

doi: 10.13241/j.cnki.pmb.2019.13.023

丹参注射液联合莫西沙星治疗老年慢阻肺急性发作患者的疗效分析*

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摘要 目的: 探讨丹参注射液联合莫西沙星治疗老年慢性阻塞性肺病急性加重患者的疗效及对血清可溶性髓样细胞触发受体-1 (sTREM-1)、白细胞介素-6 (IL-6)、中性粒细胞 CD64 (CD64) 及炎症因子水平的影响。**方法:** 选择 2015 年 5 月到 2017 年 5 月我院接诊的老年慢性阻塞性肺病急性加重患者 95 例作为研究对象, 根据随机数表法分为观察组 (n=49) 和对照组 (n=46)。对照组使用莫西沙星治疗, 观察组采用丹参注射液联合莫西沙星治疗。比较两组治疗后的疗效、治疗前后血清 sTREM-1、IL-6、CD64、炎症因子 [肿瘤坏死因子 α (TNF- α)、C 反应蛋白 (CRP)、降钙素原 (PCT)] 水平、肺功能的变化及不良反应的发生情况。**结果:** 治疗后, 观察组临床疗效总有效率为 95.92%, 显著高于对照组 (76.09%, $P<0.05$); 观察组患者血清 sTREM-1、IL-6、CD64、TNF- α 、CRP 及 PCT 水平均明显低于对照组 ($P<0.05$); 观察组 FEV1、FVC、FEV1 % 预测值均明显高于对照组 ($P<0.05$); 两组患者不良反应总发生率分别为 6.12%、13.04%, 组间比较差异无统计学意义 ($P>0.05$)。**结论:** 丹参注射液联合莫西沙星治疗老年慢性阻塞性肺病患者的临床效果显著优于单用莫西沙星治疗, 可能与其有效改善患者血清 sTREM-1、IL-6、CD64 水平及炎症因子水平有关。

关键词: 丹参注射液; 莫西沙星; 慢性阻塞性肺疾病; 可溶性髓样细胞触发受体-1; 白细胞介素-6; 中性粒细胞 CD64; 炎症因子
中图分类号: R563 **文献标识码:** A **文章编号:** 1673-6273(2019)13-2502-04

Curative Efficacy of Danshen Injection Combined with Moxifloxacin in the Treatment of Elderly Patients with AECOPD and Its Effects on the Strem-1, IL-6, CD64, and Inflammatory Factors*

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ABSTRACT Objective: To study the curative efficacy of Danshen injection combined with moxifloxacin in the treatment of elderly patients with acute exacerbation of chronic obstructive pulmonary disease and its effects on the soluble myeloid cells trigger receptor-1 (sTREM-1), interleukin-6 (IL-6), neutrophil CD64 (CD64), and inflammatory factors. **Methods:** 95 elderly patients with chronic obstructive pulmonary disease treated in our hospital from May 2015 to May 2017 were selected and divided into the observation group (n=49) and the control group (n=46) according to the randomized table. The control group was treated with moxifloxacin, and the observation group was treated with moxifloxacin combined with Danshen injection. After treatment, the clinical effects, changes of serum sTREM-1, IL-6, CD64, TNF- α , c-reactive protein (CRP), calcitonin (PCT), lung function and incidence of adverse reactions were compared between two groups. **Results:** After treatment, the total effective rate of observation group was 95.92%, which was significantly higher than that of the control group (76.09%, $P<0.05$). The serum sTREM-1, IL-6, CD64, TNF- α , CRP and PCT levels in the observation group were significantly lower than those in the control group ($P<0.05$). The predictive values of FEV1, FVC and FEV1 % in the observation group were significantly higher than those in the control group ($P<0.05$). The total incidence of adverse reactions in the two groups was 6.12% and 13.04%, respectively, and no statistically significant difference was found between the two groups ($P>0.05$). **Conclusion:** The clinical effect of Danshen injection combined with moxifloxacin is significantly better than that of moxifloxacin alone in the treatment of elderly patients with chronic obstructive pulmonary disease, which may be related to its effective improvement of serum sTREM-1, IL-6, CD64 and inflammatory factor levels.

