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百令胶囊联合信必可对中重度稳定期慢性阻塞性肺疾病患者肺功能及免疫功能的影响

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摘要 目的：探讨百令胶囊联合信必可对中重度稳定期慢性阻塞性肺疾病（COPD）患者肺功能及免疫功能的影响，为临床用药提供依据。**方法**：选取我院于2015年8月至2017年1月收治的104例COPD患者作为研究对象。采用随机数字表法将其分为单药组与联合组各52例。单药组患者单独给予信必可治疗及常规健康教育，联合组患者在单药组的基础上联用百令胶囊治疗。治疗前及治疗12周后对所有患者的用力肺活量（FVC）、第1秒用力呼气容积（FEV1）及两者之比（FEV1/FVC）进行测定，同时测定患者$CD3^+$，$CD4^+$T细胞，并计算$CD4^+/CD8^+$比值。观察并比较两组患者的临床疗效。**结果**：治疗12周后，两组患者FVC、FEV1、FEV1/FVC均明显升高（均P<0.05），且与单药组比较，联合组患者FVC、FEV1、FEV1/FVC均明显更高（均P<0.05）。治疗12周后，两组患者$CD3^+$、$CD4^+$及$CD4^+/CD8^+$均明显升高（均P<0.05），且与单药组比较，联合组患者$CD3^+CD4^+$及$CD4^+/CD8^+$均明显更高（均P<0.05）。联合组总有效率为86.54%，明显高于单药组的67.31%（P<0.05）。**结论**：百令胶囊联合信必可治疗中重度稳定期COPD患者疗效确切，能有效改善患者肺功能并提高免疫功能，值得在临床上推广。

关键词：百令胶囊；信必可；稳定期；慢性阻塞性肺疾病；肺功能；免疫功能

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Moderate to Severe Chronic Obstructive Pulmonary Disease: Effect of Bailing Capsule Combined with Symbicort on Lung Function and Immunologic Function of Patients

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ABSTRACT Objective: To investigate the effect of bailing capsule combined with symbicort on lung function and immunologic function of moderate to severe chronic obstructive pulmonary disease (COPD) patients, in order to provide the basis for clinical use of the drug. **Methods:** A total of 104 COPD patients, who were treated in Baoji Traditional Chinese Medicine Hospital of Shaanxi Province from August 2015 to January 2017, were selected and randomly divided into single drug group(n=52) and combination group(n=52). The single drug group was given single symbicort and routine health education, on the basis of which, the combination group was given bailing capsule. Forced vital capacity (FVC), forced expiratory volume in the first second (FEV1) and the ratio of them (FEV1/FVC) of all the patients before treatment and after 12 weeks of treatment were detected, and the $CD3^+$, $CD4^+$T cells and $CD4^+/CD8^+$ ratio were measured.The efficacy of patients in the two groups were observed and compared. **Results:** After 12 weeks of treatment, FVC, FEV1 and FEV1/FVC of the two groups were significantly increased, and compared with single drug group, the FVC, FEV1 and FEV1/FVC of the combination group were significantly higher (all P<0.05). After 12 weeks of treatment, $CD3^+$, $CD4^+$ and $CD4^+/CD8^+$ of the two groups were significantly increased, and compared with single drug group, the $CD3^+$, $CD4^+$ and $CD4^+/CD8^+$ of the combination group were significantly higher (all P<0.05). The total effective rate(86.54%) of the combination group was significantly higher than that(67.31%) of the single drug group (P<0.05). **Conclusion:** Bailing capsule combined with symbicort has a significant effect on moderate to severe COPD patients. It can effectively improve the patients' lung function and immune function, which is worth popularizing in clinic.

Key words: Bailing capsule; Symbicort; Stable; Chronic obstructive pulmonary disease; Lung function; Immunologic function

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前言

慢性阻塞性肺疾病（Chronic obstructive pulmonary disease，COPD）以慢性气短、胸闷、呼吸困难、咳嗽、咳痰为主要症状，是一种严重影响患者生活质量的呼吸系统重大疾病[1-3]。COPD病程长，致死、致残率高，即使是处于稳定期的COPD患者肺功能仍呈进行性下降，并伴有咳嗽、咳痰等症状[4,5]。研究表明[6-8]，在

