

doi: 10.13241/j.cnki.pmb.2019.13.026

痰热清注射液联合奈诺沙星对老年社区获得性肺炎患者血清炎症因子和免疫功能的影响 *

刘殊艳¹ 刘文田^{2Δ} 赵玉梅¹ 刘志国³ 余国勇³

(1 内蒙古医科大学第三附属医院(内蒙古包钢医院)全科 内蒙古 包头 014010;

2 陕西省汉市中心医院呼吸内科 陕西 汉中 723000; 3 陕西省汉市中心医院骨关节创伤外科 陕西 汉中 723000)

摘要 目的:探究痰热清注射液联合奈诺沙星对老年社区获得性肺炎患者血清炎症因子和免疫功能的影响。**方法:**选择 2015 年 12 月 -2017 年 12 月我院诊治的老年社区获得性肺炎患者 218 例,按照其入院顺序经随机数字表法分为两组,每组各 109 例。其中,对照组给予奈诺沙星进行治疗,研究组在对照组基础上联合痰热清注射液进行治疗,对比两组患者的治疗总有效率、临床症状改善时间、治疗前后血清肿瘤坏死因子(TNF- α)、超敏 C-反应蛋白(hs-CRP)、白细胞介素-6(IL-6)、总淋巴细胞(TT)、Th 细胞(CD4)及自然杀伤细胞(NK)水平的变化。**结果:**治疗后,研究组患者的治疗总有效率[90.8%(99/109)]显著高于对照组[74.3%(81/109)]($P<0.05$);研究组患者退热、咳嗽缓解、咳痰缓解、肺部阴影吸收 >50 等时间均明显短于对照组 ($P<0.05$);两组患者血清 TNF- α 、hs-CRP、IL-6 水平均显著低于治疗前,且研究组以上指标均显著低于对照组($P<0.05$);两组患者 TB、TT、CD4 及 NK 水平均比治疗前显著升高,且研究组以上指标均明显高于对照组($P<0.05$)。**结论:**痰热清注射液联合奈诺沙星治疗老年社区获得性肺炎的效果显著优于单用奈诺沙星治疗,其可有效改善患者的临床症状、降低血清炎症因子水平和提高免疫功能。

关键词:痰热清注射液;奈诺沙星;老年社区获得性肺炎;血清炎症因子;免疫功能

中图分类号:R563.1 **文献标识码:**A **文章编号:**1673-6273(2019)13-2515-04

Effect of Tanreqing Injection Combined with Nanofloxacin on the Serum Inflammatory Factors and Immune Function in the Elderly Patients with Community Acquired Pneumonia*

LIU Shu-yan¹, LIU Wen-tian^{2Δ}, ZHAO Yu-mei¹, LIU Zhi-guo³, YU Guo-yong³

(1 General Department, The Third Affiliated Hospital of Inner Mongolia Medical University, Baotou, Inner Mongolia, 014010, China;

2 Respiratory Medicine Department, Hanzhong Central Hospital of Shaanxi Province, Hanzhong, Shaanxi, 723000, China;

3 Osteoarticular Trauma Surgery Department, Hanzhong Central Hospital of Shaanxi Province, Hanzhong, Shaanxi, 723000, China)

ABSTRACT Objective: To investigate the effects of Tanreqing injection combined with aloxacin on the serum inflammatory factors and immune function of elderly patients with community-acquired pneumonia. **Methods:** A total of 218 cases of elderly patients with community-acquired pneumonia who were treated in our hospital from December 2015 to December 2017 were enrolled. According to the admission order, they were divided into two groups according to the random number table method, with 109 cases in each group. The control group was treated with naloxartan, and the study group was treated with Tanreqing injection on the basis of control group. The total effective rate, the time of improvement of clinical symptoms, the changes of serum tumor necrosis factor (TNF- α), high-sensitivity C-reactive protein (hs-CRP), interleukin-6 (IL-6), total lymphocytes (TT), The cells (CD4) and natural killer (NK) cells before and after treatment were compared between the two groups. **Results:** After treatment, the total effective rate of study group [90.8% (99/109)] was significantly higher than that of the control group [74.3% (81/109)] ($P<0.05$). The time of fever, cough relief, and lung shadow absorption >50 were shorter than those of the control group ($P<0.05$). The levels of serum TNF- α , hs-CRP and IL-6 of both groups were significantly lower than those before treatment, and the above indexes of study group were significantly lower than those of the control group ($P<0.05$). The levels of TB, TT, CD4 and NK in both groups were significantly higher than those before treatment, and the above indexes in the study group were significantly higher than those in the control group ($P<0.05$). **Conclusion:** Tanreqing injection combined with naloxartan is more effective than that of naloxartan alone in the treatment of elderly patients with community-acquired pneumonia, it can effectively improve the clinical symptoms, reduce the serum inflammatory factor levels and improve the immune function.

