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氨溴索注射液治疗 COPD 合并肺结核患者的疗效及对血清IL-6、TNF-α 水平的影响 *

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摘要 目的：观察氨溴索注射液治疗慢性阻塞性肺疾病(COPD)合并肺结核(PTB)患者的临床疗效及对患者血清白介素 -6(IL-6)、肿瘤坏死因子 -α(TNF-α)水平的影响。**方法：**选取 2015 年 1 月 ~2018 年 1 月我院诊治的 COPD 合并 PTB 患者 181 例，按照入院先后顺序分为对照组和观察组。对照组 90 例，给予常规对症药物治疗。观察组 91 例，在对症治疗的基础上加用氨溴索注射液。两组均持续治疗 8 周。比较两组临床有效率、病灶吸收和空洞闭合有效率、临床症状积分、肺功能及治疗前后血清 IL-6 和 TNF-α 水平的变化。**结果：**治疗后，观察组和对照组的总有效率分别为 95.60%、74.44%，观察组显著高于对照组，两组相比具有统计学差异(P＜0.05)；观察组治疗后病灶吸收有效率和症状积分均明显优于对照组(P＜0.05)，空洞闭合有效率与对照组相比差异无统计学意义(P＞0.05)；观察组治疗后用力呼气量(FVC)、一秒用力呼气容积(FEV1)和 FEV1/FVC 值显著高于对照组(P＜0.05)，血清 IL-6 和 TNF-α 水平均显著低于对照组(P＜0.05)。**结论：**氨溴索注射液可显著提高 COPD 合并 PTB 患者的临床疗效，改善临床症状、病灶吸收和空洞闭合有效率和肺功能，可能与其有效降低血清 IL-6 和 TNF-α 水平有关。

关键词：氨溴索注射液；慢性阻塞性肺疾病；肺结核；白介素 -6；肿瘤坏死因子 -α

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Clinical Efficacy of Ambroxol Injection in the Treatment of COPD Complicated with Pulmonary Tuberculosis and Its Impact on the Serum Serum IL-6 and TNF-α Levels*

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ABSTRACT Objective: To observe the clinical efficacy of ambroxol injection in the treatment of COPD combined with PTB and its impact on the serum IL-6 and TNF-α levels. **Methods:** 181 cases of patients with COPD and PTB treated in the Affiliated Hospital of Hebei University were selected from January 2015 to January 2018 and divided into the control group and the observation group according to the order of admission. In the control group, 90 cases were treated with conventional symptomatic drugs. In the observation group, 91 cases were treated with ambroxol injection on the basis of symptomatic treatment. Both groups were treated for 8 weeks. The clinical efficacy, nidus absorption status, void closure status, symptom scores, lung function and changes of serum IL-6, TNF-α levels before and after treatment were compared between two groups. **Results:** After treatment, the total effective rate of observation group and control group were 95.60% and 74.44% respectively, which was significantly higher in the observation group than that of the control group(P<0.05); the nidus absorption status and symptomatic score of observation group were better than those of the control group (P<0.05), there was no significant difference in the void closure status between two groups(P＞0.05). The values of FVC, FVC and FEV1/FVC of observation group were significantly higher than those in the control group (P<0.05), the serum levels of IL-6 and TNF-α in the observation group were significantly lower than those in the control group (P<0.05). **Conclusions:** Ambroxol injection can significantly improve the clinical symptoms, nidus absorption status, void closure status and lung function in the treatment of COPD combined with PTB, it may be related to the effective reduction of serum IL-6 and TNF-α levels.

Key words: Ambroxol Injection; COPD; PTB; IL-6; TNF-α

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前言

慢性阻塞性肺疾病(COPD)是一种以气流持续受限为特征的慢性进行性炎性疾病[1-3]。肺结核(PTB)是由结核杆菌感染引

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起的慢性传染性疾病[4,5]。两者均是呼吸系统常见病、多发病，可导致患者呼吸困难和 CO_2 潴留等，严重威胁患者的生命健康。有研究显示两种疾病之间存在密切的关系，COPD 由于呼吸道气流受限和炎症增加了发生 PTB 的风险[6,7]，而 PTB 又导致患者炎症的加重，使 COPD 病情进一步发展，二者相互影响并相互诱导。所以临床上 COPD 合并 PTB 的发生率较高，呈现出逐年上升的趋势，且病情发展加快，还影响药物的治疗效果，其治愈率低、死亡率高，已经成为目前重大的公共卫生问题[8-10]。