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COPD 稳定期积极采取措施缓解患者症状、阻止肺功能下降，对提高患者的生活质量和改善预后具有重要意义。信必可作为一种布地奈德和福莫特罗的复方制剂，对 COPD 患者的肺功能、活动耐力等有明显的改善效果[9]。中医认为 COPD 属于肺张、喘病的范畴，发展至后期为 " 肺心同病 "[10]。百令胶囊主要成分为冬虫夏草，具有抗氧化、增强免疫功能、改善肺功能等多种作用，具有补肺肾益精气之功效，研究表明[11,12]，其对 COPD 稳定期患者具有较好的治疗效果。本研究在 COPD 的治疗中联用百令胶囊与信必可，观察其对患者肺功能和免疫功能的影响，旨在为 COPD 稳定期的临床用药提供依据。

1 资料与方法

1.1 一般资料

选取我院于 2015 年 8 月至 2017 年 1 月期间收治的 104 例 COPD 患者作为研究对象，纳入标准：① 患者均经肺功能、胸片、查体等检查确诊为 COPD，并符合中医肺肾气虚证的相关诊断标准[13]；② 患者均处于稳定期：患者咳嗽、咳痰等症状轻微，且持续时间≥ 2 周；③ COPD 分级为 II~III 级[14]；④ 年龄≥ 45 岁。排除标准：① 有肺切除史者；② 合并肾衰竭、心功能障碍者；③ 合并支气管哮喘、胸腔积液等肺部疾病者；④ 合并免疫缺陷者；⑤ 处于 COPD 急性期的患者；⑥ 同期服用其他影响疗效判断的药物的患者。所有患者知情同意后，采用随机数字表法将其分为单药组与联合组各 52 例。单药组患者男 29 例，女 23 例，年龄 46~69 岁，平均（57.92± 6.31）岁，病程 2~10 年，平均（4.27± 1.63）年，COPD 分级 II 级 36 例，III 级 16 例；联合组患者男 31 例，女 21 例，年龄 45~69 岁，平均（58.13± 6.54）岁，病程 2~11 年，平均（4.39± 1.72）年，COPD 分级 II 级 34 例，III 级 18 例。两组患者一般资料无显著性差异（P>0.05），可以比较。

1.2 方法

给予单药组患者单独信必可治疗及常规健康教育：给予患者信必可（布地奈德福莫特罗粉吸入剂，AstraZeneca AB，批文准号：H20140458，每吸含 160 μg 布地奈德 +4.5 μg 福莫特罗）吸入治疗，2 次 /d，1 吸 / 次，持续 12 周。同时告知患者戒烟酒，远离污染的环境等，并给予患者心理指导，使患者能正确对待疾病，积极治疗，提高依从度。联合组在单药组的基础上给予患者百令胶囊（杭州中美华东制药有限公司，国药准字 Z10910036，规格：0.2 g/ 粒）口服，2 次 /d，5 粒 / 次，持续 12 周。

1.3 观察指标

于治疗前及治疗 12 周后采用德国 MasterScreen Pneumo 肺功能仪对所有患者的用力肺活量（FVC）、第 1 秒用力呼气容积（FEV1）及两者之比（FEV1/FVC）进行测定。治疗前及治疗 12 周后，于清晨采集两组患者空腹静脉血 3 mL，采用荧光标记法通过流式细胞仪（购自美国贝克曼库尔特有限公司）对患者 $CD3^+$，$CD4^+$T 细胞进行测定，并计算 $CD4^+/CD8^+$ 比值，观察并比较两患者的疗效。

1.4 疗效评价标准[15]

疗效评价分为临床控制、显效、有效、无效四个等级：① 临床控制：患者经过治疗后临床症状消失，肺功能恢复正常；② 显效：患者临床症状有明显改善，FEV1 增加 25%~35%；③ 有效：患者临床症状得到一定程度的改善，FEV1 增加在 15%~24%之间；④ 无效：患者症状、肺功能改善不明显或加重。总有效率 =（临床控制例数 + 显效例数 + 有效例数）/ 总例数 *100%。

1.5 统计学方法

研究数据均采用 SPSS16.0 软件进行处理，性别比例、总有效率等计数资料以 n(%) 表示，采用 x^2 检验，肺功能、免疫功能指标等计量资料以（$\bar{x}\pm s$）的形式表示，采用 t 检验。检验标准：α=0.05。

2 结果

2.1 两组患者肺功能指标比较

两组患者治疗前肺功能指标之间差异无统计学意义（P>0.05）。治疗 12 周后，两组患者 FVC、FEV1、FEV1/FVC 均明显升高（均 P<0.05），且与单药组比较，联合组患者 FVC、FEV1、FEV1/FVC 均明显更高（均 P<0.05）。见表 1。