Key words: Tanreqing injection; Naloxacin; Elderly community acquired pneumonia; Serum inflammatory factor; Immune function

Chinese Library Classification (CLC): R563.1 **Document code:** A

Article ID: 1673-6273(2019)13-2515-04

* 基金项目:内蒙古自治区自然科学基金项目(2016MS(LH)0827)

作者简介:刘殊艳(1968-),女,本科,副主任医师,研究方向:全科,电话:13848721307, E-mail: Liushuyan196809@163.com

Δ 通讯作者:刘文田(1973),男,本科,副主任医师,研究方向:中西医结合内科,电话:15891165393, E-mail: Liushuyan196809@163.com

(收稿日期:2018-11-26 接受日期:2018-12-22)

前言

社区获得性肺炎是指在院外罹患的感染性肺实质炎症,以咳嗽、胸闷、气短为主要症状,是目前临床上呼吸科常见的肺炎类型,老年人由于年龄较大,机体免疫预防能力下降,且多伴有多种基础疾病,社区获得性肺炎已成为威胁老年患者住院和死亡的重要原因^[1-3]。奈诺沙星是一种新型喹诺酮类抗菌药,其可对金黄色葡萄球菌及多药耐药性肺炎链球菌等多种临床相关性病原菌有明显的抑菌活性,且安全性较高,但频繁使用抗生素易造成细菌耐药现象的产生,使得后期治疗难度急剧上升^[4,5]。

近年来,随着中医药疗法在临床常见病、重大疾病、疑难杂症等方面的广泛应用,中西医结合疗法相比于单一西医疗法具有协同起效、不良反应少、患者耐受度高等优点。祖国医学认为社区获得性肺炎属“热肺病”、“风温肺热”等范畴,治疗应以清肺化痰为主^[6-8]。痰热清注射液是一种由黄芩、熊胆粉、山羊角、金银花、连翘等药材经提取、纯化等工艺制成的中药现代化制剂,常用于风温肺热病痰热阻肺证的治疗过程中^[9,10]。本研究以近两年我院收治的 218 例老年社区获得性肺炎患者为研究对象,通过对部分患者给予痰热清注射液联合奈诺沙星进行治疗,旨在探究该方法的治疗效果及对患者血清炎症因子和免疫功能指标的影响,为以后临床用药提供参考,具体结果报道如下。

1 资料与方法

1.1 一般资料

选择 2015 年 12 月 -2017 年 12 月我院诊治的老年社区获得性肺炎患者 218 例,纳入标准:符合《老年社区获得性肺炎诊断及治疗指南》中老年社区获得性肺炎的诊断标准者;经 X 线、肺部 CT 扫描、白细胞计数检查等确诊者^[11];对本次研究知情且自愿参与者;排除标准:合并高血压者;合并肺栓塞、肺肿瘤等肺部器质性病变者;伴有严重心肝肾功能不全者;对本研究所用药物过敏者;严重精神障碍者。218 例患者按照其入院顺序经随机数字表法分为两组,每组各 109 例。其中,研究组中

男 59 例,女 50 例,平均年龄为 73.8 ± 9.5 岁,平均病程为 5.4 ± 1.0 d;对照组中男 57 例,女 52 例,平均年龄为 73.1 ± 9.0 岁,平均病程为 5.2 ± 1.1 d。两组患者的基础资料经统计学对比差异无统计学意义($P>0.05$),具有可比性。

