

doi: 10.13241/j.cnki.pmb.2018.18.031

盐酸氨溴索对慢性阻塞性肺疾病患者免疫功能及炎症因子的影响 *

龙 瀛¹ 胡建平² 何正光¹ 罗晓彬¹ 邱 蓉¹

(1 四川省遂宁市中心医院 / 川北医学院附属遂宁医院呼吸科 四川 遂宁 629000;

2 四川省遂宁市中心医院 / 川北医学院附属遂宁医院急诊科 四川 遂宁 629000)

摘要 目的:探讨盐酸氨溴索对慢性阻塞性肺疾病(COPD)患者免疫功能及炎症因子的影响。**方法:**将2014年6月~2016年6月遂宁市中心医院收治的88例COPD患者随机分成对照组和观察组各44例。患者均先给予常规治疗,对照组再给予福莫特罗复方干粉吸入剂吸入治疗,而观察组给予盐酸氨溴索静脉滴注进行治疗,经过14d治疗后评价患者的治疗疗效,对比两组患者治疗前后的肺功能指标、免疫功能指标及炎症因子。**结果:**观察组总有效率(90.91%)显著高于对照组(75.00%)($P<0.05$)。两组患者治疗后用力肺活量(FVC)、第一秒用力呼气量(FEV1)、最大呼气峰流速值(PEF)均升高,且观察组升高更明显,差异有统计学意义($P<0.05$);两组患者治疗后 $CD3^+$ 、 $CD4^+$ 、 $CD4^+/CD8^+$ 比值均升高,同时 $CD8^+$ 降低,但观察组优于对照组($P<0.05$)。治疗后两组血清肿瘤坏死因子- α (TNF- α)、白细胞介素-6(IL-6)水平均降低,且观察组血清TNF- α 、IL-6水平均明显低于对照组($P<0.05$)。**结论:**盐酸氨溴索可改善COPD患者的肺功能、增强免疫功能,降低炎症因子水平,进而提高治疗效果。

关键词:盐酸氨溴索;慢性阻塞性肺疾病;免疫功能;肺功能;疗效;炎症因子

中图分类号:R563 **文献标识码:**A **文章编号:**1673-6273(2018)18-3538-04

The Effect of Ambroxol Hydrochloride for Immune Function and Inflammatory Factors in Patients with Chronic Obstructive Pulmonary Disease*

LONG Ying¹, HU Jian-ping², HE Zheng-guang¹, LUO Xiao-bin¹, QIU Rong¹

(1 Department of Respiration, Suining Central Hospital of Sichuan Province/Suining Affiliated Hospital of North Sichuan Medical College, Suining, Sichuan, 629000, China; 2 Department of Emergency, Suining Central Hospital of Sichuan Province/Suining Affiliated Hospital of North Sichuan Medical College, Suining, Sichuan, 629000, China)

ABSTRACT Objective: To explore the effect of ambroxol hydrochloride for immune function and inflammatory factors in patients with COPD. **Methods:** 88 patients with COPD in Suining Central Hospital from June 2014 to June 2016 were randomly divided into control group and observation group, each group with 44 cases. On the base of conventional therapy, the control group applied to symbicort turbuhaler inhalation therapy, and the observation group received ambroxol intravenous injection therapy. The therapeutic effect was evaluated After 14 days of treatment. Compared the lung function index, immune function index and inflammatory factors of two groups before and after treatment. **Results:** The total effective rate of the observation group (90.91%) was significantly higher than that of the control group (75.00%) ($P<0.05$). After the treatment, the FVC, FEV1, PEF of two groups were increased, and the observation group increased significantly, the difference was statistically significant ($P<0.05$). Two groups of $CD3^+$, $CD4^+$, $CD4^+/CD8^+$ ratio were increased, while the $CD8^+$ were reduced, but the amplitude change of observation group was significantly higher than the control group ($P<0.05$). After treatment, the serum levels of TNF- α and IL-6 in the two groups were decreased, and the serum TNF- α and IL-6 water in the observation group were significantly lower than those of the control group ($P<0.05$). **Conclusion:** Ambroxol hydrochloride can improve lung function, enhance immune function, reduce inflammatory factors, and improve therapeutic effect in patients with COPD.