表 1 两组患者治疗前及治疗 12 周后 FVC、FEV1、FEV1/FVC 比较（$\bar{x}\pm s$）

Table 1 Comparison of FVC, FEV1 and FEV1/FVC between two groups before treatment and after 12 weeks of treatment（$\bar{x}\pm s$）

Groups	Time	FVC (L)	FEV1 (L)	FEV1/FVC (%)
Single drug group（n=52）	Before treatment	2.19± 0.36	1.37± 0.32	59.32± 8.67
	After 12 weeks of treatment	2.75± 0.45	1.91± 0.39	68.37± 9.78
t		7.007	7.719	4.993
P		0.000	0.000	0.000
Combination group（n=52）	Before treatment	2.23± 0.41	1.41± 0.37	60.02± 8.45
	After 12 weeks of treatment	2.97± 0.43*	2.13± 0.48*	72.78± 10.12*
t		8.981	8.567	6.979
P		0.000	0.000	0.000

Note: Compared with single drug group, *P<0.05.

2.2 两组患者免疫功能指标比较

两组患者治疗前免疫功能指标之间差异无统计学意义（P>0.05）。治疗 12 周后，两组患者 $CD3^+$、$CD4^+$ 及 $CD4^+/CD8^+$ 均明显升高（均 P<0.05），且与单药组比较，联合组患者 $CD3^+$、$CD4^+$ 及 $CD4^+/CD8^+$ 均明显更高（均 P<0.05）。见表 2。

表 2 两组患者治疗前及治疗 12 周后 $CD3^+$、$CD4^+$ 及 $CD4^+/CD8^+$ 比较($\bar{x}\pm s$)

Table 2 Comparison of $CD3^+$, $CD4^+$ and $CD4^+/CD8^+$ between two groups before treatment and after12 weeks of treatment ($\bar{x}\pm s$)

Groups	Time	$CD3^+$(%)	$CD4^+$(%)	$CD4^+/CD8^+$
Single drug group(n=52)	Before treatment	57.36± 6.82	32.95± 5.28	0.94± 0.21
	After 12 weeks of treatment	70.43± 7.60	41.45± 6.14	1.33± 0.29
t		9.230	7.569	7.855
P		0.000	0.000	0.000
Combination group(n=52)	Before treatment	58.17± 7.27	32.69± 5.62	0.95± 0.24
	After 12 weeks of treatment	74.35± 8.31*	45.92± 6.86*	1.46± 0.32*
t		10.567	10.758	9.194
P		0.000	0.000	0.000

Note: Compared with single drug group, *P<0.05.

2.3 两组患者临床疗效比较

单药组患者总有效人数为 35 人,总有效率为 67.31%。联合组总有效人数为 45 人,总有效率为 86.54%,联合组总有效率明显高于单药组(P<0.05)。表 3。

表 3 两组患者临床疗效比较[n(%)]

Table 3 Comparison of clinical efficacy between the two groups [n (%)]

Groups	Cases	Clinical control	Effective	Valid	Invalid	Total effective rate
Single drug group	52	8(15.38)	14(26.92)	13(25.00)	17(32.69)	35(67.31)
Combination group	52	11(21.15)	18(34.62)	16(30.77)	7(13.46)	45(86.54)
x^2	-	-				5.417
P	-	-				0.020

3 讨论

临床上将 COPD 分为急性加重期和稳定期。处于急性加重期的 COPD 患者短期内病情反复发作,且症状逐步加重;处于稳定期时,COPD 患者肺功能仍然呈进行性恶化,且活动后呼吸困难,严重影响患者日常生活[16,17]。COPD 患者往往仅在疾病加重期进行治疗,而处于稳定期时,对症状有所忽视,从而错过治疗时机。随着临床研究的深入,COPD 稳定期的治疗显得十分必要,研究认为[18],采取积极有效的方式对稳定期 COPD 患者进行治疗,可控制 COPD 进行性发展,延缓肺功能下降,防止该病发展至急性加重期。

