treatment ($P < 0.05$). After treatment, compared with those of the control group, the syndrome scores for cough, aversion to cold, nasal congestion, and runny nose, and the total score in the observation group were lower ($P < 0.05$). The total effective treatment rate in the observation group (94.91%) was significantly higher than that in the control group (82.76%) ($P < 0.05$). After 10 days of treatment, the levels of $PaCO_2$, WBC, PCT, IL-6, and CRP in both groups were significantly reduced compared with those before treatment ($P < 0.05$). After treatment, the levels of $PaCO_2$, WBC, PCT, IL-6, and CRP in the observation group were lower than those in the control group ($P < 0.05$). Compared with those before treatment, PaO_2 and SaO_2 levels in both groups increased significantly after 10 days of treatment ($P < 0.05$). During the course of treatment, no severe adverse reactions, such as liver or kidney dysfunction, occurred in either group. No adverse reactions associated with Xiaoqinglong decoction were observed. No patients in either group reached mMRC grade 4 at the 1-month follow-up after discharge. The mMRC grades in both groups declined at the 1-month follow-up after discharge compared to those before treatment ($P < 0.05$). At the 1-month follow-up after discharge, the mMRC grades of patients in the observation group were lower than those of the control group ($P < 0.05$). **Conclusion** Xiaoqinglong decoction combined with the conventional protocol of western medicine deminstrates good clinical efficacy in treating patients with AECOPD of exterior cold and interior fluid retention syndrome, and can effectively improve the TCM syndromes, relieve the symptoms of dyspnea, reduce the inflammatory response, promote the resolution of infection, delay disease progression, improve short-term prognosis, and shows better safety.

[Key words] Chronic obstructive pulmonary disease Acute exacerbation Xiaoqinglong decoction Exterior cold and interior fluid retention syndrome Prognosis

流行病学调查研究估算中国慢性阻塞性肺疾病(chronic obstructive pulmonary disease, COPD)患者接近1亿[1-2]。COPD急性加重期(acute exacerbation of COPD, AECOPD)是造成COPD死亡率升高的主要原因,积极治疗AECOPD是临床关注的焦点[3]。抗菌药物、支气管扩张药物等是AECOPD的常规治疗方案,但目前的AECOPD基础治疗疗效不理想,如何提升临床疗效仍是待以解决的难题[4]。中医在AECOPD治疗中具有独特优势,AECOPD虽然在历代中医中并无记载,但根据症状体征一般将其归于"肺胀"范畴,以痰浊、水饮为标实,脏腑亏损为本虚,肺胀者在外邪入侵时易诱发内邪,故急性发作时常有表寒里饮症状体征[5-6],可采用解表散寒、温肺化饮治疗法[7]。小青龙汤为经典名方,可散表邪,并温里饮[8]。陈科伶[9]等通过小鼠实验还发现,小青龙汤具有抑制炎症反应的药理作用,可明显改善AECOPD模型小鼠的肺泡结构。小青龙汤在COPD治疗中的应用价值已得到一定认可,但在AECOPD治疗中的报道并不多见[10]。基于此,本研究分析小青龙汤联合基础西药治疗对表寒里饮证AECOPD的疗效及安全性,为AECOPD的中医药联合治疗方案提供参考数据。

1 资料与方法

1.1 一般资料

本研究为单中心随机对照试验。使用样本量计算公式 $n=\frac{(Z_\alpha\sqrt{2\overline{pq}}+Z_\beta\sqrt{p_0q_0+p_1q_1})^2}{(p_1-p_0)^2}$,其中$\alpha=0.05$(双侧),$\beta=0.1$,检验效能$1-\beta=0.9$,则$Z_\alpha=1.96$,$Z_\beta=1.28$,查阅文献[5],得到观察组与对照组治疗有效率分别为93.47%、71.43%,即$p_0=93.47$,$p_1=71.43$,带入样本量计算公式,得到每组样本量56例,考虑10%的失访率,每组样本量需62例。符合要求的124例AECOPD表寒里饮证患者入组,使用随机数字表法分为观察组(62例)与对照组(62例)。本研究获得中国注册临床试验伦理委员会审批(伦理审查文号:ChiECRCT20200195,申请审查单位:成都中医药大学附属医院),患者均自愿签署知情同意书。

1.2 中西医判断标准

1.2.1 西医诊断标准

参考《慢性阻塞性肺疾病诊治指南(2021年修订版)》[11]中的AECOPD诊断标准。有明确的COPD病史,且存在呼吸系统症状突然恶化超出日常变异,主要表现为呼吸困难加重,常伴喘息、胸闷、咳嗽加剧等。

1.2.2 表寒里饮证

参考《慢性阻塞性肺疾病中医证候诊断标准(2011版)》[12]制定的诊断标准。主证:咳痰,喘息气急,痰多,痰白稀薄、泡沫,胸闷,不能平卧,恶寒;次证:痰易咳出,喉中无痰鸣,无汗,肢体酸痛,鼻塞,流清涕;舌体胖大,舌质暗淡,舌苔白、滑,脉浮紧。

