doi: 10.13241/j.cnki.pmb.2019.09.035

头孢他啶联合氨茶碱治疗慢性阻塞性肺气肿的疗效及对血清 IGF-1、α1-AT、PDGF-B 水平的影响 *

白俊东[1] 姚华强[2] 张玉娜[3] 陈向红[2] 李延民[4] 王富军[5]

（1 邯郸市第一医院 呼吸二科 河北 邯郸 056000；2 邯郸市第一医院 内分泌一科 河北 邯郸 056000；
3 河北医科大学第四医院 内分泌科 河北 石家庄 050011；4 邯郸市第一医院 心内二科 河北 邯郸 056000；
5 河北医科大学第四医院 内分泌科 河北 石家庄 050011）

摘要 目的：探讨头孢他啶联合氨茶碱治疗慢性阻塞性肺气肿(COPD)的临床疗效及对患者血清胰岛素样生长因子 -1(IGF-1)、血清 α1- 抗胰蛋白酶(α1-AT)、血小板衍生生长因子 -B(PDGF-B)水平的影响。**方法：**选择我院 2015 年 4 月至 2018 年 4 月收治的 154 例慢性阻塞性肺气肿作为研究对象，采用随机数字表法将其分为观察组与对照组。对照组采用头孢他啶治疗，观察组在对照组基础上加用氨茶碱联合治疗。对比两组患者的临床疗效、治疗前后血清 IGF-1、α1-AT、PDGF-B 水平的变化及不良反应的发生情况。**结果：**治疗后，观察组与对照组临床疗效总有效率分别为 94.80%和 71.43%，观察组显著高于对照组(P<0.05)；观察组血清 IGF-1、PDGF-B 水平均显著低于对照组 [(110.67± 13.58) vs. (143.17± 15.74)ng/ml、(128.67± 15.33) vs. (247.69± 30.17)ng/L]，而血清 α1-AT 水平明显高于对照组[(2.79± 0.43) vs. (1.77± 0.46)g/L](P<0.05)；观察组与对照组不良反应率分别为 5.19%和 50.64%，观察组明显低于对照组(P<0.05)。**结论：**综上所述，头孢他啶联合氨茶碱治疗 COPD 的临床疗效和安全性均显著优于单用头孢他啶治疗，可能与其有效降低 COPD 患者血清 PDGF-B、IGF-1，明显提高血清 α1-AT 水平有关。

关键词：头孢他啶；氨茶碱；血清胰岛素样生长因子 -1；血清 α1- 抗胰蛋白酶；血小板衍生生长因子 -B；慢性阻塞性肺气肿
中图分类号：R563 **文献标识码：**A **文章编号：**1673-6273(2019)09-1762-04

Effects of Ceftazidime Combined with Aminophylline on Chronic Obstructive Emphysema and Its Effect on the Serum IGF-1, α1-AT and PDGF-B Levels*

BAI Jun-dong[1], YAO Hua-qiang[2], ZHANG Yu-na[3], CHEN Xiang-hong[2], LI Yan-min[4], WANG Fu-jun[5]

(1 The first hospital of Handan two Department of respiration Hebei, Handan, 056000, China; 2 Department of Endocrinology, First Hospital of Handan, Hebei, Handan, 056000, China; 3 Department of Endocrinology, the fourth hospital of Hebei Medical University, Shijiazhuang, Hebei, 050011, China; 4 The First Affiliated Hospital of Handan No. two, Hebei, Handan, 056000, China; 5 Department of Endocrinology, the fourth hospital of Hebei Medical University, Shijiazhuang, Hebei, 050011, China)