1.2 治疗方法

两组均给予止咳平喘、吸氧及营养支持、化痰、调节电解质和酸碱平衡等方法治疗等。对照组给予奈诺沙星进行治疗,口服,每次 500 mg,每天 1 次;研究组联合痰热清注射液进行治疗,每次 20 mL,加入 5%葡萄糖注射液或 0.9%氯化钠注射液 250 mL,静脉滴注,控制滴数每分钟不超过 60 滴,每天 1 次;均治疗 7d。

1.3 观察指标

① 疗效评价标准:临床症状及体征均消失,白细胞数量和体温均恢复正常,肺部炎症明显吸收,患者生活可自理即为显效;临床症状、体征、白细胞数量均得到改善,体温有所下降,肺部炎症有所吸收即为有效;未达到上述指标者即为无效;② 记录并对比两组患者的退热、咳嗽缓解、咳痰缓解、肺部阴影吸收 >50 等时间^[12];③ 于治疗前后空腹取静脉血 3 mL,离心得血清,采用免疫比浊法检测其血清 hs-CRP 水平;采用酶联免疫吸附法对其血清 IL-6、TNF- α 水平进行检测;④ 检测并对比两组患者治疗前后的总 B 淋巴细胞(TB)、总淋巴细胞(TT)、Th 细胞(CD4)及自然杀伤细胞(NK)水平^[13]。

1.4 统计学分析

采用 SPSS19.0 统计学软件进行统计学分析,临床症状改善时间、血清炎症因子和免疫功能指标等计量资料($\bar{x} \pm s$)的组间比较采用 t 检验,治疗总有效率等计数资料(%)经 χ^2 检验,以 $P<0.05$ 为差异具有统计学意义。

2 结果

2.1 两组治疗总有效率对比

经治疗后,研究组患者的治疗总有效率[90.8%(99/109)]显著高于对照组[74.3%(81/109)]($P<0.05$),详细结果见表 1。

表 1 两组治疗总有效率对比[例(%)]

Table 1 Comparison of the total effective rate between the two groups [n(%)]

Groups	n	Effective	Better	Invalid	The total effect rate
Research group	109	65(59.6)	34(31.2)	10(9.2)	99(90.8)*
Control group	109	48(44.0)	33(30.3)	28(25.7)	81(74.3)

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

2.2 两组临床症状改善时间对比

研究组患者的退热、咳嗽缓解、咳痰缓解、肺部阴影吸收 >50 等时间均短于对照组($P<0.05$),详细结果见表 2。

2.3 两组治疗前后血清 TNF- α 、hs-CRP、IL-6 水平对比

治疗前,两组患者的血清 TNF- α 、hs-CRP、IL-6 水平对比差异无统计学意义 ($P>0.05$);治疗后,两组患者的血清 TNF- α 、

表 2 两组临床症状改善时间对比($\bar{x} \pm s$, d)

Table 2 Comparison of the improvement time of clinical symptom between the two groups($\bar{x} \pm s$, d)

Groups	n	Antipyretic	Cough relief	Expectoration relief	Lung shadow absorption >50
Research group	109	$3.13 \pm 1.06^*$	$6.42 \pm 1.27^*$	$3.40 \pm 1.01^*$	$7.41 \pm 1.32^*$
Control group	109	4.09 ± 1.22	7.25 ± 1.35	4.15 ± 1.08	8.49 ± 1.39

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

hs-CRP、IL-6 水平平均比治疗前显著降低,且研究组以上指标均显著低于对照组($P<0.05$),详细结果见表 3。

表 3 两组治疗前后血清 TNF- α 、hs-CRP、IL-6 水平对比($\bar{x}\pm s$)

Table 3 Comparison of the serum TNF- α , hs-CRP and IL-6 levels before and after treatment between the two groups($\bar{x}\pm s$)

Groups	TNF- α (pg/mL)		hs-CRP(mg/L)		IL-6(pg/mL)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Research group (n=109)	130.79 $\pm$ 13.55	65.38 $\pm$ 10.11**	14.92 $\pm$ 3.25	4.13 $\pm$ 1.03**	61.81 $\pm$ 6.76	24.31 $\pm$ 2.49**
Control group (n=109)	128.81 $\pm$ 14.58	89.91 $\pm$ 12.23 [#]	15.06 $\pm$ 3.50	9.12 $\pm$ 2.31 [#]	62.29 $\pm$ 6.53	40.62 $\pm$ 3.73 [#]

Note: Compared with the control group, * $P<0.05$; compared with before treatment, [#] $P<0.05$.