1.3 纳入标准

①符合AECOPD诊断标准。②符合表寒里饮证诊断标准。③急性发作至入院时间≤24 h。④年龄40~75岁。⑤入组前2个月内无肺炎、支气管炎等呼吸系统疾病史。

⑥入组前1个月内未使用糖皮质激素治疗或中药治疗。

1.4　排除标准

①合并哮喘等其他呼吸系统疾病。②合并免疫系统疾病。③有荨麻疹、过敏性鼻炎等变态反应性疾病史。④合并心力衰竭、肾衰竭等其他重要器官功能障碍。⑤高血压或糖尿病经药物治疗难以控制。⑥存在认知障碍或神经精神疾病史。

1.5　剔除、脱落标准

①试验中途主动要求退出。②试验期间不遵循医嘱要求。③试验期间失访。

1.6　治疗方法

对照组给予抗菌药物及支气管舒张剂等基础西药治疗: 盐酸左氧氟沙星0.5 g/次, 1次/d, 静脉滴注; 注射用多索茶碱0.2 g/次, 1次/d, 静脉滴注; 吸入用布地奈德混悬液1 mg/次, 2次/d; 硫酸特布他林雾化吸入用溶液5 mg/次, 2次/d; 盐酸氨溴索片30 mg/次, 3次/d, 口服; 连续治疗10 d。观察组在对照组治疗方案的基础上联合小青龙汤治疗: 桂枝、半夏各15 g, 麻黄、五味子、白芍各10 g, 干姜6 g, 细辛、甘草各3 g, 每日1剂, 连续治疗10 d; 随症加减: 若咳而上气, 喉中如水鸡声, 表寒较轻者, 加射干、紫菀、款冬、大枣, 使用射干麻黄汤治疗(观察组中有6例符合该表现, 加用射干麻黄汤治疗10 d); 饮郁化热, 烦躁而喘, 脉浮者, 加石膏兼清郁热(有4例患者符合该表现, 加用石膏使用10 d)。

1.7　观察指标

1.7.1　主要结局指标

评估治疗前及治疗10 d后主要中医证候积分: 评估咳嗽、喘息、恶寒、鼻塞、流涕、肢体酸痛的轻重程度, 计分为无(0分)、轻(2分)、中(4分)、重(6分), 评分相加为总积分。疗效评估标准: 采用尼莫地平法评估中医疗效, 以治疗前及治疗10 d后主要中医证候积分变化差值/治疗前主要中医证候积分×100%, 计算疗效指数, 以> 95%、> 70%且≤95%、30%> 且≤70%、≤30%分为临床控制、显效、有效和无效4个疗效等级。以每组临床控制、显效、有效的人数为分子, 以每组纳入例数为分母, 计算总有效率。

1.7.2　次要结局指标

在治疗前、治疗10 d后评估以下指标:

①感染及炎症指标: 采集入院当日及治疗后清晨的外周肘静脉血3 ~ 4 mL, 使用血细胞分析仪(美国Beckman Coulter公司, 型号: UniCel DxH800)白细胞计数(white blood cell, WBC); 常温高速离心后获得血清标本, 化学发光免疫法(德国Roche公司, 货号: 0513764200)检测血清降钙素原(procalcitonin, PCT)水平, 酶联免疫分析法(法国Bio Mérieux公司, 货号: JN0424、JK-a-1499)检测血清白细胞介素(interleukin, IL)-6、C反应蛋白(C-reactive protein, CRP)。

②动脉血气: 在入院当日及治疗后清晨, 使用专用动脉采血管采集桡动脉血, 使用血气分析仪(德国Roche公司, 型号: cobas b 123)检测动脉血氧分压(arterial partial pressure of oxygen, PaO_2)、动脉血二氧化碳分压(arterial partial pressure of carbon dioxide, $PaCO_2$)、动脉血氧饱和度(arterial oxygen saturation, SaO_2)。

③安全性评价 治疗期间监测血常规、肝肾功能、心电图及肺部CT、患者不适症状表现, 记录不良反应。

④出院后随访1个月, 调查患者呼吸困难程度, 使用改良英国医学研究委员会呼吸困难量表(modified Medical Research Council dyspnea scale, mMRC)[13], 分为0 ~ 4级, 级别越高, 呼吸困难越严重。

1.8　统计学方法

采用SPSS24.0处理数据; 中医证候积分、感染及炎症指标等符合正态分布且方差齐性的连续性数据以$\bar{x} \pm s$表示, 组间同一时间点的两两采用独立样本t检验, 组内两两时间点的比较使用配对样本t检验; 总有效率等分类数据以例数(%)表示, 行χ^2检验, mMRC分级为等级资料, 行Mann-Whitney U检验; α= 0.05。

2　结果

2.1　基线资料

研究期间观察组3例脱落, 对照组有4例脱落, 两组脱落率无统计学意义, 实际入组117例, 其中观察组59例, 对照组58例。两组一般资料比较, 差异无统计学意义, 见表1。

