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玉屏风颗粒联合重组人干扰素 α-1b 雾化吸入治疗对反复呼吸道感染患儿炎性因子和 T 细胞亚群的影响 *

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摘要 目的：探讨在重组人干扰素 α-1b 雾化吸入治疗的基础上加用玉屏风颗粒对反复呼吸道感染（RRTI）患儿炎性因子和 T 细胞亚群的影响。**方法**：将我院于 2018 年 3 月 ~2020 年 2 月期间收治的 RRTI 患儿 180 例根据信封抽签法分为对照组（n=90）和实验组（n=90），均给予止咳、退热、平喘、抗感染等常规治疗的基础上，对照组患儿予以重组人干扰素 α-1b 雾化吸入治疗，实验组患儿则在对照组的基础上联合玉屏风颗粒治疗，比较两组患儿疗效、症状消失时间、炎性因子、T 细胞亚群和不良反应。**结果**：实验组治疗 3 周后的临床总有效率为 91.11%（82/90）高于对照组的 78.89%（71/90）（*P*<0.05）。实验组肺部啰音、发热、喘息、咳嗽症状消失时间较对照组短（*P*<0.05）。两组治疗 3 周后血清白介素 -6（IL-6）、肿瘤坏死因子 -α（TNF-α）、白介素 -10（IL-10）水平均下降，且实验组低于对照组（*P*<0.05）。两组治疗 3 周后 $CD8^+$ 较治疗前降低，且实验组低于对照组（*P*<0.05）；$CD4^+/CD8^+$、$CD3^+$、$CD4^+$ 均较治疗前升高，且实验组高于对照组（*P*<0.05）。比较两组不良反应发生率未见统计学差异（*P*>0.05）。**结论**：玉屏风颗粒联合重组人干扰素 α-1b 雾化吸入治疗 RRTI 患儿，可迅速改善患儿临床症状、T 细胞亚群以及炎性因子水平，且不增加不良反应发生率，疗效令人满意。

关键词：玉屏风颗粒；重组人干扰素 α-1b；雾化吸入；反复呼吸道感染；炎性因子；T 细胞亚群

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The Effect of Yupingfeng Granules Combined with Recombinant Human Interferon α-1b Aerosol Inhalation on Inflammatory Factors and T Cell Subsets in Children with Recurrent Respiratory Tract Infection*

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ABSTRACT Objective: To investigate the effect of Yupingfeng granules combined with recombinant human interferon α-1b aerosol inhalation on inflammatory factors and T cell subsets in children with recurrent respiratory tract infection (RRTI). **Methods:** 180 children with RRTI who were admitted to our hospital from March 2018 to February 2020 were selected, children were divided into control group (n=90) and experimental group (n=90) according to the envelope lottery method. On the basis of routine treatment such as cough relief, antipyretic, antiasthmatic and anti infection, the children in the control group were treated with recombinant human interferonα-1b aerosol inhalation. The children in the experimental group were treated with Yupingfeng granules on the basis of the control group. The curative effect, symptom disappearance time and inflammation factors, T cell subsets and adverse reactions of the two groups were compared. **Results:** The total clinical effective rate of the experimental group was 91.11%(82/90) at 3 weeks after treatment was higher than that 78.89% (71/90) of the control group (*P*<0.05). The disappearance time of lung rale, fever, wheeze, and cough of the experimental group were shorter than those of the control group (*P*<0.05). The levels of serum interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α) and interleukin-10 (IL-10) in two groups at 3 weeks after treatment decreased, and the levels of the experimental group were lower than those of the control group (*P*<0.05). $CD8^+$ decreased compared with that before treatment, and that in the experimental group was lower than that in the control group (*P*<0.05). $CD4^+/CD8^+$, $CD3^+$, $CD4^+$ in two groups at 3 weeks after treatment increased, and the experimental group was higher than the control group (*P*<0.05). There was no significant difference in the incidence of adverse reactions between the two groups (*P*>0.05). **Conclusion:** Yupingfeng granules combined with recombinant human interferon α-1b aerosol inhalation in treatment of children with RRTI, which can rapidly improve the clinical symptoms, T cell subsets and inflammatory factors levels, and does not increase the incidence of adverse reactions, and the efficacy is satisfactory.