2.4 两组治疗前后免疫功能指标对比

治疗前,两组患者的 TT、TB、NK、CD4 等指标对比差异无统计学意义($P>0.05$);治疗后,两组患者的上述指标水平平均比治

疗前显著升高,且研究组明显高于对照组($P<0.05$),详细结果见表 4。

表 4 两组治疗前后免疫功能指标对比($\bar{x}\pm s, \%$)

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

Groups	TT		TB		NK		CD4	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Research group(n=109)	56.92 $\pm$ 3.27	89.33 $\pm$ 4.71**	28.26 $\pm$ 3.67	39.55 $\pm$ 4.14**	15.67 $\pm$ 4.14	23.92 $\pm$ 4.76**	1.52 $\pm$ 0.28	2.36 $\pm$ 0.55**
Control group (n=109)	57.21 $\pm$ 3.55	68.53 $\pm$ 4.36 [#]	28.64 $\pm$ 3.52	33.73 $\pm$ 3.96 [#]	15.72 $\pm$ 4.03	19.86 $\pm$ 4.54 [#]	1.57 $\pm$ 0.24	1.93 $\pm$ 0.46 [#]

Note: Compared with the control group, * $P<0.05$; compared with before treatment, [#] $P<0.05$.

3 讨论

中医认为老年社区获得性肺炎的发病机制主要为风热毒邪,侵袭肺脏,化热生痰,痰热壅肺,治疗应以清肺化痰为主。中药制剂痰热清注射液主要含黄芩、熊胆粉、山羊角、金银花、连翘等药品成分^[14,15]。黄芩清热燥湿、泻火解毒;熊胆粉清热平肝;山羊角平肝镇惊;金银花清热解毒、疏散风热;连翘清热解毒、消肿散结^[16,17];诸药配伍,共奏清热、化痰、解毒之功效;现代药理研究结果也显示,痰热清注射液具有较好的抗病毒、抗炎、退热、止咳、化痰作用^[18-20]。本研究结果显示治疗后,研究组患者的治疗总有效率显著高于对照组,患者退热、咳嗽缓解、咳痰缓解、肺部阴影吸收 >50 等时间均短于对照组,表明痰热清注射液联合奈诺沙星治疗老年社区获得性肺炎的效果显著,该方法可有效改善患者的临床症状。

hs-CRP 是一种由肝脏合成的急性时相反应蛋白,其水平高低可反映机体的炎症程度^[21]。TNF- α 又名肿瘤坏死因子,是一种由单核-巨噬细胞分泌的炎症因子,可参与机体的炎症反应和免疫应答过程,还具有抑制和杀伤肿瘤细胞的作用^[22,23]。IL-6 作为参与炎症反应重要的炎症因子之一,其水平升高会使肺组织血管内皮细胞中黏附分子的表达能力增强,引发血管炎性反应的加重,同时,IL-6 可促进氧自由基的释放,进一步损害肺组织^[24-26]。本研究结果显示两组患者治疗后的上述血清炎症因子水平平均显著低于治疗前,且研究组更低,表明痰热清注射液联合奈诺沙星可有效改善老年社区获得性肺炎患者的血

清炎症因子水平。

免疫功能作为机体重要的抗感染防御机制,与感染发生、发展、恢复、预后均具有重要关系。NK 细胞是机体重要的免疫细胞,活化后的 NK 细胞可合成和分泌多种细胞因子,从而发挥调节机体免疫功能的作用^[27,28]。CD4 细胞是人体免疫系统的一种重要免疫细胞,其水平下降标志着免疫系统受到严重损害^[29]。B 淋巴细胞具有产生抗体、提呈抗原及分泌细胞内因子参与免疫调节的作用^[30]。本研究结果显示两组患者治疗后的 TB、TT、CD4、NK 等免疫功能指标水平平均比治疗前显著升高,且研究组更高,表明痰热清注射液联合奈诺沙星可有效改善老年社区获得性肺炎患者的免疫功能。分析其原因可能与痰热清注射液中黄芩的有效成分黄芩苷具有免疫抑制和免疫增强的双向调节作用有关。