Key words: Danshen injection; Moxifloxacin; Chronic obstructive pulmonary disease; Soluble myeloid cells trigger receptor-1; Interleukin-6; Neutrophil CD64; Inflammatory cytokines

Chinese Library Classification (CLC): R563 **Document code:** A

Article ID: 1673-6273(2019)13-2502-04

* 基金项目: 陕西省自然科学基金研究计划项目 (2014JM3586)

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(收稿日期: 2019-01-23 接受日期: 2019-02-18)

前言

慢性阻塞性肺疾病 (chronic obstructive pulmonary disease, COPD)呈进行性发展,与气道的慢性炎性反应增强有关,以 40 岁左右中老年人多发人群,临床表现为咳嗽咳痰、气促等症状,且具有反复发作的特点,严重影响患者的生活质量^[1,2]。COPD 若不及时治疗可发生肺源性心脏病、呼吸衰竭,因此,在治疗上应以控制炎症反应为主^[3,4]。抗菌药物特别是在肺组织浓度高的呼吸喹诺酮类抗生素的使用是 AECOPD 患者临床治疗的关键药物。但因 AECOPD 患者因组织缺氧,多合并心脑血管合并症。

研究表明丹参注射液可有效扩张小动脉,抑制血小板聚集,提高氧自由基的清除效果,缓解组织损伤^[5,6],可显著改善慢性阻塞性肺病、肺炎等的临床症状^[7,8]。近年来,STREM-1、IL-6、CD64 作为重要的炎症标志物,对呼吸机相关性肺炎、脓毒症等的临床诊治具有重要意义^[9,10],但对 COPD 诊断价值研究鲜有报道。因此,本研究主要探讨 COPD 患者采用丹参注射液联合莫西沙星治疗的疗效及对血清 STREM-1、IL-6、CD64、炎症因子的影响,现报道如下。

1 资料与方法

1.1 一般资料

选择 2015 年 5 月到 2017 年 5 月于我院进行治疗的 95 例老年 COPD 患者作进行研究。采用简单随机分组法分为 2 组,观察组男 28 例,女 21 例;61-83 岁,平均(67.25± 9.89)岁,病程 2~13 年,平均(5.87± 3.25)年;对照组男 27 例,女 19 例;年龄 60~84 岁,平均(68.19± 9.68)岁,病程 3~14 年,平均(5.89± 3.26)年。两组患者年龄、性别等一般资料比较差异无明显统计学意义($P>0.05$),具有可比性。

纳入标准:(1)符合《慢性阻塞性肺疾病全球倡议 (GOLD, 2018)》中 AECOPD 的诊断标准^[11](2)无长期服用影响检测结果的药物;排除标准:(1)预计生存期<3 个月;(2)意识障碍者;(3)

合并重症肺炎、病情危重合并呼吸衰竭需进一步机械通气者。(4)对本次研究药物过敏、禁忌者。

1.2 治疗方法

两组患者常规给予化痰、抗感染治疗,对照组在此基础上给予莫西沙星(规格 2mg,厂家:金花企业(集团)股份有限公司西安金花制药厂,国药准字 H20010648)50 μ g 吸入治疗,1d2 次。观察组在对照组的基础上加用丹参注射液(规格 10 mL,厂家:四川三精升和制药有限公司,国药准字 Z51021304)20 mL 加入 5%的葡萄糖注射液 250 mL 静脉滴注,1d 1 次。

1.3 观察指标

所有患者于治疗前及治疗后 3 天抽取空腹静脉血 5 mL,抗凝后以 3000 $r \cdot min^{-1}$ 的速度进行离心,时间 10 min,提取上层血清后,置于零下 20℃ 的冷冻箱内存储以备检测,采用双抗体夹心酶联免疫吸附法 (ELISA) 测定 STREM-1、IL-6、CD64、CRP、PCT 及 TNF- α 水平;FEV1、FVC、FEV1 % 预测值水平采用 HI-101 肺功能检测仪测定。

疗效评定标准^[12]:显效:临床症状消失,肺部体征消失,复查炎症指标正常或下降。有效:发热、咳嗽、咳痰、呼吸困难、紫绀等临床症状明显改善,肺部体征减轻,低氧血症较前缓解,复查炎症指标正常或下降;无效:临床症状加重或无改善。显效+有效=总有效率。

1.4 统计学分析

以 SPSS18.0 软件包处理数据,计量资料均为正态分布,用均数 $\pm$ 标准差($\bar{x} \pm s$)表示,组间比较使用独立样本 t 检验,计数资料以率表示,组间比较采用 χ^2 检验,以 $P<0.05$ 表示差异具有统计学意义。