表 1　两组患者一般资料比较

Table 1　Comparison of general data between the two groups of patients

General data	Observation group (n = 59)	Control group (n = 58)	χ^2/t	P
Male/Female	35/24	36/22	0.093	0.761
Age/yr.	61.25 ± 7.22	60.90 ± 6.91	0.274	0.785
Disease course/years	16.42 ± 3.14	16.00 ± 3.06	0.739	0.461
Smoking history	36 (61.02)	34 (58.62)	0.070	0.792
Hypertension	14 (23.73)	12 (20.69)	0.156	0.693
Diabetes mellitus	6 (10.17)	4 (6.90)	0.092	0.762#
Hyperlipidemia	6 (10.17)	5 (8.62)	0.082	0.774

is continuous correction chi-square test. Data presented as $\bar{x} \pm s$, case or case (%).

2.2　主要结局指标

与本组治疗前比较, 治疗后两组各项积分及总分均

降低($P<0.05$)；治疗后与对照组比较，观察组患者咳嗽、恶寒、鼻塞、流涕证候积分及总积分降低($P<0.05$)。见表2。治疗10 d后，观察组临床控制7例，显效18例，有效31例，无效3例；对照组临床控制2例，显效10例，有效36例，无效10例；相较于对照组的82.76%(48/58)，观察组总有效率94.91%(56/59)明显更高($P<0.05$)。

表 2 两组表寒里饮证AECOPD患者主要中医证候积分比较

Table 2 Comparison of main TCM syndromes scores between the two groups of AECOPD patients presenting exterior cold and interior fluid retention syndrome

Main TCM syndromes scores	Observation group (n = 59)	Control group (n = 58)
Cough		
Before treatment	4.03 ± 0.69	3.97 ± 0.59
After treatment	1.90 ± 0.44$^{*,\#}$	2.21 ± 0.61*
Wheezing		
Before treatment	3.90 ± 0.58	3.86 ± 0.63
After treatment	0.98 ± 1.01*	1.41 ± 0.92*
Aversion to cold		
Before treatment	3.90 ± 0.69	3.83 ± 0.68
After treatment	0.85 ± 0.99$^{*,\#}$	1.34 ± 0.95*
Nasal congestion		
Before treatment	2.10 ± 0.44	2.03 ± 0.26
After treatment	0.54 ± 0.90$^{*,\#}$	0.97 ± 1.01*
Runny nose		
Before treatment	4.14 ± 0.51	4.10 ± 0.45
After treatment	1.56 ± 0.84$^{*,\#}$	1.97 ± 0.59*
Limb soreness		
Before treatment	2.24 ± 0.65	2.17 ± 0.57
After treatment	1.56 ± 0.84*	1.86 ± 0.51*
Total score		
Before treatment	20.31 ± 1.22	19.97 ± 1.70
After treatment	7.40 ± 1.94$^{*,\#}$	9.76 ± 2.09*

$^{*}P < 0.05$, vs. this group before treatment; $^{\#}P < 0.05$, vs. control group after treatment.

2.3 次要结局指标

与本组治疗前比较，治疗后两组患者WBC及PCT、IL-6、CRP、$PaCO_2$明显降低($P<0.05$)，治疗后与对照组比较，观察组更低($P<0.05$)；治疗后两组患者PaO_2、SaO_2明显升高($P<0.05$)，治疗后与对照组比较，观察组更高($P<0.05$)。见表3。观察组治疗期间出现1例头晕，1例头痛，2例口干；对照组有1例头晕，1例口干，1例皮疹；组间不良反应总发生率分别为6.78%、5.17%，$P>0.05$。两组患

表 3 两组表寒里饮证AECOPD患者次要结局指标比较

Table 3 Comparison of secondary outcome indicators between the two groups of AECOPD patients presenting exterior cold and interior fluid retention syndrome

Indicator	Observation group (n = 59)	Control group (n = 58)
WBC/×10^9·L^{-1}		
Before treatment	12.16 ± 1.95	12.05 ± 1.91
After treatment	8.13 ± 1.56$^{*,\#}$	9.20 ± 1.63*
PCT/μg·L^{-1}		
Before treatment	1.29 ± 0.24	1.26 ± 0.21
After treatment	0.54 ± 0.12$^{*,\#}$	0.78 ± 0.16*
IL-6/ng·L^{-1}		
Before treatment	36.12 ± 5.04	35.46 ± 5.37
After treatment	16.01 ± 3.15$^{*,\#}$	19.68 ± 4.03*
CRP/mg·L^{-1}		
Before treatment	24.59 ± 4.22	23.76 ± 4.10
After treatment	7.60 ± 1.78$^{*,\#}$	10.75 ± 2.24*
PaO_2/mmHg		
Before treatment	55.49 ± 4.07	56.12 ± 3.82
After treatment	81.39 ± 3.85$^{*,\#}$	78.07 ± 4.15*
$PaCO_2$/mmHg		
Before treatment	53.12 ± 4.12	52.90 ± 3.89
After treatment	40.19 ± 3.08$^{*,\#}$	42.45 ± 3.27*
SaO_2/%		
Before treatment	85.78 ± 2.03	86.10 ± 2.15
After treatment	95.81 ± 1.80$^{*,\#}$	94.19 ± 2.03*
mMRC grading/case(%)		
Before treatment		
Grade 0	0 (0.00)	0 (0.00)
Grade 1	3 (5.08)	6 (10.34)
Grade 2	25 (42.37)	26 (44.83)
Grade 3	26 (44.07)	23 (39.66)
Grade 4	5 (8.47)	3 (5.17)
After discharge		
Grade 0	8 (13.56)$^{*,\#}$	4 (6.90)*
Grade 1	27 (45.76)	19 (32.76)
Grade 2	18 (30.51)	23 (39.66)
Grade 3	6 (10.17)	12 (20.69)
Grade 4	0 (0.00)	0 (0.00)