ABSTRACT Objective: To investigate the clinical efficacy of ceftazidime combined with aminophylline in the treatment of chronic obstructive emphysema and the effect on the serum insulin-like growth factor-1, serum 1-antitrypsin and platelet-derived growth factor-b levels. **Methods:** 154 cases of patients with chronic obstructive emphysema admitted to our hospital from April 2015 to April 2018 were selected and were divided into the observation group and the control group by random number table method. The control group was treated with ceftazidime, and the observation group was treated with aminophylline on the basis of control group. The clinical efficacy, changes of serum IGF-1, α1-AT and PDGF-B levels before and after treatment and the occurrence of adverse reactions were compared between the two groups. **Results:** After treatment, the total effective rates of observation group and the control group were 94.80% and 71.43% respectively, and which was significantly higher in the the observation group than that of the control group (P<0.05). The serum IGF-1 and PDGF-B levels in the observation group were significantly lower than those in the control group [(110.67 13.58) vs. (143.17 15.74)ng/mL, (128.67 15.33) vs. (247.69 30.17)ng/L], while serum α1-AT level was significantly higher than that in the control group [(2.79 0.43) vs. (1.77 0.46)g/L](P<0.05). The incidence of adverse reactions in the observation group and the control group were 5.19% and 50.64% respectively, which were significantly lower in the observation group than that of the control group (P<0.05). **Conclusion:** The clinical efficacy and safety of ceftazidime combined with aminophylline in the treatment of COPD are significantly better than that of ceftazidime alone, which may be related to the effective reduction of serum PDGF-B and IGF-1 levels and the significant increase of serum α1-AT level.

* 基金项目：河北省科技攻关项目(06276179)
作者简介：白俊东(1974-)，男，本科，主治医师，研究方向：呼吸科疾病，电话：13111393157，E-mail：zhaohua732@163.com
（收稿日期：2018-12-04 接受日期：2018-12-27）

Key words: Ceftazidime; Aminophylline. Serum insulin-like growth factor-1; Serum 1-antitrypsin; Platelet derived growth factor-b; Chronic obstructive emphysema

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

Article ID: 1673-6273(2019)09-1762-04

前言

慢性阻塞性肺气肿（Chronic obstructive emphysema，COPD）是一种呼吸系统的病理改变，吸烟、大气污染、感染等是诱发因素，其临床症状主要表现为呼吸困难、缺氧、酸中毒等[1]，若治疗不及时，会诱发其并发症，如肺源性心脏病、呼吸衰竭和心理衰竭等，严重者甚至危及生命[2]。研究表明[3]血清 PDGF-B、α1-AT、IGF-1 水平变化与 COPD 病情严重性有一定相关性，有助于了解病情。α1-AT 是蛋白溶解酶抑制物活性最强的一种，而 COPD 患者血清α1-AT 明显减少[4]。研究显示[5]肺内 IGF-1D 增多与肺间质纤维化的严重程度呈正相关。。PDGF-B 是氧化应激反应的下游产物，在 COPD 病情中扮演重要角色，且对病情发展和预后具有重要意义[6]。

头孢他啶治疗 COPD 的效果佳，能够提高患者的生活质量[7]；氨茶碱可作用于支气管平滑肌，有效缓解支气管粘膜的水肿、充血情况，明显减轻炎症反应，改善呼吸功能[8]。本研究主要探讨了头孢他啶联合氨茶碱治疗慢性阻塞性肺气肿的临床疗效及对患者血清 IGF-1、α1-AT、PDGF-B 水平的影响，现将结果报道如下。

1 材料与方法

1.1 一般资料

选择我院 2015 年 4 月至 2018 年 4 月收治的 154 例慢性阻塞性肺气肿作为研究对象，采用随机数字表法将其分为观察组与对照组。观察组 77 例，男 43 例，女 34 例；年龄 53~77 岁，平均(65.12± 7.28)岁，病程 3~11 年，平均(9.28± 1.03)年，体重指数(21.79± 3.15)kg/m^2；对照组 77 例，男 47 例，女 30 例；年龄 55~79 岁，平均(64.77± 7.59)岁，病程 2~12 年，平均(9.78± 1.54)年，体重指数(21.88± 3.55)kg/m^2。两组一般临床资料比较差异均统计学意义(P>0.05)，具有可比性。

纳入标准[9]：符合《阻塞性肺气肿的首诊症状与诊断》诊断标准，且符合以下条件者：① 年龄 41~81 岁，② 患者及家属签署同意书；排除标准：① 具有免疫性疾病、恶性肿瘤者，② 近期手术及出现心肌梗死者，③ 对本次研究药物过敏者，④ 不配合者。