本研究将 104 例中重度稳定期 COPD 患者纳入研究,治疗 12 周后,两组患者 FVC、FEV1、FEV1/FVC 均明显升高,且与单药组比较,联合组患者 FVC、FEV1、FEV1/FVC 均明显更高。提示百令胶囊联合信必可对患者肺功能有更为明显的改善效果。福莫特罗和布地奈德是信必可的两种成分,其中福莫特罗对 β2- 受体有选择性激动作用,是一种长效的选择性β2- 受体激动剂,同时可通过活化蛋白激酶,将糖皮质激素受体从无活性的状态激活,从而有舒张患者支气管平滑肌、提升糖皮质激素抗炎能力的作用;而布地奈德作为一种糖皮质激素,能提高平滑肌细胞、内皮细胞、溶酶体膜的稳定性,起到减弱支气管的收缩作用,并对局部炎症效应有明显的拮抗作用[20-23]。冬虫夏草是百令胶囊的主要成分,其可润精气、降虚火,有助肾阳,可补肺益肾[24]。临床研究表明[25,26],百令胶囊能有效舒张患者支气管平滑肌,在止咳化痰方面有明显的效果。百令胶囊与信必可协同作用,对 COPD 患者肺功能的改善效果优于信必可单药的改善效果。

本研究同时观察了两组患者治疗前后免疫指标的变化情况。$CD3^+$T 细胞是成熟的 T 淋巴细胞,$CD3^+$ 降低时,患者免疫功能减弱;$CD4^+$T 细胞是免疫应答的主要细胞,又被称为辅助性 T 淋巴细胞;$CD4^+/CD8^+$ 比值变化提示了人体内免疫平衡的改变[27]。研究结果显示,治疗 12 周后,两组患者 $CD3^+$、$CD4^+$ 及 $CD4^+/CD8^+$ 均明显升高,且与单药组比较,联合组患者 $CD3^+$、$CD4^+$ 及 $CD4^+CD8^+$ 均明显更高。提示两组患者免疫功能均得到改善,而联合组患者免疫功能改善更为明显。相关药理学研究表明[28],百令胶囊对机体 T 细胞有保护作用,在其作用下 T 淋巴细胞受到刺激后的转换率得到明显提高,同时高单核 - 巨噬细胞系统的吞噬功能也得到加强,从而使机体免疫力得到提高。而目前尚没有研究报道信必可单药提高患者免疫功能的作用机制,推测其成分中福莫特罗与布地奈德共同作用有明显的抗炎作用,能提高糖皮质激素的抗炎活性,阻止炎症细胞的粘附、集聚,在减轻 COPD 患者炎症反应的同时,患者免疫功能也得到恢复。信必可与百令胶囊联用时能从不同机制提高 COPD 患者的免疫能力,较信必可单药效果更好。而比较两组患者临床疗效也发现联合组总有效率为 86.54%,明显高于单药组的 67.31%,提示联合组的临床疗效优于单药组。

综上所述,百令胶囊联合信必可治疗中重度稳定期 COPD 患者疗效确切,能有效改善患者肺功能并提高免疫功能,值得在临床上推广。

参考文献(References)

[1] Rennard SI. The Promise of Observational Studies (ECLIPSE, SPIROMICS, and COPDGene) in Achieving the Goal of Personalized Treatment of Chronic Obstructive Pulmonary Disease [J]. Semin Respir Crit Care Med, 2015, 36(4): 478-490

[2] Chronic obstructive pulmonary disease: The golden decade. Implications for the diagnosis, prevention and treatment of chronic obstructive pulmonary disease[J]. Med Clin (Barc), 2015, 144(11): 507-513

[3] 李金玲,杨林瀛,庞桂芬,等.慢性阻塞性肺疾病急性加重期合并深静脉血栓形成的相关因素分析[J].医学与哲学, 2016, 37(10): 39-41
Li Jin-ling, Yang Lin-ying, Pang Gui-fen, et al. Analysis of Factors Related of Chronic Obstructive Pulmonary Disease with Acute Exacerbation Complicated with Deep Vein Thrombosis Merger [J]. Medicine & Philosophy, 2016, 37(10): 39-41

[4] Kawada T. Approaches to daily body condition management in patients with stable chronic obstructive pulmonary disease [J]. J Clin Nurs, 2016, 25(21-22): 3279-3290

[5] Ekkernkamp E, Storre JH, Windisch W, et al. Impact of intelligent volume-assured pressure support on sleep quality in stable hypercapnic chronic obstructive pulmonary disease patients: a randomized, crossover study[J]. Respiration, 2014, 88(4): 270-276