WBC: white blood cell; PCT: procalcitonin; IL-6: interleukin-6; CRP: C-reactive protein; PaO_2: arterial partial pressure of oxygen; $PaCO_2$: arterial partial pressure of carbon dioxide; SaO_2: arterial oxygen saturation. mMRC: modified Medical Research Council dyspnea scale. 1 mmHg=0.133 kPa. $^{*}P < 0.05$, vs. this group before treatment; $^{\#}P < 0.05$, vs. control group after treatment.

者出院后1个月随访时均无mMRC4级病例，与本组治疗前比较，出院后1个月两组患者mMRC分级均降低（$P<0.05$）；出院后1个月与对照组比较，观察组患者mMRC分级更低（$P<0.05$）。

3　讨论

肺主气，邪客于肺脉，肺气受阻则不能发泄，宣降不利，引发咳喘，肺为脾之子，久病则子盗母气，损耗脾气，脾又为生痰之源，脾气虚则运化失调，脾肺两虚，导致咳痰、咳嗽症状持续[14]。肺为肾之母，肺久病则肾气亏虚，水液运行输布失调，阻滞气机，肾不纳气不归元，故气短难续[15]。肺朝百脉，肺气弱则无法助心行血，日久则心气不足，最终诱发多脏同病。AECOPD的病机以实证为主，痰瘀互结则气机不畅，久则气道壅滞，肺气不能肃降，外邪入侵则风、寒、湿邪等与痰瘀搏结，引发喘息、咳痰、恶寒等实证表现[16]。表寒里饮证为AECOPD最常见的证候，肺气亏损，水液停聚成内饮，寒邪侵袭肺卫，与内饮搏结并停于肺内，表现为表寒里饮证，是目前报道较多的证候[17]。AECOPD的常规西药治疗以对症处理为主，如抗感染、多索茶碱扩张支气管等，但临床疗效仍有很大的提升空间。故本研究通过临床试验分析中药汤剂联合基础西药治疗表寒里饮证AECOPD的应用价值。

小青龙汤为经典名方，《金匮要略》“痰饮咳嗽病篇”第35条：“咳逆倚息不得卧，小青龙汤主之。”主治表寒里饮证。小青龙汤中麻黄、桂枝为君药，发汗解表；半夏与干姜配伍可温化内饮，结合细辛可宣化水饮，三者为臣药；白芍、五味子、甘草结合可酸甘化阴，三者为佐药，补肺阴及脾阴；干姜与细辛、五味子配伍又辛散化饮敛降，全方热药与寒药并用，升散与降气之药并用，阴阳平衡，既能散表寒，又可温里饮[18]。水饮聚集于肺则不能平躺，躺则咳甚，肺中水气过盛而引发喘息，小青龙汤上输于脾，脾气散精，上归于肺，通调水道，去肺中水气，喘息、咳痰等症状则可随之缓解。现代药理学研究发现[19-20]，小青龙汤中麻黄的主要成分——麻黄生物碱，可通过调控环磷酸腺苷信号通路，抑制多种促炎因子的表达，发挥良好的抗炎作用；桂枝则能作用于多个基因靶点，通过调控肿瘤坏死因子信号通路，抑制炎症反应。也有学者通过动物实验发现[21]，小青龙汤加减方能抑制核因子κB降解，并激活环氧化酶2表达，减轻COPD+香烟模型小鼠气道炎症和气道重塑。上述研究提示小青龙汤具有抗炎作用，在控制气道炎症及病情进展方面具有良好疗效。本研究也发现，观察组治疗10 d后血清IL-6、CRP水平明显低于对照组，其中IL-6、CRP为临床常用的炎症指标[22-23]，表明小青龙汤能发挥抗炎作用，与上述药理学研究结果相似，可减轻AECOPD患者气道炎症，缓解疾病进展。此外，呼吸道感染是诱发AECOPD的重要原因，患者气道炎症反应增强，呼吸道防御能力下降，感染与炎症交错刺激，造成病情加重及反复发作[24-25]。WBC是临床观察感染及炎症状况的常用指标，PCT是观察细菌感染的敏感指标，可反映全身炎症反应活跃程度，PCT监测可用于预测AECOPD患者预后[26]。本研究中，观察组治疗10 d后血清PCT也低于对照组，提示小青龙汤抗炎作用良好，联合抗生素等西药对症治疗能促进炎症及感染消退，控制疾病进展。