Key words: Ambroxol hydrochloride; COPD; Immune function; Pulmonary function; Efficacy; Inflammatory factors

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

Article ID: 1673-6273(2018)18-3538-04

前言

慢性阻塞性肺疾病 (Chronic Obstructive Pulmonary Disease, COPD)是呼吸科常见的慢性疾病,且发病率呈逐年上升的

趋势^[1-3]。该患者的临床表现多以咳嗽、喘息、咳痰、胸闷、气短为主,且肺功能和免疫功能降低^[4,5]。COPD好发于中老年人群,随着年龄的增加,该病的病死率也逐渐升高^[6,7]。有研究显示,COPD在全国导致死亡的疾病病因中高居第4位^[8,9]。目前,临

* 基金项目:国家科技支撑计划项目(2012BAI05B136);四川省卫生厅科研基金项目(1302095)

作者简介:龙瀛(1983-),女,本科,主治医师,从事呼吸科相关方面的研究,E-mail:kgtssg@163.com

(收稿日期:2018-04-04 接受日期:2018-04-27)

床上治疗 COPD 多以药物治疗为主,手术治疗为辅,抗感染和改善通气功能是常用的治疗手段,但患者大多有咳痰,此类治疗手段祛痰效果不明显,而盐酸氨溴索是常用的祛痰药物,在治疗 COPD 方面具有较好的疗效^[10,11],但是该药对 COPD 患者肺功能、免疫功能以及炎症因子影响的研究还尚有不足。本研究应用盐酸氨溴索治疗 COPD 患者取得不错的疗效,现进行如下报道。

1 资料与方法

1.1 一般资料

选择 2014 年 6 月~2016 年 6 月在遂宁市中心医院就诊并且采取治疗的 88 例 COPD 患者作为研究对象,纳入标准:患者均符合《慢性阻塞性肺疾病诊治指南》^[12]的诊断标准,患者以气流受限为主要特征,并伴有咳嗽、喘息、咳痰、胸闷、气短等症状体征,同时患者的肺功能及免疫功能降低。排除标准:患有其他慢性肺部疾病如肺结核、各型肝炎、慢性肾脏疾病、严重神经系统疾病、严重血液病、肿瘤等疾病的患者。其中男性有 42 例、女性有 46 例,年龄为 42-75 岁,病程 1-10 年。采用随机数字表法将纳入的 88 例患者随机分成对照组和观察组。对照组 44 例,其中男 19 例,女 25 例,年龄 43-75 岁,平均年龄为 (57.5 ± 9.5) 岁,病程 1-10 年,平均病程为 (4.4 ± 3.0) 年;合并糖尿病患者 8 例,高血压患者 10 例,冠心病患者 6 例,高血脂患者 5 例。观察组 44 例,其中男 23 例,女 21 例,年龄 42-75 岁,平均年龄为 (60.2 ± 7.3) 岁,病程 1-10 年,平均病程为 (4.5 ± 2.6) 年;合并糖尿病患者 7 例,高血压患者 11 例,冠心病患者 8 例,高血脂患者 6 例。两组临床基线资料组间均无统计学差异($P > 0.05$)。本研究经患者知情同意,获得我院伦理委员会审核批准。

1.2 治疗方法

两组患者入院后均进行相同的常规治疗,即吸氧治疗,另给予解痉平喘、祛痰、抗生素抗感染、具有扩张支气管功能的 β 受体激动剂和氨茶碱、营养支持等常规治疗。在常规治疗的基础上,对照组的 COPD 患者加用布地奈德福莫特罗粉吸入剂(厂家:瑞典阿斯利康有限公司(AstraZeneca AB,规格:30 μ g/格),国药准字 H201440458)吸入治疗,用量与用法为 1 格/次,2 次/d。观察组患者在常规治疗的基础上联合盐酸氨溴索

(厂家:天津药物研究院药业有限责任公司,规格:15 mg,国药准字 H20113062)30 mg+5%葡萄糖注射液(厂家:东北制药有限公司,国药准字 H20113174)250 mL 静脉滴注治疗,2 次/d。在治疗期间,两组患者均保持清淡饮食,大便通畅,适量运动,戒烟限酒并保持积极乐观的心态。两组患者疗程均为 2 周。