综上所述,痰热清注射液联合奈诺沙星治疗老年社区获得性肺炎的效果显著优于单用予奈诺沙星治疗,其可有效改善患者的临床症状、降低血清炎症因子水平和提高免疫功能。

参考文献(References)

- [1] Diamantis P, Kofteridis MD PhD, Giannoula Giourgouli M D, Plataki M N, et al. Community-Acquired Pneumonia in Elderly Adults with Type 2 Diabetes Mellitus [J]. Journal of the American Geriatrics Society, 2016, 64(3): 649
- [2] Cataudella E, Giraffa C M, Di M S, et al. Neutrophil-To-Lymphocyte Ratio: An Emerging Marker Predicting Prognosis in Elderly Adults with Community-Acquired Pneumonia [J]. Journal of the American Geriatrics Society, 2017, 65(8): 1796-1801

- [3] Melgaard D, Baandrup U, Bøgsted M, et al. The Prevalence of Oropharyngeal Dysphagia in Danish Patients Hospitalised with Community-Acquired Pneumonia[J]. *Dysphagia*, 2016, 32(3): 1-10
- [4] Roychoudhury S, Makin K, Twinem T, et al. In Vitro Resistance Development to Nemonoxacin in *Streptococcus pneumoniae*: A Unique Profile for a Novel Nonfluorinated Quinolone[J]. *Microbial Drug Resistance*, 2016, 22(7): 578-584
- [5] Poole R M. Nemonoxacin: first global approval [J]. *Drugs*, 2014, 74(12): 1445-1453
- [6] De-Min L I, Tang S H, Qiang L, et al. Literature study on prevention and treatment of community acquired pneumonia by traditional Chinese medicine [J]. *China Journal of Chinese Materia Medica*, 2017, 42(8): 1418-1422
- [7] Zhi Y J, Liao X, Xie Y M, et al. Methodological quality assessment of community-acquired pneumonia clinical practice guidelines in China based on AGREE II tool [J]. *China Journal of Chinese Materia Medica*, 2017, 42(11): 2175-2180
- [8] Wang K, Xi W, Yang D, et al. Rhinovirus is associated with severe adult community-acquired pneumonia in China. [J]. *J Thorac Dis*, 2017, 9(11): 4502-4511
- [9] Pei W, Xing L, Xie Y M, et al. Tanreqing injection for acute bronchitis disease: A systematic review and meta-analysis of randomized controlled trials [J]. *Complementary Therapies in Medicine*, 2016, 25(4): 143-158
- [10] Li C, Liu S, Luo G, et al. Comparison of Plasma Pharmacokinetics of Tanreqing Solution between Intratracheal Aerosolization and Intravenous Injection in Rats [J]. *Biomedical Chromatography*, 2017, 25(25): 3843-3857
- [11] Mulder T, van Werkhoven C H, Huijts S M, et al. Treatment restrictions and empirical antibiotic treatment of community-acquired pneumonia in elderly patients [J]. *Netherlands Journal of Medicine*, 2016, 74(1): 56
- [12] Diao W Q, Shen N, Yu P X, et al. Efficacy of 23-valent pneumococcal polysaccharide vaccine in preventing community-acquired pneumonia among immunocompetent adults: A systematic review and meta-analysis of randomized trials [J]. *Vaccine*, 2016, 34(13): 1496-1503
- [13] Chalmers J D, Akram A R, Singanayagam A, et al. Risk factors for *Clostridium difficile* infection in hospitalized patients with community-acquired pneumonia[J]. *Journal of Infection*, 2016, 73(1): 45-53
- [14] Qu J M, Cao B. Guidelines for the diagnosis and treatment of adult community acquired pneumonia in China (2016 Edition) [J]. *Zhonghua Jie He He Hu Xi Za Zhi*, 2016, 39(4): 241-242
- [15] Zhao D, Chen H, Yang Q, et al. Value of clinical signs in the identification of *Mycoplasma pneumoniae* in community acquired pneumonia in children[J]. *Zhonghua Er Ke Za Zhi Chinese Journal of Pediatrics*, 2016, 54(2): 104
- [16] Liu D S, Han X D, Liu X D. Current Status of Community-Acquired Pneumonia in Patients with Chronic Obstructive Pulmonary Disease [J]. *Chinese Medical Journal*, 2018, 131(9): 1086-1091