另有研究指出[27]，小青龙汤还有抗组胺的作用，可拮抗组胺释放引起的气管平滑肌痉挛，减轻气道阻力。因此，小青龙汤在呼吸系统疾病治疗中常用，能减轻气道炎症及支气管痉挛，改善患者呼吸困难等症状[28-30]。本研究中，观察组治疗10 d后动脉血气（PaO_2、$PaCO_2$、SaO_2）改善效果优于对照组，出院后随访1个月时mMRC分级显著低于对照组，提示联合小青龙汤治疗，AECOPD患者缺氧状态及呼吸困难症状显著缓解，患者近期预后更佳。本研究结果还显示，观察组患者治疗10 d后咳嗽、恶寒、鼻塞、流涕证候积分及总积分低于对照组，治疗总有效率为94.91%，也高于对照组的82.76%，提示小青龙汤对表寒里饮证AECOPD治疗有效，联合西药治疗可提升疗效，缓解患者症状体征。此外，本研究两组患者药物方案均未出现肝肾毒性等严重不良事件，并未发现与小青龙汤相关的不良反应，提示小青龙汤联合西药基础治疗的安全性良好。

综上所述，小青龙汤联合西药基础治疗表寒里饮证AECOPD效果较好，可有效减轻炎症反应，促进感染消退，改善肺通气，缓解临床症状及中医证候，并改善短期预后，是一种安全可靠的治疗方案，值得临床推广应用。

*　　*　　*

作者贡献声明　唐文君负责经费获取、调查研究、研究方法、验证、初稿写作和审读与编辑写作，曾珠负责正式分析和可视化，周鹏程负责数据审编，贾国兵负责研究项目管理，孟铠瑞负责软件，何成诗负责论文构思、提供资源和监督指导。所有作者已经同意将文章提交给本刊，且对将要发表的版本进行最终定稿，并同意对工作的所有方面负责。

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利益冲突 所有作者均声明不存在利益冲突

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参 考 文 献

[1] 郑丹蕾, 王红梅, 刘耘充, 等. 慢性阻塞性肺疾病患者血嗜酸粒细胞分布及临床特征. 中华结核和呼吸杂志, 2021, 44(3): 218-224. doi: 10.3760/cma.j.cn112147-20200617-00715.
ZHENG D L, WANG H M, LIU Y C, *et al*. The distribution of blood eosinophils and the related clinical characteristics in chronic obCOPD patients. Chin J Tubercul Respirat Dis, 2021, 44(3): 218-224. doi: 10.3760/cma.j.cn112147-20200617-00715.

[2] ZENG S, ARJOMANDI M, LUO G. Automatically explaining machine learning predictions on severe chronic obstructive pulmonary disease exacerbations: retrospective cohort study. JMIR Med Inform, 2022, 10(2): e33043. doi: 10.2196/33043.

[3] ZECCHI R, FRANCESCHI P, TIGLI L, *et al*. Sample preparation strategy for the detection of steroid-like compounds using MALDI mass spectrometry imaging: pulmonary distribution of budesonide as a case study. Anal Bioanal Chem, 2021, 413(16): 4363-4371. doi: 10.1007/s00216-021-03393-6.

[4] 朱美君, 孙芳, 涂水余, 等. 噻托溴铵联合布地格福吸入对慢性阻塞性肺疾病急性加重期患者肺功能及血清特异因子的影响. 山西医药杂志, 2023, 52(14): 1083-1086. doi: 10.3969/j.issn.0253-9926.2023.14.009.
ZHU M J, SUN F, TU S Y, *et al*. Effects of tiotropium bromide combined with budegforo inhalation on lung function and serum specific factors in patients with acute exacerbation of chronic obstructive pulmonary disease. Shanxi Med J, 2023, 52(14): 1083-1086. doi: 10.3969/j.issn.0253-9926.2023.14.009.

[5] 张美萃, 杜世拔, 范良. 小青龙汤联合常规治疗对外寒内饮型慢性阻塞性肺疾病急性期患者的临床疗效. 中成药, 2022, 44(1): 78-82. doi: 10.3969/j.issn.1001-1528.2022.01.015.
ZHANG M C, DU S B, FAN L. Clinical effects of Xiaoqinglong Decoction combined with conventional treatment on patients with chronic obstructive pulmonary disease in acute phase due to External Cold and Internal Fluid. Chin Tradit Patent Med, 2022, 44(1): 78-82. doi: 10.3969/j.issn.1001-1528.2022.01.015.