1.3 观察指标

(1)肺功能:于治疗前后应用呼吸功能监护仪检测患者第一秒用力呼气量(FEV1)、用力肺活量(FVC)、最大呼气峰流速值(PEF)变化情况。(2)免疫功能:采用流式细胞仪 TBNK 计数方法测定 COPD 患者的免疫功能,比较治疗前后两组患者的 CD3⁺、CD4⁺、CD8⁺ 及 CD4⁺/CD8⁺ 水平变化。(3)炎症因子:空腹采集患者静脉血 6 mL,以 2200 r/min 的转速,15 cm 的离心半径离心 8 min 以分离血清待检。检测患者治疗前后血清肿瘤坏死因子- α (TNF- α)、白细胞介素-6(IL-6)水平,采用双抗夹心酶联免疫(ELISA)法,试剂盒由北京普恩光德生物科技开发有限公司提供。

1.4 疗效评价

参考文献^[12]对将疗效分为 3 等级:其中治疗后患者的肺功能得到有效改善,痰培养结果转阴,相关症状及体征消失或有明显的好转,且治疗过程未复发,定义为显效;治疗后肺功能有一定程度的改善,痰培养转阴性,相关症状、体征好转,但未完全消失为有效;治疗后患者肺功能改善不明显,痰培养阳性,相关症状和体征无明显好转甚至加重为无效。总有效率 = 显效率 + 有效率。

1.5 统计学方法

本文数据应用 SPSS20.0 进行分析,肺功能、免疫功能、炎症因子等计量资料以 $(\bar{x} \pm s)$ 表示,采用 t 检验;治疗有效率等计数资料以率(%)表示,行 χ^2 检验, $P < 0.05$ 定义为有统计学差异。

2 结果

2.1 疗效

观察组总有效率为 90.91% (40/44), 对照组为 75.00% (33/44),两组之间差异具有统计学意义($\chi^2=3.938, P=0.047$)。见表 1。

表 1 两组临床疗效比较[n(%)]

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

Groups	n	Excellent	Effectivity	Invalid	Total effectivity
Observation group	44	26 (59.09)	14 (31.82)	4 (9.09)	40 (90.91)
Control group	44	24 (54.55)	9 (20.45)	11 (25.00)	33 (75.00)

2.2 肺功能

治疗后,两组患者的 FVC、FEV1、PEF 水平均升高,且观察

组以上各指标均高于对照组($P < 0.05$),见表 2。

表 2 治疗前后两组患者肺功能指标的变化情况 $(\bar{x} \pm s)$

Table 2 Changes of lung function index in two groups of patients before and after treatment $(\bar{x} \pm s)$

Groups	Time	FEV1(L)	FVC(L)	PEF(L/s)
Control group (n=44)	Before treatment	1.53 $\pm$ 0.23	1.65 $\pm$ 0.20	3.21 $\pm$ 0.22
	After treatment	2.01 $\pm$ 0.26 ^a	2.27 $\pm$ 0.32 ^a	3.94 $\pm$ 0.32 ^a
Observation group (n=44)	Before treatment	1.56 $\pm$ 0.21	1.67 $\pm$ 0.18	3.22 $\pm$ 0.24
	After treatment	2.87 $\pm$ 0.34 ^{ab}	2.95 $\pm$ 0.36 ^{ab}	4.38 $\pm$ 0.36 ^{ab}

Note: Compare with before treatment, ^a $P < 0.05$, Compare with the control group after treatment, ^b $P < 0.05$.

2.3 免疫功能

经过治疗,两组 CD3⁺、CD4⁺、CD4⁺/CD8⁺ 均上升,而 CD8⁺

降低,且观察组 CD3⁺、CD4⁺、CD4⁺/CD8⁺ 高于对照组,CD8⁺ 低于对照组(P<0.05),见表 3。

表 3 治疗前后两组患者免疫功能指标变化情况($\bar{x} \pm s$)

Table 3 Changes of immune function indexes in two groups of patients before and after treatment($\bar{x} \pm s$)

Groups	Time	CD3 ⁺ (%)	CD4 ⁺ (%)	CD8 ⁺ (%)	CD4 ⁺ /CD8 ⁺
Control group(n=44)	Before treatment	68.41± 9.32	41.34± 5.14	37.14± 3.95	1.12± 0.04
	After treatment	73.71± 8.33 ^a	44.91± 6.35 ^a	32.46± 4.37 ^a	1.42± 0.02 ^a
Observation group (n=44)	Before treatment	68.74± 9.65	41.17± 5.35	37.35± 3.72	1.12± 0.01
	After treatment	84.27± 8.74 ^{ab}	54.45± 6.57 ^{ab}	24.77± 4.67 ^{ab}	2.24± 0.02 ^{ab}

Note: Compare with before treatment, ^aP<0.05, Compare with the control group after treatment, ^bP<0.05.