- [17] Min J C, Song J Y, Ji Y N, et al. Disease burden of hospitalized community-acquired pneumonia in South Korea: Analysis based on age and underlying medical conditions [J]. *Medicine*, 2017, 96(44): e8429
- [18] Li W, Zeng L, Li J, et al. Development of indicators for assessing rational drug use to treat community-acquired pneumonia in children in hospitals and clinics: A modified Delphi study[J]. *Medicine*, 2017, 96(51): e9308
- [19] Man S C, Fufezan O, Sas V, et al. Performance of lung ultrasonography for the diagnosis of community-acquired pneumonia in hospitalized children[J]. *Medical Ultrasonography*, 2017, 19(3): 276
- [20] Mukhopadhyay A, Maliapen M, Ong V, et al. Community-Acquired Pneumonia Case Validation in an Anonymized Electronic Medical Record-Linked Expert System [J]. *Clinical Infectious Diseases An Official Publication of the Infectious Diseases Society of America*, 2017, 64(suppl_2): S141
- [21] Agnello L, Bellia C, Gangi M D, et al. Utility of serum procalcitonin and C-reactive protein in severity assessment of community-acquired pneumonia in children[J]. *Clinical Biochemistry*, 2016, 49(1): 47-50
- [22] Andrade D C, Borges I C, Adrian P V, et al. Effect of Pneumococcal Conjugate Vaccine on the Natural Antibodies and Antibody Responses Against Protein Antigens from *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Moraxella catarrhalis* in Children with Community-Acquired Pneumonia [J]. *Pediatric Infectious Disease Journal*, 2016, 35(6): 683
- [23] Ceccato A, Torres A, Cilloniz C, et al. Invasive Disease versus Urinary Antigen Confirmed Pneumococcal Community-Acquired Pneumonia[J]. *Chest*, 2017, 123(4): 977-978
- [24] Saghaian-Hedengren S, Mathew J L, Hagel E, et al. Assessment of Cytokine and Chemokine Signatures as Potential Biomarkers of Childhood Community-acquired Pneumonia Severity: A Nested Cohort Study in India [J]. *Pediatric Infectious Disease Journal*, 2017, 36(1): 102-108
- [25] Chen L, Cheng J, Wang Y L. Effects of different anaesthetics on cytokine levels in children with community-acquired pneumonia undergoing flexible fiberoptic bronchoscopy [J]. *Journal of International Medical Research*, 2016, 44(3): 462-471
- [26] Daniel P, Rodrigo C, McKeever T M, et al. Time to first antibiotic and mortality in adults hospitalised with community-acquired pneumonia: a matched-propensity analysis[J]. *Thorax*, 2016, 71(6): 568-570
- [27] Ghj W, Bjm V, van Kessel D A, et al. Pneumococcal conjugate vaccination response in patients after community-acquired pneumonia, differences in patients with *S. pneumoniae* versus other pathogens[J]. *Vaccine*, 2017, 35(37): 4886
- [28] Cilloniz C, Torres A, Niederman M, et al. Community-acquired pneumonia related to intracellular pathogens [J]. *Intensive Care Medicine*, 2016, 42(9): 1-13
- [29] Bader M S, Yi Y, Abouchehade K, et al. Community-Acquired Pneumonia in Patients With Diabetes Mellitus: Predictors of Complications and Length of Hospital Stay [J]. *American Journal of the Medical Sciences*, 2016, 352(1): 30-35
- [30] Ebrahimi F, Giaglis S, Hahn S, et al. Markers of Neutrophil Extracellular Traps Predict Adverse Outcome in Community-Acquired Pneumonia: Secondary Analysis of a Randomised Controlled Trial [J]. *European Respiratory Journal*, 2018, 51(4): 1701389