[6] 何光辉,黄民强,伍北寿,等.脉冲震荡肺功能在稳定期COPD治疗中的应用价值[J].现代生物医学进展, 2016, 16(11): 2099-2101
He Guang-hui, Huang Min-qiang, Wu Bei-shou, et al. Appling Value of Impulse Oscillometry in Patients with COPD in Stable Stage [J]. Progress in Modern Biomedicine, 2016, 16(11): 2099-2101

[7] Narsingam S, Bozarth AL, Abdeljalil A. Updates in the management of stable chronic obstructive pulmonary disease [J]. Postgrad Med, 2015, 127(7): 758-770

[8] Grindrod K. Management of stable chronic obstructive pulmonary disease[J]. Br J Community Nurs, 2015, 20(2): 58, 60-64

[9] Lee SD, Xie CM, Yunus F, et al. Efficacy and tolerability of budesonide/formoterol added to tiotropium compared with tiotropium alone in patients with severe or very severe COPD: A randomized, multicentre study in East Asia[J]. Respirology, 2016, 21(1): 119-127

[10] 王胜,叶海勇,陈悦,等.302例慢性阻塞性肺疾病急性加重期中医证候分型[J].北京中医药大学学报, 2015, 38(1): 57-62
Wang Sheng, Ye Hai-yong, Chen Yue, et al. TCM syndrome distribution in 302 patients with acute exacerbation of chronic obstructive pulmonary disease [J]. Journal of Beijing University of Traditional Chinese Medicine, 2015, 38(1): 57-62

[11] 杜强,陶连珊,朱成华,等.百令胶囊对高风险慢性阻塞性肺疾病稳定期患者的临床疗效和诱导痰中IL-17表达的影响[J].实用药物与临床, 2016, 19(8): 978-980
Du Qiang, Tao Lian-shan, Zhu Cheng-hua, et al. Effect of Bailing capsule and its influence on IL-17 expression of induced sputum in patients with stable high risk chronic obstructive pulmonary disease [J]. Practical Pharmacy and Clinical Remedies, 2016, 19(8): 978-980

[12] 孙志芬,曲桂红,张媚霞,等.阿奇霉素联合百令胶囊治疗慢性阻塞性肺疾病疗效观察[J].中国药师, 2016, 19(7): 1311-1313
Sun Zhi-fen, Qu Gui-hong, Zhang Mei-xia, et al. Effect Observation of Azithromycin Combined with Bailing Capsules on Chronic Obstructive Pulmonary Disease [J]. China Pharmacist, 2016, 19 (7): 1311-1313

[13] 胡强,宋本艳,潘嘉,等.刺五加注射液治疗慢性阻塞性肺疾病稳定期肺肾气虚证临床疗效的观察[J].世界科学技术-中医药现代化, 2016, 18(3): 511-515
Hu Qiang, Song Ben-yan, Pan Jia, et al. Clinical Observation on Acanthopanax Senticosus Injection in Treatment of COPD at Stable Stage with Lung and Kidney Qi Deficiency Syndrome [J]. World Science and Technology-Modernization of Traditional Chinese Medicine, 2016, 18(3): 511-515

[14] Subramanian, Ragulan, Jindal A, et al. The Study of Efficacy, Tolerability and Safety of Theophylline Given Along with Formoterol Plus Budesonide in COPD[J]. J Clin Diagn Res, 2015, 9(2): OC10-13

[15] 郭洁,张勇,赵妍,等.综合外治疗法治疗COPD缓解期的临床疗效及对肺功能的影响[J].现代中西医结合杂志, 2016, 25(1): 21-24
Guo Jie, Zhang Yong, Zhao Yan, et al. Effect of comprehensive external therapy on stable COPD and pulmonary function[J]. Modern Journal of Integrated Traditional Chinese and Western Medicine, 2016, 25 (1): 21-24

[16] Is it possible to shorten the antibiotic therapy in patients hospitalized for acute COPD exacerbation? [J]. Rev Mal Respir, 2017, 34 (3): 275-277

[17] Nguyen MS, Nguyen Dang D, Schleich F, et al. Asthma-COPD overlap syndrome among patients with stable COPD [J]. Rev Med Liege, 2015, 70(1): 37-43

[18] Brill SE, Law M, El-Emir E, et al. Effects of different antibiotic classes on airway bacteria in stable COPD using culture and molecular techniques: a randomised controlled trial [J]. Thorax, 2015, 70 (10): 930-938