2.4 炎症因子

经过治疗,两组血清 TNF-α、IL-6 水平均降低,且观察组的

炎症指标水平均明显低于对照组(P<0.05)。见表 4。

表 4 两组治疗前后 TNF-α、IL-6 水平比较($\bar{x} \pm s$)

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

Groups	Time	TNF-α (ng/L)	IL-6 (umol/L)
Control group(n=44)	Before treatment	253.25± 28.12	41.52± 3.25
	After treatment	231.58± 18.25 ^a	35.68± 2.59 ^a
Observation group(n=44)	Before treatment	260.42± 28.98	40.95± 3.49
	After treatment	198.24± 15.89 ^{ab}	28.74± 2.67 ^{ab}

Note: Compare with before treatment, ^aP<0.05, Compare with the control group after treatment, ^bP<0.05.

3 讨论

COPD 是临床上常见的呼吸系统疾病之一,尤其在 40 岁以上的中老年人群中具有较高的发病率,全球 40 岁以上人群 COPD 的发病率达到 9%^[13-15],但该病目前越来越趋向于年轻化,且 COPD 的发病率仍呈增长趋势,给社会、家庭造成极大压力和负担,同时 COPD 患者的病死率也较高^[16,17]。另外,COPD 患者由于气道阻塞导致呼吸急促、通气不畅,并且痰液不易咳出,加重了气道阻塞和感染,造成肺气体交换功能削弱,使患者的肺功能下降^[18,19]。除此以外,COPD 患者长期处于炎症抵制,加上患者处于中老年阶段,体质明显下降,长期以往很容易出现机体细胞免疫功能降低,主要表现为免疫功能的 T 淋巴细胞中的 CD8⁺ 增加,CD4⁺ 以及 CD3⁺ 均减少^[20-22]。目前临床上治疗 COPD 时主要通过保守治疗,即以药物治疗为主,手术治疗为辅,来缓解 COPD 患者的的相关症状和体征和改善肺功能及免疫功能^[23-25]。

注射用盐酸氨溴索为新型黏液溶解剂,并且是一种祛咳止痰类内科药物,其能够显著促进肺泡表面活性物质分泌,并促进纤毛运动以及呼吸液的分泌,增加呼吸道黏膜浆液腺的分泌,减少黏液腺分泌,缓解气道阻塞,进而改善 COPD 患者的肺功能^[26]。同时盐酸氨溴索还具有一定的细胞免疫调节作用,在 T 淋巴细胞分化、成熟过程中起着重要的作用^[27,28]。在本次研究中,治疗后,两组患者的肺功能指标 FVC、FEV1、PEF 均呈上升趋势,且观察组显著高于对照组(P<0.05);治疗后,两组患者的细胞免疫功能指标,即 T 细胞中的 CD8⁺ 数降低,而 CD4⁺、CD3⁺ 及 CD4⁺/CD8⁺ 比值均升高,且观察组的变化幅度显著高于对照组(P<0.05)。推测可能是因为盐酸氨溴索具有前述的促

进痰液排出、缓解气道阻塞等特性,能够有效地改善 COPD 患者的肺功能、免疫功能。经过 2 周治疗后,观察组总有效率为 90.91%(40/44),对照组为 75.00%(33/44),提示氨溴索具有增加痰液中抗菌药物浓度的作用,其可协同抗菌药物提高抗感染的功效,从而进一步改善及提升 COPD 患者的肺功能及免疫功能,提高临床治疗效果,优化 COPD 患者的临床预后,最终提升其生活质量。经治疗,两组患者的炎症指标均降低,且观察组下降更明显,提示氨溴索能够明显降低 COPD 患者的血清炎症因子水平。COPD 受到病原菌、环境污染物等因素影响,释放大量子道炎性细胞和介质,从而加重气道炎症反应,引起支气管痉挛、水肿、黏液分泌物增多等,另外肺部炎症的溢出还能够引起全身性炎症反应^[29]。氨溴索可能通过抑制炎症细胞因子的产生,减轻肺部炎症反应,降低血清炎症因子水平^[30]。

综上所述,在常规治疗 COPD 的基础上,加用盐酸氨溴索静脉注射,临床治疗效果显著,并且能够有效改善及提高 COPD 患者的肺功能及免疫功能,增强对疾病的免疫力,降低炎症反应。

参考文献(References)