1.2 治疗方法

对照组采用氨茶碱治疗，口服氨茶碱(连云港泰邦药业有限公司，2 ml:0.25 g，20170312)0.2 g/ 次，3 次 /d。观察组在对照组治疗基础上注射头孢他啶 (广州白云山制药股份有限公司，1 g/ 支，20171221) 静脉注射 1.0 g/ 次，12 h 注射一次，7 天为 1 个疗程。两组患者治疗疗程均为 14 天。

1.3 观察指标

所有试验者均抽取静脉血 6 mL，以 3000 转 /min 离心分离血清，置于 -20℃冻存待检。血清 IGF-1、α1-AT、PDGF-B 水平采用 ELISA 法检测，以上指标均严格按照试剂盒（上海哈灵生物科技有限公司，96T/ 盒，20170412）说明操作。

疗效评定参照相关文献进行[10]：显效：2 周后，患者呼吸困难消失，血清 IGF-1、α1-AT、PDGF-B 水平改善明显；有效：2 周后，患者呼吸困难好转，血清 IGF-1、α1-AT、PDGF-B 水平改善一部分；无效：2 周后，患者呼吸困难无改善，血清 IGF-1、α1-AT、PDGF-B 水平无改变。

1.4 统计学分析

研究数据选用 spss18.0 进行统计分析，符合正态分布的计量资料以均数± 标准差($\bar{x}$± s)表示，组间比较采用独立样本 t 检验，计数资料以率(%)表示，组间比较采用 x^2 检验，以 P<0.05 表示差异具有统计学意义。

2 结果

2.1 两组治疗后的临床疗效比较

治疗后，观察组总有效率为 94.8%，明高高于对照组和(71.43%)，组间差异具有统计学意义(P<0.05)，见表 1。

表 1 两组治疗后临床疗效比较[例(%)]

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

Groups	n	Significantly	Effective	Invalid	Otal efficiency
Observation group	77	46(59.74)	27(35.06)	4(5.20)	73(94.80)[a]
Control group	77	37(48.05)	18(23.38)	22(28.57)	55(71.43)

Note: compared with the control group, after treatment [a]P<0.05.

2.2 两组治疗前后血清 IGF-1、α1-AT、PDGF-B 水平的比较

治疗前，两组患者血清 IGF-1、α1-AT、PDGF-B 水平比较差异均无统计学意义 (P>0.05)；治疗后，观察组血清 IGF-1 和 PDGF-B 水平均显著低于对照组，而血清α1-AT 明显高于对照组，差异均具有统计学意义(P<0.05)，见表 2。

2.3 两组治疗后不良反应情况的比较

治疗后，观察组与对照组总不良反应率分别为(5.19%)和(50.64%)，差异具有统计学意义(P<0.05)。见表 3。

3 讨论

COPD 是属于肺气肿常见的临床病理类型，通过靠人体内呼气流速降低和肺用力呼气时间延长为特征，表现最为常见是终末细支气管远端气腔过度膨胀，同时伴有气泡壁破坏，患者肺功能下降[11,12]。相关研究显示[13,14]COPD 的好发人群多为老年

群体，其主要原因是老年人免疫功能逐渐下降和随着年龄增长累积了部分基础疾病等原因，为此在临床上增加了治疗难度[15]。此外，在 COPD 的病变发生过程中，体内相关气道慢性炎性反应引发支气管平滑肌收缩，同时大量释放了急性感染激活炎症介质，导致患者病情加重。因此，及早治疗尤为重要[16,17]。

表 2 两组治疗前后血清 IGF-1、α1-AT、PDGF-B 水平的比较($\bar{x}\pm s$)

Table 2 Comparison of the serum IGF-1, α1-AT, PDGF-B levels between two groups of patients before and after treatment($\bar{x}\pm s$)

Groups	n	IGF-1(ng/mL)		α1-AT(g/L)		PDGF-B(ng/L)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	77	153.27± 18.31[a]	110.67± 13.58[b]	1.95± 0.31[a]	2.79± 0.43[b]	513.28± 61.83[a]	128.67± 15.33[b]
Control group	77	152.97± 17.28	143.17± 15.74	1.94± 0.28	2.05± 0.39	510.72± 60.01	247.69± 30.17

Note: compared with the control group, before treatment [a]P>0.05, compared with the control group, after treatment [b]P<0.05.

