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痰热清注射液联合孟鲁司特治疗慢性阻塞性肺疾病急性加重期患者的疗效观察

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摘要 目的:探讨痰热清注射液联合孟鲁司特治疗慢性阻塞性肺疾病急性加重期(AECOPD)患者的疗效。**方法:**将2014年5月至2016年12月我院收治的AECOPD患者116例按照随机数字表法分为研究组和对照组,每组58例,对照组患者给予AECOPD常规治疗,同时口服孟鲁司特10 mg/d,研究组则在此基础上静脉滴注痰热清注射液20 mL/d,两组疗程均为2周。观察两组临床疗效、患者临床症状改变,并对比两组治疗前后血清白细胞介素-6(IL-6)、白细胞介素-8(IL-8)和肿瘤坏死因子-α(TNF-α)水平。**结果:**研究组总有效率为98.28%,明显高于对照组的87.93%(P<0.05)。研究组患者咳嗽消失时间、气促消失时间、哮鸣音消失时间明显低于对照组(P<0.05)。治疗后两组患者血清IL-6、IL-8以及TNF-α水平均降低(P<0.05),且研究组较对照组降低(P<0.05)。**结论:**痰热清注射液联合孟鲁司特治疗AECOPD能够有效缓解患者症状,降低患者炎症反应,临床效果较好。

关键词:慢性阻塞性肺疾病;痰热清注射液;孟鲁司特;临床疗效

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Clinical Observation of Tanreqing Injection Combined with Montelukast in the Treatment of Patients with Acute Exacerbation of Chronic Obstructive Pulmonary Disease

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ABSTRACT Objective: To observe the clinical efficacy of Tanreqing injection combined with montelukast in the treatment of patients with acute exacerbation of chronic obstructive pulmonary disease (AECOPD). **Methods:** 116 patients with AECOPD in our hospital from May 2014 to December 2016 were randomly divided into study group and control group, 58 cases in each group, the control group were treated with AECOPD conventional treatment, oral montelukast 10 mg/d, study group were treated with intravenous dripping Tanreqing injection 20 mL/d on the basis of the control group, and two groups were treated for 2 weeks. The clinical efficacy, clinical symptoms change of two groups were observed, and the levels of serum interleukin-6 (IL-6), interleukin-8 (IL-8) and tumor necrosis factor-α (TNF-α) were compared between the two groups before and after treatment. **Results:** The total effective rate of the study group was 98.28%, which was significantly higher than that of the control group(87.93%) (P<0.05). The disappearance time of cough, shortness of breath, wheezing in study group were significantly lower than the control group (P<0.05). There was no significant difference in serum IL-6, IL-8 and TNF-α levels between the two groups before treatment (P>0.05). After treatment, the serum levels of IL-6, IL-8 and TNF-α were significantly decreased in the two groups (P<0.05), and the serum levels of IL-6, IL-8 and TNF-α in the study group were significantly lower than those in the control group (P<0.05). **Conclusion:** Tanreqing injection combined with montelukast can effectively alleviate the symptoms of patients with AECOPD, reduce the inflammatory response of patients, the clinical effect is better.

Key words: Chronic obstructive pulmonary disease; Tanreqing injection; Montelukast; Clinical efficacy

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前言

慢性阻塞性肺疾病(Chronic obstructive pulmonary disease,COPD)是以慢性进行性阻塞性通气功能障碍为主要特征,病变持续进展,可能进一步发展成为肺心病以及呼吸衰竭等[1]。COPD发病机制非常复杂,目前仍未完全明确,临床上根据患者的病情将COPD分为稳定期和急性加重期[2]。其中,慢性阻

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塞性肺疾病急性加重期(AECOPD)通常继发感染出现,是患者死亡的主要原因[3]。目前临床上对于 AECOPD 尚缺乏特效的治疗手段,一般给予控制性氧疗、解痉、平喘以及抗感染等对症治疗,疗效不佳。孟鲁司特是白三烯受体拮抗剂,它可以抑制呼吸道中白三烯受体,起到控制喘息,缓解气道炎症的效果,治疗 COPD 有一定疗效[4]。痰热清注射液具有化痰止咳、清热解毒等功效的一种中药制剂,主要是由连翘、山羊角、黄芩、金银花、熊胆粉等组成,以往被广泛用于急、慢性呼吸道感染,取得有很好的效果[5]。为进一步观察痰热清注射液联合孟鲁司特治疗 AECOPD 患者的疗效,我们进行了对照研究,现报道如下。