- [1] 罗丽.氨溴索治疗慢性阻塞性肺疾病的临床疗效及其对肺功能的影响[J].临床合理用药杂志,2016,9(18): 21-22
Luo Li. Clinical effect of ambroxol in treating chronic obstructive pulmonary disease and the impact for pulmonary function[J]. Chinese journal of clinical rational drug use, 2016, 9(18): 21-22
- [2] Wang Y, Su NX, Chen ZQ, et al. Inhibitor of metalloproteinase-1 in lung tissue of rats with chronic obstructive pulmonary disease [J]. Chin J Integr Med, 2014, 20(3): 224-231
- [3] 门翔,尚喜雨.COPD 患者 Th17 细胞和 Treg 细胞介导的免疫应答变化及免疫失衡与肺功能的关系研究[J].中国免疫学杂志,2016, 32

- (12): 1826-1829
- Men xiang, Shang Xi-yu. Relationship of immune response and immune imbalance mediated by Th17 cells and Treg cells with pulmonary function in COPD patients[J]. Chinese Journal of Immunology, 2016, 32(12): 1826-1829
- [4] Qiang G, Yu Q, Liang C, et al. Impact of Chronic Obstructive Pulmonary Disease on Risk of Recurrence in Patients with Resected Non-small Cell Lung Cancer [J]. Zhongguo Fei Ai Za Zhi, 2018, 21(3): 215-220
- [5] Gentry S, Gentry B. Chronic Obstructive Pulmonary Disease: Diagnosis and Management [J]. American family physician, 2017, 95(7): 433-441
- [6] Agarwal A, Batra S, Prasad R, et al. A study on the prevalence of depression and the severity of depression in patients of chronic obstructive pulmonary disease in a semi-urban Indian population[J]. Monaldi Arch Chest Dis, 2018, 88(1): 902
- [7] 丁飞,李奎,胡学进,等.盐酸氨溴索治疗 COPD 患者的疗效及其对肺功能和血气分析指标的影响 [J]. 现代医药卫生, 2016, 32(15): 2384-2386
- Ding Fei, Li Kui, Hu Xue-jing, et al. The effect of ambroxol hydrochloride for pulmonary function and blood gas analysis index and the efficacy in patients with COPD [J]. Journal of Modern Medicine, 2016, 32(15): 2384-2386
- [8] Jaswal S, Saini V, Kaur J, et al. Association of Adiponectin with Lung Function Impairment and Disease Severity in Chronic Obstructive Pulmonary Disease[J]. Int J Appl Basic Med Res, 2018, 8(1): 14-18
- [9] 乔中会,李俊萍.慢性阻塞性肺疾病急性加重期患者死亡原因探讨 [J].临床肺科杂志, 2012, 17(7): 1309-1310
- Qiao Zhong-hui, Li Jun-ping. The cause of death in patients with acute exacerbation of chronic obstructive pulmonary disease [J]. Journal of Clinical Pulmonary Medicine, 2012, 17(7): 1309-1310
- [10] Jaswal S, Saini V, Kaur J, et al. Association of Adiponectin with Lung Function Impairment and Disease Severity in Chronic Obstructive Pulmonary Disease [J]. Int J Appl Basic Med Res, 2018, 8(1): 14-18
- [11] 钟武源. 盐酸氨溴索雾化吸入疗法治疗老年慢性支气管炎临床疗效研究[J].北方药学, 2016, 13(12): 75
- Zhong Wu-yuan. Clinical efficacy of ambroxol hydrochloride atomization inhalation in the treatment of chronic bronchitis in the elderly [J]. Journal of North Pharmacy, 2016, 13(12): 75
- [12] 中华医学会呼吸病学分会慢性阻塞性肺疾病学组. 慢性阻塞性肺疾病诊治指南 (2013 年修订版)[J]. 中国医学前沿杂志, 电子版, 2014, 36(2): 67-79
- Chinese Medical Association of Chronic obstructive pulmonary disease group of Respiratory Diseases Branch. Guidelines for the diagnosis and treatment of chronic obstructive pulmonary disease[J]. Chinese Journal of Tuberculosis and Respiratory Diseases, 2014, 36(2): 67-79