表 3 两组治疗后不良反应发生情况的比较[例(%)]

Table 3 Comparison of the incidence of adverse reactionss between two groups[n(%)]

Groups	n	Nausea	Vomiting	Diarrhea	Much sputum	Short of breath	Adverse reaction rate
Observation group	77	1(1.30)	0(0.00)	0(0.00)	1(1.30)	2(2.60)	4(5.19)a
Control group	77	8(10.39)	6(7.79)	7(9.09)	9(11.69)	9(11.69)	39(50.64)

Note: compared with the control group, after treatment [a]P<0.05.

在人体内的诸多炎性因子中，血清 PDGF-B 主要能刺激体内血管平滑肌细胞、成纤维细胞、胶质细胞的分裂增生，属于人体内血小板 a 颗粒中的一种碱性蛋白质，且具有趋化活性、缩血管活性、促分裂效应、参与磷酸酯酶激活与前列腺素代谢等特点[18-20]。当肝受损时大量分泌的 PDGF 刺激间质星形细胞增殖，从而转化为肌纤维祥母细胞，聚集炎症受损区，其是评估 COPD 病情的重要参考指标之一。α1-AT 是人体内一种糖蛋白，占 10%-20%含糖率，主要由肝脏合成，是人体血清中最主要的蛋白酶抑制剂。α1-AT 在炎症性疾患时可直接进入人体内毛细血管组织液，对急性炎性疾病有一定限制作用。当α1-AT 缺乏时，人体内炎症时白细胞和巨噬细胞释放蛋白分解酶，从而导致肺气肿，α1-AT 在预防肺气肿中起着重要作用[21,22]。IGF-1 是人体内促细胞生长多肽，由人体内多种细胞合成，优点是可在人体组织局部发挥作用，同时分泌或旁分泌，对促进人体各种细胞分化和增殖具有一定效果。同时，其还可直接调节血管的收缩和舒张作用[23,24]。由此可见，血清 IGF-1 水平变化与 COPD 发生密切相关，可能参与了 COPD 的发生和发展过程。因此，血清 PDGF-B、α1-AT、IGF-1 水平的变化对于评估 COPD 的病情具有一定的临床参考价值[25]。

头孢他啶是由第三代头孢菌素半合成的药物，和其他三代的先锋霉素类似，对抗绿脓杆菌、呼吸道感染、泌尿、腹内感染、生殖系统感染病情药效显著[26]。相关文献显示该药物还能够和结合人体内细菌细胞膜表面青霉素的结合蛋白，迫使转肽酶发生酰化，有效阻碍其细胞壁的合成。且快速阻碍其细胞分裂及生长，加速人体内细菌凋亡，对通气状况有良好的临床效果[27,28]。但是单一使用头孢他啶治疗的 COPD 患者血清 PDGF-B、α1-AT、IGF-1 水平并不理想。氨茶碱可有效作用于支气管平滑肌，缓解支气管粘膜的水肿、充血情况，对改善炎症、呼吸功能效果明显[29]。

本研究结果显示头孢他啶联合氨茶碱治疗 COPD 的临床总有效率明显高于单一使用头孢他啶治疗，且血清 IGF-1 和 PDGF-B 水平均低于单一使用头孢他啶者，而血清α1-AT 水平高于单一使用头孢他啶者。此外，头孢他啶联合氨茶碱治疗后的不良反应率明显低于单一使用头孢他啶治疗者，提示两者联合治疗不仅显著提高了 COPD 的临床疗效，治疗安全性也更高，，其主要原因可能是头孢他啶与氨茶碱能有效抗菌、抗感染和提高抗生素疗效，从而减少了不良反应的发生[30]。

综上所述，头孢他啶联合氨茶碱治疗 COPD 的临床疗效和安全性均显著优于单用头孢他啶治疗，可能与其有效降低COPD 患者血清 PDGF-B、IGF-1，明显提高血清 α1-AT 水平有关。

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