临床对 COPD 合并 PTB 的治疗以平喘、抗炎、止咳化痰、抗结核和营养支持等对症治疗为主，但由于抗结核治疗不良反应较大，患者的免疫功能受到影响，免疫力下降，且细菌耐药性的不断出现，使得治疗效果不理想[11-13]。优化治疗方法、选择更好的治疗药物对患者的治疗更有意义。氨溴索注射液具有改善气道炎症和通气的作用[14,15]。因此，本研究观察分析了氨溴索注射液治疗 COPD 合并 PTB 患者的疗效及对血清白介素 -6(IL-6)、肿瘤坏死因子 - α(TNF-α)的影响。

1 资料与方法

1.1 一般资料

选取 2015 年 1 月 ~2018 年 1 月我院诊治的 COPD 合并 PTB 患者 181 例，按照入院先后顺序分为对照组和观察组。对照组 90 例，男 51 例，女 39 例；年龄 51~75 岁，平均 59.65± 5.4 岁；COPD 病程 0.5~10.1 年，平均 4.2± 1.1 年，初治 79 例，复治 11 例。观察组 91 例，男 53 例，女 38 例；年龄 50~76 岁，平均 58.54± 4.8 岁；COPD 病程 0.6~10.3 年，平均 4.9± 1.2 年，初治 82 例，复治 9 例。两组一般资料比较无显著性差异(P＜0.05)。入选标准：① 符合 COPD 和 PTB 的诊断标准[16,17]；② 有咳嗽、气喘、发热、咳血等症状，肺部可闻及罗鸣音；③ 签署知情同意书。排除标准：① 合并严重心血管疾病、癌症及肝肾功能损伤者；② 治疗依从性差者；③ 对药物过敏者。本研究获得医院医学伦理委员会批准。

1.2 治疗方法

对照组根据患者的临床症状给予支气管扩张、抗结核、吸氧、纠正电解质紊乱、抗感染、抗凝和营养支持等治疗。观察组在对照组的基础上加用氨溴索注射液治疗，方法：30 mL 氨溴索注射液加入 2 mL 0.9%氯化钠注射液，采用雾化器进行雾化治疗，1 次 / 天，连续治疗 8 周。

1.3 观察指标

① 临床有效率：显效：临床症状和罗鸣音明显改善或消失；有效：临床症状有一定缓解或部分症状明显改善；无效：临床症状未改善或加重。② 治疗后两组临床症状积分、病灶吸收和空洞闭合有效率。病灶吸收标准：完全吸收：病灶吸收完全；吸收：病灶吸收面积＜ 1/2；无效：无吸收或有弥散趋势。空洞闭合标准：完全闭合：空洞闭合；明显缩小：缩小直径≥ 1/2；缩小：缩小直径＜ 1/2；无效：无缩小甚至扩大。临床症状积分：按照 COPD 症状积分标准进行评分，轻度为 1 分、中度为 2 分、重度为 3 分。③ 治疗后患者的肺功能：采用肺功能检测仪测定治疗后患者的 FVC、FEV1 和 FEV1/FV 值，评价患者的肺功能。④ 治疗前后抽取患者空腹静脉血 5 mL，采用 ELISA 测定血清 IL-6 和 TNF-α 水平，试剂盒购自武汉博士德生物有限公司。

1.4 统计学方法

采用 SPSS 20.0 统计学软件分析，计量资料用($\bar{x}$± s)表示，组间比较采用 t 检验；计数资料采用例和%表示，组间比较采用 x^2 检验。以 P<0.05 表示差异有统计学意义。

2 结果

2.1 两组临床疗效的比较

治疗后，观察组的总有效率为 95.60%，对照组为 74.44%，观察组显著高于对照组，两组相比具有统计学差异(P＜0.05)，见表 1。

表 1 两组临床疗效的比较[例(%)]

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

Groups	n	Excellent	Valid	Inefficient	Total Effective Rate
Control Group	90	36(40.00)	31(34.44)	23(25.56)	67(74.44)
Observation Group	91	50(54.95)	37(40.66)	4(4.40)	87(95.60)*

Note: Compared with control group, *P＜0.05.

2.2 两组临床症状积分、病灶吸收和空洞闭合有效率的比较

观察组治疗后病灶吸收有效率和症状积分优于对照组(P＜0.05)，空洞闭合有效率与对照组相比无显著性差异 (P＜0.05)，见表 2。

表 2 两组临床症状积分、病灶吸收和空洞闭合有效率比较[例(%)]($\bar{x}$± s)

Table 2 Comparison of the void closure status, void closure status and symptom scores between the two groups[n(%)]($\bar{x}$± s)

Groups	n	Nidus absorption status	Void closure status	Symptom scores
Control Group	90	81(90.00)	80(88.89)	90.38± 15.34
Observation Group	91	72(79.12)*	75(82.42)	84.75± 11.27*

Note: Compared with control group, *P＜0.05.