[19] Boeck L, Soriano JB, Brusse-Keizer M, et al. Prognostic assessment in COPD without lung function: the B-AE-D indices[J]. Eur Respir J, 2016, 47(6): 1635-1644

[20] Efficacy and tolerability of budesonide/formoterol added to tiotropium compared with tiotropium alone in patients with severe or very severeCOPD: A randomized, multicentre study in East Asia [J]. Respirology, 2016, 21(1): 119-127

[21] 李凡敏,梁宗安,胡丽佳,等.慢性阻塞性肺疾病和支气管哮喘吸入布地奈德/福莫特罗的肺功能变化趋势研究[J].中国煤炭工业医学杂志, 2015, 18(9): 1494-1496
Li Fan-min, Liang Zong-an, Hu Li-jia, et al. A study on lung function trends in the treatment of copd and bronchial asthma by budesonide / formoterol inhalation [J]. Chinese Journal of Coal Industry Medicine, 2015, 18(9): 1494-1496

[22] 叶青,张立波,范荣梅,等.布地奈德福莫特罗联合噻托溴铵对重度慢性阻塞性肺疾病稳定期患者的疗效分析[J].中华肺部疾病杂志(电子版), 2014, 7(3): 45-48
Ye Qing, Zhang Li-bo, Fan Rong-mei, et al. Curative effect of the combination of Symbicort Turbuhaler and Tiotropium Bromide in the treatment of severe stable chronic obstructive pulmonary disease patients[J]. Chinese Journal of lung Disease(Electronic Edition), 2014, 7 (3): 45-48

[23] Effect of inhalation profile and throat geometry on predicted lung deposition of budesonide and formoterol (BF) in COPD: An in-vitro comparison of Spiromax with Turbuhaler [J]. Int J Pharm, 2015, 491 (1-2): 268-276

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macrovascular complications of type 2 diabetic mellitus in Central, Kingdom of Saudi Arabia[J]. Saudi Med J, 2016, 37(12): 1408-1411

[12] Duan J, Zheng C, Gao K,et al.Ultrasonography of lower limb vascular angiopathy and plaque formation in type 2 diabetes patients and finding its relevance to the carotid atherosclerotic formation[J]. Pak J Med Sci, 2014, 30(1): 54-58

[13] Hernández M, López C, Real J, et al. Preclinical carotid atherosclerosis in patients with latent autoimmune diabetes in adults (LADA), type 2 diabetes and classical type 1 diabetes [J]. Cardiovasc Diabetol, 2017, 16(1): 94

[14] Agarwal AK, Singh M, Arya V, et al. Prevalence of peripheral arterial disease in type 2 diabetes mellitus and its correlation with coronary artery disease and its risk factors[J]. J Assoc Physicians India, 2012, 7 (60): 28-32

[15] Nomair AM, ElDeeb MM, Maharem DA.Aldose reductase (-106) C/T gene polymorphism and possibility of macrovascular complications in Egyptian type 2 diabetic patients [J]. Indian J Endocrinol Metab, 2016, 20(5): 648-655

[16] Inoue M, Oribe J, Seike M, et al. High alanine aminotransferase level as a predictor for the incidence of macrovascular disease in type 2 diabetic patients with fatty liver disease [J]. Hepatol Int, 2013, 7(2): 555-561

[17] Kurihara O, Takano M, Mizuno K, et al. Impact of Diabetic Retinopathy on Vulnerability of Atherosclerotic Coronary Plaque and Incidence of Acute Coronary Syndrome [J]. Am J Cardiol, 2016, 118 (7): 944-949

[18] Papa G, Degano C, Iurato MP, et al. Macrovascular complication phenotypes in type 2 diabetic patients [J]. Cardiovasc Diabetol, 2013, 18(12): 20-22

[19] Ribeiro A, Baptista SB, Faustino M, et al. Diabetes Screening in Patients with Macrovascular Coronary Disease: Are the New European Guidelines a Step Backwards? [J]. Acta Med Port, 2017, 30 (6): 434-442

[20] Miranda Garduño LM, Bermúdez Rocha R, Gómez Pérez FJ, et al. Relationship between the ankle-arm index determined by Doppler ultrasonography and cardiovascular outcomes and amputations, in a group of patients with type 2 diabetes mellitus from the Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán [J]. Gac Med Mex, 2011, 147(2): 111-116