[6] 刘宏祥, 赵永辰, 周胜男, 等. 经方序贯疗法治疗嗜酸性粒细胞增高型慢性阻塞性肺疾病急性加重期外寒内饮证的中医证候疗效及对炎症指标和凝血指标的影响. 河北中医, 2021, 43(4): 566-570, 652. doi: 10.3969/j.issn.1002-2619.2021.04.009.
LIU H X, ZHAO Y C, ZHOU S N, *et al*. Effect of sequential treatment of classical prescription on acute exacerbation of chronic obstructive pulmonary disease with external cold and internal drinking of peripheral blood eosinophils increased and its influence on inflammatory and coagulation index. Hebei J Tradit Chin Med, 2021, 43(4): 566-570, 652. doi: 10.3969/j.issn.1002-2619.2021.04.009.

[7] 王琳君, 李耀辉, 钟珍, 等. 形寒寒饮则伤肺述评. 河北中医, 2023, 45(1): 122-124. doi: 10.3969/j.issn.1002-2619.2023.01.030.
WANG L J, LI Y H, ZHONG Z, *et al*. Form cold cold drink injury lung review. Hebei J Tradit Chin Med, 2023, 45(1): 122-124. doi: 10.3969/j.issn.1002-2619.2023.01.030.

[8] 龚李萍, 王玉兰, 郭超峰. 基于数据挖掘分析小青龙汤的方证关系. 山东中医药大学学报, 2022, 46(4): 487-492. doi: 10.16294/j.cnki.1007-659x.2022.04.014.
GONG L P, WANG Y L, GUO C F. Relationship between Formula and Syndrome of Xiaoqinglong Decoction Based on Data Mining. J Shandong Univ Tradit Chin Med, 2022, 46(4): 487-492. doi: 10.16294/j.cnki.1007-659x.2022.04.014.

[9] 陈科伶, 付正丰, 黄青松, 等. 小青龙汤化学成分分析及其对慢性阻塞性肺疾病急性发作期小鼠的作用. 中成药, 2022, 44(12): 4037-4040. doi: 10.3969/j.issn.1001-1528.2022.12.051.
CHEN K L, FU Z F, HUANG Q S, *et al*. Chemical composition analysis of Xiaoqinglong Decoction and its effect on mice with acute exacerbation of chronic obstructive pulmonary disease. Chin Tradit Patent Med, 2022, 44(12): 4037-4040. doi: 10.3969/j.issn.1001-1528.2022.12.051.

[10] 张平安, 高娜, 陈明哲, 等. 基于网络药理学探讨小青龙汤治疗慢性阻塞性肺疾病的作用机制. 世界中医药, 2021, 16(24): 3585-3590, 3595. doi: 10.3969/j.issn.1673-7202.2021.24.003.
ZHANG P A, GAO N, CHEN M Z, *et al*. Mechanism of Xiaoqinglong decoction in the treatment of chronic obstructive pulmonary disease based on network pharmacology. World Chi Med, 2021, 16(24): 3585-3590, 3595. doi: 10.3969/j.issn.1673-7202.2021.24.003.

[11] 中华医学会呼吸病学分会慢性阻塞性肺疾病学组, 中国医师协会呼吸医师分会慢性阻塞性肺疾病工作委员会. 慢性阻塞性肺疾病诊治指南(2021年修订版). 中华结核和呼吸杂志, 2021, 44(3): 170-205. doi: 10.3760/cma.j.cn112147-20210109-00031.
Chronic obstructive pulmonary Disease Group, Respiratory Society, Chinese Medical Association, Working Committee of Chronic obstructive Pulmonary Disease, Respiratory Physician Branch, Chinese Medical Doctor Association. Guidelines for the diagnosis and management of chronic obstructive pulmonary disease (revised version 2021). Chin J Tubercul Respirat Dis, 2021, 44(3): 170-205. doi: 10.3760/cma.j.cn112147-20210109-00031.

[12] 中华中医药学会内科分会肺系病专业委员会. 慢性阻塞性肺疾病中医证候诊断标准(2011版). 中医杂志, 2012, 53(2): 177-178. 无doi
Chinese Society of Traditional Chinese Medicine Branch of internal medicine specialty committee of pulmonary diseases. TCM Syndrome Diagnosis Criteria for Chronic obstructive Pulmonary Disease (2011 edition). J Tradit Chin Med, 2012, 53(2): 177-178.

[13] ZHOU M, WANG T, WEI D, *et al*. Incidence, severity and tolerability of pneumothorax following low-dose CT-guided lung biopsy in different severities of COPD. Clin Respir J, 2021, 15(1): 84-90. doi: 10.1111/crj.13272.

[14] 姚富科, 李素云, 杨建雅, 等. 基于"气主呴之"探讨肾阳在慢性阻塞性肺疾病炎癌转化中的作用. 国际中医中药杂志, 2023, 45(6): 657-662. doi: 10.3760/cma.j.cn115398-20220707-00079.
YAO F K, LI S Y, YANG J Y, *et al*. To explore the role of kidney-yang in the transformation of inflammatory carcinoma in chronic obstructive pulmonary disease based on "Qi controlling Xu". Int J Tradit Chin Med, 2023, 45(6): 657-662. doi: 10.3760/cma.j.cn115398-20220707-00079.