2.3 两组治疗后肺功能的比较

治疗后，观察组 FVC、FEV1 和 FEV1/FVC 值显著高于对照组(P＜0.05)，见表 2。

2.4 两组治疗前后血清 IL-6、TNF-α 水平的变化比较

治疗后，两组血清 IL-6 和 TNF-α 水平均显著低于治疗前(P＜0.05)，且观察组治疗后以上指标显著低于对照组 (P＜0.05)，见表 4。

表 3 两组治疗后肺功能的比较($\bar{x}\pm s$)

Table 3 Comparison of clinical effect between the two groups after treatment($\bar{x}\pm s$)

Groups	n	FVC(L)	FEV1 (L)	FEV1/FVC(%)
Control Group	90	2.12± 0.54	1.38± 0.31	73.59± 25.64
Observation Group	91	2.68± 0.61*	1.72± 0.42*	91.08± 28.53*

Note: Compared with control group, *P＜0.05.

表 4 两组治疗前后血清 IL-6、TNF-α 水平的变化比较($\bar{x}\pm s$)

Table 4 Comparison of the changes of serum levels of IL-6 and TNF-α between the two groups before and after treatment($\bar{x}\pm s$)

Groups	n	IL-6		TNF-α	
		Before treatment	After treatment	Before treatment	After treatment
Control Group	90	70.32± 11.25	45.89± 9.35*	81.25± 18.54	67.34± 15.28*
Observation Group	91	69.38± 10.54	33.74± 8.25*#	80.87± 19.04	60.28± 14.36*#

Note: Compared with control group, *P＜0.05; Compared withbefore treatment, #P＜0.05.

3 讨论

COPD 是一种不完全可逆的气流受限性疾病，常进行性加重，与异常炎症反应有关，以气道、肺实质和肺血管的慢性炎症为重要特征。当炎症细胞激活后，多种炎性介质和细胞因子包括 IL-6、TNF-α 等释放，这些介质能够破坏肺结构并促进中性粒细胞炎症反应，导致气道壁损伤，结构重构，进而产生气腔狭窄，引起气道阻塞[18-20]。有研究显示 COPD 患者血清 IL-6 和 TNF-α 水平明显升高[21-23]，在气道炎症中发挥重要作用。TNF-α 是炎症反应过程中出现最早、最重要的促炎因子，是 COPD 的诱导剂[24-26]。IL-6 可促进 T 细胞和 B 细胞的分化和增殖，参与早期炎症反应[27]。PTB 患者的血清 IL-6 和 TNF-α 水平明显升高，广泛参与了结核病的免疫过程，TNF-α 水平升高可引起结核病变加重，组织坏死等。另有研究显示 COPD 合并 PTB 患者血清 IL-6 和 TNF-α 水平明显高于 COPD 患者和 PTB 患者，IL-6 和 TNF-α 在 COPD 合并 PTB 患者的病情发展过程中起到重要作用[28]。

血清 IL-6 和 TNF-α 水平在一定程度上可反映肺部炎症状况。本研究结果显示加用氨溴索注射液治疗后，患者血清 IL-6和 TNF-α 水平显著低于常规对症治疗，可能是由于氨溴索注射液是一种粘液溶解剂，具有多种生物效应，能够显著抑制肺泡巨噬细胞和嗜中性粒细胞释放自由基，抑制嗜中性粒细胞的趋化作用，降低对机体组织的损害，减少 IL-6 和 TNF-α 的产生，减轻肺部炎性反应，具有抗氧化和减少炎性介质释放的作用[29]。

氨溴索注射液对分泌细胞的作用可调节浆液和粘液的分泌，提高气道表面的含水量，促进呼吸道分泌物的排出并减少滞留，从而达到改善患者通气的作用[30]。同时，氨溴索注射液能够促使肺泡和支气管腺体的分泌，裂解黏蛋白和粘多糖，抑制酸性粘多糖的合成，从而降低痰液的粘稠度，从而稀释痰液并易排出，并能够增加纤毛的摆动、抗黏连和倒伏能力，增大粘液的清除，改善呼吸状况。从而改善患者的肺功能。本研究中，加用氨溴索注射液治疗后临床有效率显著提升，临床症状积分、病灶吸收和空洞闭合有效率、肺功能得到显著改善，可能与其可显著降低 IL-6 和 TNF-α 水平，并改善患者的肺功能有关。

综上所述，氨溴索注射液可显著提高 COPD 合并 PTB 患者的临床疗效，改善临床症状、病灶吸收和空洞闭合有效率和肺功能，可能与其有效降低血清 IL-6 和 TNF-α 水平有关。

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