2 结果

2.1 两组患者临床疗效的比较

治疗后,两组总有效率分别为 95.92%、76.09%,观察组显著高于对照组($P<0.05$),见表 1。

表 1 两组患者临床疗效的比较[例(%)]

Table 1 Comparison of the clinical efficacy between the two groups[n(%)]

Groups	n	Effective	Valid	Invalid	Total effective rate
Observation group	49	35(71.43)	12(24.49)	2(4.08)	47(95.92)
Control group	46	27(58.70)	8(17.39)	11(23.91)	35(76.09)
χ^2 value					7.900
P value					0.005

2.2 两组患者治疗前后血清 STREM-1、IL-6、CD64 水平的比较

治疗后,两组患者血清 STREM-1、IL-6、CD64 水平均较治疗前显著降低,且观察组患者以上指标均明显低于对照组($P<0.05$),见表 2。

2.3 两组患者治疗前后血清炎症因子水平的比较

治疗后,两组患者血清 TNF- α 、CRP 及 PCT 水平均较治疗前显著降低,且观察组以上指标均显著低于对照组($P<0.05$),见表 3。

2.4 两组患者治疗前后肺功能的比较

两组患者经治疗后各肺功能指标如 FEV1、FVC、FEV1 % 预测值均较治疗前显著升高 ($P<0.05$),且观察组 FEV1、FVC、FEV1 % 预测值均明显高于对照组($P<0.05$),见表 4。

2.5 两组患者并发症发生情况的比较

两组患者并发症总发生率分别 6.12%、13.04%,组间比较差异无统计学意义($P>0.05$),见表 5。

3 讨论

表 2 两组患者治疗前后血清 STREM-1、IL-6、CD64 水平的比较($\bar{x} \pm s$)

Table 2 Comparison of the serum levels of STREM-1, IL-6 and CD64 levels between the two groups before and after treatment($\bar{x} \pm s$)

Groups	n	STREM-1(ng/mL)		IL-6(ng/L)		CD64(%)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	49	133.29± 20.75	18.13± 6.57	481.21± 76.14	50.37± 8.42	85.36± 12.51	39.47± 3.12
Control group	46	133.51± 21.23	59.48± 12.84	479.86± 77.63	201.12± 45.13	86.03± 13.63	61.24± 9.26
t value		0.051	19.938	0.086	22.968	0.250	15.548
P value		0.959	0.000	0.932	0.000	0.803	0.000

表 3 两组患者治疗前后血清炎症因子水平的比较($\bar{x} \pm s$)

Table 3 Comparison of the serum inflammatory factor levels between the two groups before and after treatment($\bar{x} \pm s$)

Groups	n	TNF- α (ng/L)		CRP(mg/L)		PCT(ng/mL)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	49	533.04± 134.52	61.13± 18.74	31.68± 2.51	7.87± 0.52	1.89± 0.56	0.23± 0.18
Control group	46	531.25± 138.40	240.73± 52.06	31.71± 3.27	10.29± 1.15	1.87± 0.61	0.86± 0.35
t value		0.064	22.643	0.050	13.351	0.167	11.132
P value		0.949	0.000	0.960	0.000	0.868	0.000

表 4 两组患者治疗前后肺功能的比较($\bar{x} \pm s$)

Table 4 Comparison of the lung function between the two groups before and after treatment($\bar{x} \pm s$)

Groups	n	FEV1(L)		FEV1 /FVC		Fev1% predicted value	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	49	1.62± 0.29	1.90± 0.56	52.19± 5.37	65.82± 6.10	51.28± 6.53	65.29± 7.85
Control group	46	1.60± 0.24	1.61± 0.58	51.90± 4.77	56.18± 5.29	50.90± 5.44	56.63± 8.07
t value		0.365	2.479	0.278	8.206	0.307	5.301
P value		0.716	0.015	0.782	0.000	0.760	0.000

表 5 两组患者不良反应发生情况的比较[例(%)]

Table 5 Comparison of the incidence of adverse reactions between the two groups[n(%)]

Groups	n	Nausea	Itchy skin	Heart palpitations	Gastrointestinal reaction	The total incidence of
Observation group	49	1	0	1	1	3(6.12)
Control group	46	2	1	1	2	6(13.04)
χ^2 value						1.325
P value						0.250