- [13] Yeh JJ, Wei YF, Lin CL, et al. Effect of the asthma-chronic obstructive pulmonary disease syndrome on the stroke, Parkinson's disease, and dementia: a national cohort study [J]. Oncotarget, 2017, 9(15): 12418-12431
- [14] 杨萍,洪旭初.盐酸氨溴索治疗慢性阻塞性肺疾病的临床疗效及对患者肺功能与免疫功能的影响[J].临床合理用药杂志, 2016, 9(30): 23-24, 30
- Yang Ping, Hong Xu-chu. The clinical efficacy of ambroxol hydrochloride in the treatment of chronic obstructive pulmonary disease and effect on pulmonary function and immune function of patients[J]. Chinese Journal of Clinical Rational Drug Use, 2016, 9(30): 23-24, 30
- [15] 丁婷婷,陈军,李仙龙,等.盐酸氨溴索辅助治疗对慢性阻塞性肺病患者血清 BNP、TNF- α 及脂联素水平的影响 [J]. 现代生物医学进展, 2017, 17(05): 901-904
- Ding Ting-ting, Chen Jun, Li Xian-long, et al. Effects of Ambroxol Hydrochloride Adjuvant Therapy on the Levels of Serum BNP, TNF- α and Adiponectin in Patients with Chronic Obstructive Pulmonary Disease [J]. Progress in Modern Biomedicine, 2017, 17(05): 901-904
- [16] Li W, Mao B, Wang G, et al. A study of the mechanism of Qingre Huatan therapy in treatment of acute exacerbation of chronic obstructive pulmonary disease by improving airway inflammation and mucus hypersecretion [J]. Journal of Chinese integrative medicine, 2008, 6(8): 799-805
- [17] 薛志丽,赵晔,苏芳,等.无创正压通气治疗慢性阻塞性肺疾病合并 II 型呼吸衰竭的临床效果 [J]. 现代生物医学进展, 2016, 16(25): 4929-4931, 4940
- Xue Zhi-li, Zhao Ye, Su Fang, et al. Clinical Effect of Noninvasive Positive Pressure Ventilation on Treatment of Chronic Obstructive Pulmonary Disease with Type II Respiratory Failure [J]. Progress in Modern Biomedicine, 2016, 16(25): 4929-4931, 4940
- [18] 薛菲. 盐酸氨溴索辅助治疗慢性阻塞性肺疾病对肺功能及免疫功能的改善作用[J].中国药业, 2016, 25(24): 53-56
- Xue Fei. Improvement Effect of Ambroxol Hydrochloride on Pulmonary Function and Immune Function in Patients with Chronic Obstructive Pulmonary Disease[J]. China Pharmaceuticals, 2016, 25(24): 53-56
- [19] Sato M, Inoue S, Igarashi A, et al. Heart-type fatty acid binding protein as a prognostic factor in patients with exacerbated chronic obstructive pulmonary disease[J]. Respir Investig, 2018, 56(2): 128-135
- [20] 唐焕新,魏娜,薛继红.COPD 急性加重易感人群免疫功能及高危因素研究[J].河北医学, 2016, 22(3): 378-380
- Tang Huan-xin, Wei Na, Xue Ji-hong. Study on Immune Function and Risk Factors in Acute Exacerbation of COPD in Susceptible[J]. Hebei Medicine, 2016, 22(3): 378-380
- [21] Li J, Yi W, Jiang P, et al. Effects of ambroxol hydrochloride on concentrations of paclitaxel and carboplatin in lung cancer patients at different administration times [J]. Cellular and molecular biology (Noisy-le-Grand, France), 2016, 62(13): 85-89
- [22] Newsome BR, McDonnell K, Hucks J, et al. Chronic Obstructive Pulmonary Disease: Clinical Implications for Patients With Lung Cancer [J]. Clin J Oncol Nurs, 2018, 22(2): 184-192
- [23] 龙仁贵. 盐酸氨溴索治疗慢性阻塞性肺疾病疗效及对患者肺功能与免疫功能的影响[J].海南医学院学报, 2014, 5(09): 1193-1195, 1198
- Long Ren-gui. Effect of ambroxol hydrochloride on pulmonary function and immune function of patients with chronic obstructive pulmonary disease [J]. Journal of Hainan Medical University, 2014, 5(09): 1193-1195, 1198