1 资料和方法

1.1 临床资料

将 2014 年 5 月至 2016 年 12 月我院收治的 AECOPD 患者 116 例作为研究对象,纳入标准:(1)所有入组患者均符合中华医学会呼吸病学分会制定的《COPD 诊断治疗指南》中的诊断标准[6],临床表现为短期内出现呼吸困难或原有呼吸困难加重,咳嗽、咳痰或痰量 / 性状改变,伴有或不伴有发热。(2)患者及家属自愿参加研究。排除标准:(1)合并恶性肿瘤者;(2)具有肝肾功能不全、严重心力衰竭、自身免疫疾病者;(3)对本研究药物过敏者;(4)不能配合治疗者。其中男 62 例,女 54 例。年龄 26~68 岁,平均年龄为(46.5± 4.8)岁。将患者按照随机数字表法分成研究组和对照组。其中研究组 58 例,男 34 例,女 24 例。年龄 28~67 岁,平均年龄为(46.2± 3.5)岁;病程 2~15 年,平均病程(8.4± 3.4)年。对照组 58 例,男 32 例,女 26 例。年龄 26~68 岁,平均年龄为(46.9± 3.7)岁;病程 2~16 年,平均病程(8.6± 3.2)年。两组患者一般资料经统计学分析无统计学差异(P>0.05)。

1.2 研究方法

对照组患者给予 AECOPD 常规治疗方案治疗, 主要包含控制性氧疗和解痉、平喘以及抗感染等,依据患者常见的病原菌经验性选取二\三代头孢菌类以及喹诺酮类抗生素等。在治疗期间均不应用糖皮质激素制剂,合并有呼吸衰竭患者施以无创机械通气,同时给予孟鲁斯特钠(杭州默沙东制药有限公司,规格:5 mg× 5 片,批号:140422)10 mg,口服,1 次 /d。研究组在此基础之上静脉滴注痰热清注射液(上海凯宝药业股份有限公司,规格:10 mg/ 支,批号:140712),将 20 mL 痰热清注射液加入生理盐水 250 mL 中,静脉滴注,1 次 /d。所有患者治疗疗程均为 2 周。

1.3 观察指标

1.3.1 临床疗效评价 按照《COPD 诊断治疗指南》中疗效评定标准进行评定:(1)显效:治疗足疗程后患者喘息、气促等临床症状明显改善,呼吸平稳,听诊肺部哮鸣音消失;(2)好转:治疗足疗程后患者喘息、气促等临床症状明有所改善,呼吸平稳,听诊哮鸣音减少,但仍有哮鸣音;(3)无效:治疗足疗程后患者临床症状无改善甚至加重,听诊肺部哮鸣音无改变甚至加重[7]。

1.3.2 临床症状消失时间 观察两组患者咳嗽消失时间、气促消失时间、哮鸣音消失时间。

1.3.3 血清学指标观察 分别于治疗前一天和疗程结束后次日采集清晨空腹静脉血 5 mL, 经 4000 r/min 离心 10 min 后分离血清,应用双抗体酶联免疫吸附法测定各血清白细胞介素 -6(IL-6)、白细胞介素 -8(IL-8)和肿瘤坏死因子 -α(TNF-α)水平,操作方法和步骤严格按照试剂盒(购自北京科瑞美科技有限公司)说明进行。

1.4 统计学方法

所有数据应用 SPSS21.0 统计软件进行分析, 临床有效率为计数资料,实施 x^2 检验,临床症状消失时间、血清学指标等为计量资料,以均数± 标准差($\bar{x}$± s)表示,实施 t 检验,x^2 检验标准为 α=0.05。

2 结果

2.1 两组临床疗效对比

研究组治疗总有效率较对照组升高(P<0.05),见下表 1。

表 1 两组治疗后疗效对比[n(%)]

Table 1 Comparison of curative effects in the two groups after treatment [n(%)]

Groups	n	Effective	Better	Invalid	Total effective rate
Study group	58	49(84.48)	8(13.79)	1(1.72)	57(98.28)
Control group	58	40(68.97)	11(18.97)	7(12.07)	51(87.93)
x^2	-				4.833
P	-				0.027

2.2 两组临床症状消失时间对比

研究组患者咳嗽消失时间、气促消失时间和哮鸣音消失时间均明显短于对照组(P<0.05),见下表 2。

2.3 两组患者治疗前及治疗后各血清因子水平比较

治疗前两组患者各血清因子水平无统计学差异(P>0.05),治疗后两组患者血清 IL-6、IL-8 及 TNF-α 水平均较治疗前明显降低(P<0.05),且研究组患者较对照组降低(P<0.05),见下表 3。

3 讨论

我国是 COPD 患病大国,近年来随着空气质量的下降和人口老龄化,我国 COPD 的患病率正逐年增高,有报道显示,我国 COPD 患病率约为 8.2%,患病人数超过 4000 万人,COPD 已成为我国农村死亡原因的第一位, 城市死亡原因的第四位[8]。COPD 病情进展缓慢,发病机制较为复杂,临床上将其分为稳定期和急性加重期。其中 AECOPD 患者呼吸功能恶化、临床症状加重,如不给予有效治疗,病死率较高。目前,临床上对于 AECOPD 多采用解痉、平喘以及抗感染等治疗方法,效果不甚理想。其中孟鲁斯特是治疗 AECOPD 的常用药物。孟鲁斯特是