慢性阻塞性肺疾病的本质是气道慢性炎症性疾病,其复杂的炎性细胞及其分泌的细胞因子相互诱导,发生气道慢性炎症,导致病理改变造成粘液高分泌、气腔狭窄、气流受限引起的气道阻塞。急性加重期,在感染、污染等诱发因素作用下,气道炎症加剧,引起咳嗽、脓痰、喘息、呼吸困难等呼吸道症状^[13,14];另一方面,肺部炎症溢出,导致全身性的炎症反应。有研究显示 40 岁以上人群慢性阻塞性肺病的患病率达 8.2%,且老年人免疫功能下降,容易合并并发症,受疾病影响更严重^[15,17]。

如上所述,78%的 AECOPD 患者有明确的病毒或细菌感染依据,在临床治疗中,首选抗菌药物治疗,而莫西沙星属第四

代喹诺酮类抗菌药物。其抗菌谱能够完全覆盖 AECOPD 的常见病原体,组织分布较广,在支气管黏膜及分泌物中,杀菌能力较强,见效快,治疗时间短,其可以快速的渗透肺组织,因而也被称为“呼吸喹诺酮”^[18-20]。但 COPD 患者在急性加重期往往因存在呼吸功能下降 CO₂ 潴留,从而引起组织缺氧,进而红细胞、纤维蛋白原增多,且因常伴有发热、脱水血液粘稠度升高等一系列全身病理生理改变,而丹参注射液的主要作用为活血化瘀,同时还能加快氧自由基的清除,抗支气管平滑肌痉挛,提高局部组织的药物浓度^[21,22]。有研究报道,丹参注射液能缓解慢性阻塞性肺病的炎症反应^[23,24]。相关文献显示丹参注射液可有效

扩张小动脉,抑制血小板聚集,提高氧自由基的清除效果,缓解肺组织损伤。慢性阻塞性肺病在中医中属于“喘证”“咳嗽”“肺胀”的范畴,大多与肺、脾、肾的功能失调相关,因此,治疗上以补肾、补脾、痰浊瘀血为主^[25,26]。

本研究结果显示联合丹参注射液治疗的患者的临床总有效率达 95.92%, 明显高于单独使用莫西沙星治疗的患者,且 FEV1、FVC、FEV1 % 预测值均明显高于使用莫西沙星治疗的患者,说明丹参注射液联合莫西沙星治疗老年慢性阻塞性肺病能明显提高其临床效果,改善患者的肺功能。分析原因是由于莫西沙星能通过抗生素的强大活性减轻细菌负荷,减轻中性粒细胞、CD8T 淋巴细胞为主的炎症细胞浸润,从而减轻由炎性介质引起的支气管痉挛,缓解慢性阻塞性肺病的临床症状;而丹参注射液则能通过改善血液流变性能,降低血浆黏度,提高微循环,增加心脏血管血流量,减轻组织缺氧,缓解肺动脉高压,改善右心功能,提高心输出量。两药通过不同机制发挥各自的作用,最终改善肺功能指标,提高临床效果。且两组患者治疗期间不良反应无明显差异,说明联合用药未增加药物不良反应, Bozinovski S^[27]等研究显示丹参注射液对慢性阻塞性肺病效果显著,安全性高,不会增加不良反应的发生。

正常人群中 STREM-1 水平较低,一旦发生慢性阻塞性肺病 STREM-1 水平则明显升高^[28]。STREM-1 在嗜中性粒细胞和巨噬细胞表面表达,于感染过程中释放入血液或体液中。IL-6 属于白细胞介素的一种,参与免疫反应中细胞的分化、增殖;CD64 属于免疫球蛋白超家族的成员,是免疫球蛋白 G 的高亲和受体,正常情况下呈低水平表达,当机体发生感染时表达增高^[29]。本研究结果显示联合丹参注射液治疗的患者的血清 STREM-1、IL-6、CD64、TNF- α 、CRP 及 PCT 水平明显低于使用莫西沙星治疗的患者,说明丹参注射液联合莫西沙星能有效改善患者的炎症因子水平,这与 Karloh M^[30]研究结果相似。分析原因是由于丹参注射液可有效扩张动脉,预防微血栓形成,红细胞变形能力因此得到加强,从而抑制动脉壁斑块的形成,最终改善氧化应激及下调血清 IL-6、CRP 等炎症细胞因子表达。

综上所述,丹参注射液联合莫西沙星治疗老年慢性阻塞性肺病患者的临床效果显著优于单用莫西沙星治疗,可能与其有效改善患者血清 STREM-1、IL-6、CD64 水平及炎症因子水平有关。

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