- sus magnetic resonance imaging for the prenatal diagnosis of placenta accreta[J]. *J Matern Fetal Neonatal Med*, 2016, 29(2): 218-223
- [22] 张石. 产前检测外周血 AFP CK 水平联合彩超检查对胎盘植入的诊断价值[J]. *浙江临床医学*, 2017, 19(9): 1680-1682
- Zhang Shi. Prenatal detection of peripheral blood AFP CK level combined with color Doppler ultrasound in diagnosis of placenta accreta [J]. *Zhejiang Clinical Medical Journal*, 2017, 19(9): 1680-1682
- [23] Balcacer P, Pahade J, Spektor M, et al. Magnetic Resonance Imaging and Sonography in the Diagnosis of Placental Invasion [J]. *J Ultrasound Med*, 2016, 35(7): 1445-1456
- [24] Kumar I, Verma A, Ojha R, et al. Invasive placental disorders: a prospective US and MRI comparative analysis[J]. *Acta Radiol*, 2017, 58(1): 121-128
- [25] Rochkind S, Shainberg A. Muscle Response to Complete Peripheral Nerve Injury: Changes of Acetylcholine Receptor and Creatine Kinase Activity over Time [J]. *J Reconstr Microsurg*, 2017, 33 (5): 352-357
- [26] Mar WA, Berggruen S, Atueyi U, et al. Ultrasound imaging of placenta accreta with MR correlation[J]. *Ultrasound Q*, 2015, 31(1): 23-33
- [27] 汪波,林保冠,石挺慧,等.急性重度敌敌畏中毒患者血清儿茶酚胺水平与其心脏损伤的关系 [J]. *现代生物医学进展*, 2014, 14(31): 6139-6141, 6196
- Wang Bo, Lin Bao-guan, Shi Ting-hui, et al. Relationship between the Heart Injury and Catecholamine Level of Patients with Severe Acute Dichlorvos Poisoning [J]. *Progress in Modern Biomedicine*, 2014, 14 (31): 6139-6141, 6196
- [28] Liu J, Song G, Lin X, et al. Upregulated unique long 16 binding protein 1 detected in preeclamptic placenta affects human extravillous trophoblast cell line (HTR-8/SVneo) invasion by modulating the function of uterine natural killer cells[J]. *Exp Ther Med*, 2017, 13(4): 1447-1455
- [29] Sato T, Mori N, Hasegawa O, et al. Placental recess accompanied by a T2 dark band: a new finding for diagnosing placental invasion[J]. *Abdom Radiol (NY)*, 2017, 42(8): 2146-2153
- [30] Uyanikoglu H, Turp AB, Hilali NG, et al. Serum endothelin-1 and placental alkaline phosphatase levels in placenta percreta and normal pregnancies[J]. *J Matern Fetal Neonatal Med*, 2018, 31(6): 777-782
-
- (上接第 3541 页)
- [24] Van Buul AR, Kasteleyn MJ, Chavannes NH, et al. Physical activity in the morning and afternoon is lower in patients with chronic obstructive pulmonary disease with morning symptoms [J]. *Respir Res*, 2018, 19(1): 49
- [25] Rosrita NN, Yunus F, Ginting TT, et al. Depression in patients with stable chronic obstructive pulmonary disease: a cross-sectional study in the national center for respiratory diseases in Indonesia [J]. *Pneumologia*, 2016, 65(4): 197-200
- [26] Jimborean G, Iano?i ES, Postolache P, et al. The role of quantitative computed tomography in the diagnosis of chronic obstructive pulmonary disease[J]. *Pneumologia*, 2016, 65(4): 184-188
- [27] Amin AN, Bollu V, Stensland MD, et al. Treatment patterns for patients hospitalized with chronic obstructive pulmonary disease[J]. *Am J Health Syst Pharm*, 2018, 75(6): 359-366
- [28] Zhong XM, Li L, Wang HZ, et al. Associations of Polymorphism of rs9944155, rs1051052, and rs1243166 Locus Allele in Alpha-1-antitrypsin with Chronic Obstructive Pulmonary Disease in Uygur Population of Kashgar Region[J]. *Chin Med J (Engl)*, 2018, 131(6): 684-688
- [29] Ingadottir AR, Beck AM, Baldwin C, et al. Association of energy and protein intakes with length of stay, readmission and mortality in hospitalised patients with chronic obstructive pulmonary disease [J]. *Br J Nutr*, 2018, 119(5): 543-551
- [30] Firoozabadi MD, Sheikhi MA, Rahmani H, et al. Risks of on-pump coronary artery bypass grafting surgery in patients with chronic obstructive pulmonary disease due to sulfur mustard[J]. *Postepy Dermatol Alergol*, 2017, 34(5): 429-432