白三烯受体拮抗剂，它可以特异性的阻断白三烯与炎症细胞表面的受体结合，从而发挥抗炎的作用对 AECOPD 有一定疗效[9-11]。但孟鲁斯特对 AECOPD 患者体内的炎症因子网络抑制功能有限，需要与糖皮质激素结合使用才能发挥更好的疗效，使其治疗受到限制[12,13]。痰热清注射液是国家乙类中药，其主要成分为连翘、山羊角、黄芩、金银花、熊胆粉等[14]。有相关研究表明，痰热清注射液能够有效抑制炎症信号通路的相关活化过程，使得炎症细胞因子的表达受到抑制，减缓体内的炎症反应[15,16]。

表 2 两组临床症状消失时间对比（d, $\bar{x}\pm s$）

Table 2 Comparison of the disappearance time of clinical symptoms in the two groups（d, $\bar{x}\pm s$）

Groups	n	Disappearance time of cough	Disappearance time of shortness of breath	Disappearance time of wheezing
Study group	58	6.2± 1.6	5.7± 2.0	4.7± 1.9
Control group	58	8.7± 2.6	9.0± 2.9	5.8± 2.0
t value	-	3.036	3.034	2.736
P value	-	0.000	0.000	0.003

表 3 两组患者治疗前后血清 IL-6、IL-8、TNF-α 比较（ng/L，$\bar{x}\pm s$）

Table 3 Comparison of serum IL-6, IL-8 and TNF-α before and after treatment in the two groups（ng/L, $\bar{x}\pm s$）

Groups	n	IL-6		IL-8		TNF-α	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Study group	58	58.2± 13.4	35.2± 11.4*	29.3± 4.6	11.3± 3.8*	48.3± 10.8	26.4± 7.2*
Control group	58	61.4± 11.8	46.7± 12.8*	28.6± 5.3	15.6± 2.7*	48.5± 12.1	37.6± 6.8*
t value	-	0.453	2.845	0.528	2.642	0.183	2.923
P value	-	0.773	0.000	0.380	0.025	0.879	0.000

Note: compared with before treatment, *P<0.05.

本研究中对照组给予 AECOPD 常规治疗，同时口服孟鲁司特，研究组应用痰热清注射液联合孟鲁斯特治疗，结果研究组总有效率较对照组升高。同时研究组患者咳嗽消失时间，气促消失时间及哮鸣音消失时间均明显短于对照组，这与 Zhu JJ 等研究一致[17,18]，表明痰热清注射液联合孟鲁司特治疗 AECOPD 可以显著改善患者临床症状，促进患者康复，临床疗效更佳。我们认为这与痰热清注射液的药理作用有关。痰热清注射液中的黄芩为君药，具有清热润燥，泻火解毒的功效。熊胆粉和山羊角为臣药，具有解毒祛痰、镇咳平喘的效果[19]。而金银花为佐药，具有宣肺解表、清热化痰的功效[20,21]。连翘为使药，可将诸药引入肺经，发挥药理作用。该药对各类急慢性支气管炎、肺炎和上呼吸道感染有很好的治疗作用[22,23]。现代药理学研究发现，痰热清注射液对肺炎链球菌、流感嗜血杆菌、金黄色葡萄球菌均有一定抑制作用[24,25]。本研究中研究组临床效果优于对照组也证实了痰热清注射液联合孟鲁司特对 AECOPD 有很好的治疗作用。

本研究还对两组患者治疗前后血清 IL-6、IL-8、TNF-α 水平进行了比较。其中 IL-6 是机体重要的炎症介质，它可以诱导 B 淋巴细胞的增殖活化，对病原菌差生杀伤作用，同时也是 COPD 中损伤气道的重要分子[26,27]。IL-8 则具有很强的趋化作用，它可以诱导中性粒细胞和嗜酸性粒细胞浸润气道粘膜，从而加重气道的损伤[28]。而 TNF-α 可以引起炎症细胞聚集并释放花生四烯酸，加重局部损伤[29,30]。本研究中治疗后两组患者血清 IL-6、IL-8、TNF-α 均显著降低，观察组患者血清 IL-6、IL-8、TNF-α 显著低于对照组，结果表明痰热清注射液联合孟鲁司特可以有效的降低机体炎症反应，这对 AECOPD 患者的康复有很好的作用。同时我们认为孟鲁司特作为一种非激素类抗炎药物，而痰热清注射液为中药制剂，两者结合可以发挥很好的治疗作用，同时适用于成年人以及 1 岁以上儿童哮喘的预防以及长期治疗，治疗范围更加广泛。

综上所述，痰热清注射液联合孟鲁司特能够有效缓解 AECOPD 患者症状，降低患者炎症反应，临床效果较好。

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