[15] 丁静, 周进, 张艳红, 等. 补肺保元膏联合无烟灸治疗老年慢性阻塞性肺疾病稳定期肺肾气虚证患者的临床疗效观察. 实用心脑肺血管病杂志, 2023, 31(1): 95-101. doi: 10.12114/j.issn.1008-5971.2023.00.008.
DING J, ZHOU J, ZHANG Y H, *et al*. Clinical efficacy of bufei baoyuan ointment combined with smokeless moxibustion in the treatment of elderly patients with COPD in stable phase with lung-kidney Qi deficiency syndrome. Pract J Card Cereb Pneu Vascul Dis, 2023, 31(1): 95-101. doi: 10.12114/j.issn.1008-5971.2023.00.008.

[16] 李书娇, 许蓉姗, 马佳佳, 等. 老年慢性阻塞性肺疾病急性加重合并冠心病患者的中医证候观察. 中国中医急症, 2022, 31(8): 1262-1265. doi: 10.3969/j.issn.1004-745X.2022.08.037.
LI S J, XU R S, MA J J, *et al*. Influence of coronary heart disease on TCM syndrome of elderly patients with acute exacerbation of chronic obstructive pulmonary disease. J Emerg Tradit Chin Med, 2022, 31(8): 1262-1265. doi: 10.3969/j.issn.1004-745X.2022.08.037.

[17] 党惠子, 李珊, 吴蔚. 慢性阻塞性肺疾病急性加重期药物配伍应用举隅. 国际中医中药杂志, 2022, 44(7): 822-824. doi: 0.3760/cma.j.cn115398-20210524-00236. doi: 10.3760/cma.j.cn115398-20210524-00236.
TANG H Z, LI S, WU W. Application of drug compatibility in acute exacerbation of chronic obstructive pulmonary disease. Int J Tradit Chin Med, 2022, 44(7): 822-824. doi: 0.3760/cma.j.cn115398-20210524-00236. doi: 10.3760/cma.j.cn115398-20210524-00236.

[18] 符琼方, 胡朋, 杨文秀, 等. 钩藤饮子合小青龙汤辨证治疗咳嗽变异性哮喘(风邪犯肺证)的效果及对外周血白三烯D4、C4及尿白三烯E4水平的影响. 天津中医药大学学报, 2022, 41(3): 317-321. doi: 10.11656/j.issn.1673-9043.2022.03.10.
FU Q F, HU P, YANG W X, *et al*. Efficacy of Gouteng Yinzi with Xiaoqinglong Decoction in the dialectical treatment of cough variant

asthma (pathogenic wind invading the lung) and its influence on levels of peripheral blood leukotriene D4 and C4 and urinary leukotriene E4. J Tianjin Univ Tradit Chin Med, 2022, 41(3): 317-321. doi: 10.11656/j.issn.1673-9043.2022.03.10.

[19] 郑亚娟, 袁培培, 傅阳, 等. 基于cAMP/PKA/CREB信号通路探讨麻黄生物碱组分对过敏性哮喘大鼠的抗炎机制. 中药新药与临床药理, 2022, 33(11): 1453-1459. doi: 10.19378/j.issn.1003-9783.2022.11.002.
ZHENG Y J, YUAN P P, FU Y, *et al*. Exploring the anti-inflammatory mechanism of ephedra herba alkaloid components in allergic asthmatic rats based on cAMP/PKA/CREB signaling pathway. Tradit Chin Drug Res Clin Pharmacol, 2022, 33(11): 1453-1459. doi: 10.19378/j.issn.1003-9783.2022.11.002.

[20] 陈雪猛, 王勇, 吴维. 基于网络药理学分析桂枝治疗类风湿关节炎的作用机制. 中南医学科学杂志, 2023, 51(1): 45-48. doi: 10.15972/j.cnki.43-1509/r.2023.01.011.
CHEN X M, WANG Y, WU W. Mechanism of cassia twig in treating rheumatoid arthritis based on network pharma-cology. Med Sci J Cent South China, 2023, 51(1): 45-48. doi: 10.15972/j.cnki.43-1509/r.2023.01.011.

[21] 符秀曼, 张美萃, 范良, 等. 基于NF-κB通路和COX-2水平探讨小青龙汤加减方对LPS联合香烟烟雾诱导的COPD小鼠气道炎症和气道重塑的影响. 中药材, 2021, 44(11): 2692-2696. doi: 10.13863/j.issn1001-4454.2021.11.036.
FU X M, ZHANG M C, FAN L, *et al*. To investigate the effects of Xiaoqinglong Decoction on airway inflammation and airway remodeling induced by LPS combined with cigarette smoke in COPD mice based on NF-κB pathway and COX-2 level. J Chin Med Mater, 2021, 44(11): 2692-2696. doi: 10.13863/j.issn1001-4454.2021.11.036.