[21] Kim BY, Jung CH, Mok JO. Prevalences of diabetic retinopathy and nephropathy are lower in Korean type 2 diabetic patients with non-alcoholic fatty liver disease[J]. J Diabetes Investig, 2014, 5(2): 170-175

[22] Gale R, Scanlon PH, Evans M, et al. Action on diabetic macular oedema: achieving optimal patient management in treating visual impairment due to diabetic eye disease [J]. Eye (Lond), 2017, 31(S1): S1-S20

[23] Furukawa S, Sakai T, Niiya T, et al. Macrovascular Complications and Prevalence of Urgency Incontinence in Japanese Patients with Type 2 Diabetes Mellitus: The Dogo Study [J]. Intern Med, 2017, 56 (8): 889-893

[24] Celik M, Cerrah S, Arabul M, et al. Relation of asymmetric dimethylarginine levels to macrovascular disease and inflammation markers in type 2 diabetic patients [J]. J Diabetes Res, 2014, 1 (2014): 139215-139216

[25] Yokomichi H, Nagai A, Hirata M, et al. Survival of macrovascular disease, chronic kidney disease, chronic respiratory disease, cancer and smoking in patients with type 2 diabetes: BioBank Japan cohort [J]. J Epidemiol, 2017, 27(3S): S98-S106

（上接第 2372 页）

[24] 舒成喆,顾亮.沙美特罗/丙酸氟替卡松联合百令胶囊治疗慢性阻塞性肺疾病的临床研究 [J]. 中国临床药理学杂志, 2015, 31(4): 247-249

Shu Cheng-zhe, Gu Liang. Salmeterol/fluticasone propionate combined with bailing capsule in the treatment of acute chronic obstructive pulmonary disease [J]. The Chinese Journal of Clinical Pharmacology, 2015, 31(4): 247-249

[25] 李春红,王飞.百令胶囊联合呼吸康复训练对矽肺合并慢阻肺患者白细胞介素 -6 及肺功能的影响 [J]. 中国生化药物杂志, 2016, 36 (5): 139-141

Li Chun-hong, Wang Fei. Effects of Bailing capsules combined with respiratory rehabilitation training on interleukin-6 and lung function in silicosis patients with COPD [J]. Chinese Journal of Biochemical Pharmaceutics, 2016, 36(5): 139-141

[26] Li X, Peng K, Zhou Y, et al. Inhibitory effect of Bailing capsule on hypoxia-induced proliferation of rat pulmonary arterial smooth muscle cells[J]. Saudi Med J, 2016, 37(5): 498-505

[27] Di Gennaro P, Gerlini G, Urso C, et al. $CD4^+FOXP3^+$T regulatory cells decrease and $CD3^+CD8^+$T cells recruitment in TILs from melanoma metastases after electrochemotherapy [J]. Clin Exp Metastasis, 2016, 33(8): 787-798

[28] 郝文东,王国芳,张彩莲.百令胶囊联合布地奈德福莫特罗粉吸入剂治疗稳定期慢性阻塞性肺疾病的疗效及机制 [J]. 临床肺科杂志, 2016, 21(9): 1603-1606

Hao Wen-dong, Wang Guo-fang, Zhang Cai-lian. Efficacy and mechanism of Bailing capsule combined with budesonide and formoterol fumarate powder in the treatment of stable COPD patients[J]. Journal of Clinical Pulmonary Medicine, 2016, 21(9): 1603-1606

[29] 厉洪江,刘翠华,田明,等.百令胶囊辅助治疗过敏性紫癜肾炎患儿的临床观察[J].中国药房, 2016, 27(32): 4546-4548

Li Hong-jiang, Liu Cui-hua, Tian Ming, et al. Clinical Observation of Bailing Capsules in Adjunctive Treatment of Children with Henoch-schonlein Purpu-ra Nephritis [J]. China Pharmacy, 2016, 27 (32): 4546-4548

[30] 林甄,陈文庆,罗素华,等.信必可都保与舒利迭对轻中度支气管哮喘患儿免疫因子 IL4、IFNγ 及肺功能影响的比较[J].现代诊断与治疗, 2014, 25(8): 1712-1714

Lin Zhen, Cheng Wen-qing, Luo Su-hua, et al. Compare the Impact of Symbicort Turbuhaler and Seretide for Immune Factor IL 4, IFN γ and Lung Function in Children with Mild to Moder-ate Asthma [J]. Modern Diagnosis & Treatment, 2014, 25(8): 1712-1714