[22] ZU C, WANG K, ZHANG Q, *et al*. Clinical features of hemophagocytic syndrome following BCMA CAR-T cell therapy in patients with relapsed/refractory multiple myeloma. Zhejiang Da Xue Xue Bao Yi Xue Ban, 2022, 51(2): 160-166. English. doi: 10.3724/zdxbyxb-2022-0039.

[23] ZULPA AK, BARATHAN M, IYADORAI T, *et al*. Release of pro-inflammatory cytokines TNF-α, IFN-γ and IL-6 by Burkholderia pseudomallei- stimulated peripheral blood mononucleocytes of acute myeloid leukemia patients. Trop Biomed, 2021, 38(2): 180-185. doi: 10.47665/tb.38.2.055.

[24] 严思, 湛文世, 颜光寰, 等. 合并细菌感染对AECOPD患者血浆氨基酸水平及TNF-α/TNFR/NF-κB通路的影响. 中华医院感染学杂志, 2023, 33(7): 1011-1015. doi: 10.11816/cn.ni.2023-221224.
YAN S, ZHAN W S, YAN G H, *et al*. Effects of bacterial infection on plasma amino acid and TNF-a/TNFR/NF-κB pathways in AECOPD patients. Chin J Nosocomiol, 2023, 33(7): 1011-1015. doi: 10.11816/cn.ni.2023-221224.

[25] 邵远江, 黄炳红. AECOPD患者感染呼吸道病毒特征及呼吸道合胞病毒感染与血清IP-10的关系. 中国病原生物学杂志, 2021, 16(10): 1207-1210, 1215. doi: 10.13350/j.cjpb.211019.
SHAO Y J, HUANG B H. The characteristics of a respiratory virus infection in patients with AECOPD and the relationship between respiratory syncytial virus infection and the expression of serum IP-10. J Parasit Biol, 2021, 16(10): 1207-1210, 1215. doi: 10.13350/j.cjpb.211019.

[26] ZHANG Q, LIU JX, BAI JS, *et al*. D-Dimer and Procalcitonin Improve the Sensitivity of BAP-65 Score in Predicting AECOPD Patients Admission to ICU. Clin Lab, 2023, 69(2): e220343. doi: 10.7754/Clin.Lab.2022.220343.

[27] 张迪, 张冬梅, 陆瑞敏, 等. 基于"肺主行水"理论探究小青龙汤调节肺水转运蛋白的作用机制. 中国实验方剂学杂志, 2022, 28(8): 1-11. doi: 10.13422/j.cnki.syfjx.20220736.
ZHANG D, ZHANG D M, LU R M, *et al*. Mechanism of Xiao Qinglongtang regulating lung water transport-related proteins based on theory of lung controlling water movement. Chin J Experiment Tradit Med Formu, 2022, 28(8): 1-11. doi: 10.13422/j.cnki.syfjx.20220736.

[28] 李成辉, 黄镛, 任宝琦. 基于临床文献研究的小青龙汤方证规律分析. 西部中医药, 2023, 36(2): 80-83. doi: 10.12174/j.issn.2096-9600.2023.02.17.
LI C H, HUANG Y, REN B Q. Analysis of syndromes rules of Xiao Qinglong decoction based on clinical literature. West J Tradit Chin Med, 2023, 36(2): 80-83. doi: 10.12174/j.issn.2096-9600.2023.02.17.

[29] 彭梦薇, 刘燕, 陈玉龙, 等. 基于NF-κB/miR-494信号调控MUC5AC和CFTR研究小青龙汤与清气化痰丸改善病理性气道黏液的机制. 中华危重病急救医学, 2022, 34(8): 831-836. doi: 10.3760/cma.j.cn121430-20220310-00234.
PENG M W, LIU Y, CHEN Y L, *et al*. Mechanism of Xiaoqinglong Decoction and Qingqi Huatan Pills in improving pathological airway mucus based on nuclear factor-κB/microRNA-494 signaling regulation of mucin 5AC and cystic fibrosis transmembrane conductance regulator. Chin Crit Care Med, 2022, 34(8): 831-836. doi: 10.3760/cma.j.cn121430-20220310-00234.

[30] 赵艳菊, 肖玉琴, 王玲玲. 动脉血气分析、凝血功能及肺动脉收缩压监测在慢性阻塞性肺疾病急性加重防治中的应用分析. 实用医院临床杂志, 2022, 19(3): 154-157. doi: 10.3969/j.issn.1672-6170.2022.03.043.
ZHAO Y J, XIAO Y Q, WANG L L. Application analysis of arterial blood gas analysis, coagulation function and pulmonary artery systolic pressure monitoring in the prevention and treatment of acute exacerbation of chronic obstructive pulmonary disease. Pract J Clin Med, 2022, 19(3): 154-157. doi: 10.3969/j.issn.1672-6170.2022.03.043.

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