Key words: Yupingfeng granules; Recombinant human interferon α-1b; Aerosol inhalation; Recurrent respiratory tract infection; Inflammatory factors; T cell subsets

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前言

反复呼吸道感染(RRTI)是儿科的常见疾病,是指小儿在 1 年内发生呼吸道感染的次数超过一定范围的一种临床综合征[1-3]。以往研究数据显示[4],小儿 RRTI 在儿科疾病中约占 20%。该病临床主要表现为发热、鼻塞、流涕、喷嚏伴轻咳等症状,若未能予以及时治疗,可引起哮喘、肾炎和心肌炎等,严重危害患儿生长发育及其生命健康[5-7]。现临床针对该病的治疗尚无特异性方案,一般是予以止咳化痰、抗病毒等常规对症治疗。重组人干扰素 α-1b 是临床治疗 RRTI 的常用药物,可发挥较好的抗病毒效应[8,9],但仍有部分患儿使用重组人干扰素α-1b 治疗后,效果一般。近年来中西医结合治疗在 RRTI 中的效果逐渐凸显,玉屏风颗粒具有扶正固本的功效, 还可增强机体免疫功能,在治疗 RRTI 方面具有一定的效果[10]。本研究通过对我院收治的部分 RRTI 患儿给予玉屏风颗粒联合重组人干扰素α-1b 雾化吸入治疗,取得了较好的效果。现报道如下。

1 资料与方法

1.1 一般资料

将我院于 2018 年 3 月 ~2020 年 2 月期间收治的 RRTI 患儿 180 例,纳入标准:(1)符合 RRTI 相关诊断标准[11];(2)经临床检查等确诊为 RRTI;(3)患儿精神状态良好;(4)患儿监护人知情研究且签署同意书。排除标准:(1)未能按医嘱用药或监护人要求退出研究;(2)脑、肾、肝等重要脏器病变者;(3)合并肺部畸形、心脏病、肺结核等疾病;(4)合并全身感染性疾病者;(5)对本研究用药方案耐受;(6)严重营养不良者。根据信封抽签法分为对照组(n=90)和实验组(n=90),其中对照组女 41 例,男 49 例,年龄 3~7 岁,平均(4.79±0.53)岁;病程 1~4 年,平均(2.31±0.36)年;感染位置:下呼吸道感染 42 例,上呼吸道感染 48 例。实验组女 44 例,男 46 例,年龄 3~6 岁,平均(4.86±0.67)岁;病程 1~3 年,平均(2.19±0.42)年;感染位置:下呼吸道感染 44 例,上呼吸道感染 46 例。两组一般资料对比无显著性差异(P>0.05),具有可比性。本次研究已获取我院伦理学委员会批准进行。

1.2 方法

给予两组患者止咳、退热、平喘、抗感染等常规治疗,治疗期间请家属或监护人协助确保饮食、生活习惯规律。在此基础上,对照组予以重组人干扰素 α-1b(北京三元基因药业股份有限公司,国药准字:S20040039,规格:10 μg:0.5 mL/ 支)1-2 μg/kg·次,经 3 mL 灭菌注射液稀释后雾化吸入,1 次 /d。实验组在对照组基础上联合玉屏风颗粒 (国药集团广东环球制药有限公司,国药准字:Z10930036,规格:每袋装 5 g)治疗,口服,其中 3~5 岁患儿 5 g/ 次,5~7 岁患儿 7. 5 g/ 次,均为 3 次 /d。两组均治疗 3 周。

1.3 观察指标

(1)记录两组患儿临床总有效率。疗效判定标准如下[12]:总有效率 =(有效例数 + 显效例数)/ 总例数×100%。无效:咳嗽、发热、喘息、肺部啰音等临床表现未见改善甚至加重。有效:咳嗽、发热、喘息、肺部啰音等临床表现有一定改善。显效:咳嗽、发热、喘息、肺部啰音等临床表现完全消失。(2)记录两组治疗期间不良反应发生情况。(3)记录两组咳嗽、发热、喘息、肺部啰音等症状消失时间。(4)抽取所有患儿治疗前、治疗 3 周后的空腹肘静脉血 4 mL,分为两管,一管经常规离心处理(离心半径 11.5 cm,3100 r/min 离心 13 min)分离上清液,置于 -42℃冰箱中待测,采用酶联免疫吸附试验法检测炎性因子指标:肿瘤坏死因子 -α(TNF-α)、白介素 -10(IL-10)、白介素 -6(IL-6),严格遵守试剂盒(青岛瑞斯凯尔生物科技有限公司)说明书步骤操作;另一管采用 FACSCalibur 流式细胞仪(艾森生物(杭州)有限公司) 检测患儿 T 淋巴细胞亚群:$CD4^+$、$CD8^+$、$CD3^+$, 并计算 $CD4^+/CD8^+$ 值。

1.4 统计学方法

采用 SPSS27.0 软件分析数据。感染位置、性别、总有效率等计数资料以率或例数表示,采用 χ^2 检验。症状消失时间、平均年龄、炎性因子水平等计量资料以($\bar{x}\pm s$)表示,采用 t 检验。检验水准设置为 α=0.05。

2 结果

2.1 两组症状消失时间比较

治疗 3 周后实验组发热、肺部啰音、喘息、咳嗽症状消失时间均短于对照组(P<0.05);见表 1。

表 1 两组症状消失时间比较($\bar{x}\pm s$,d)

Table 1 Comparison of symptom disappearance time between the two groups($\bar{x}\pm s$, d)

Groups	Disappearance time of cough	Disappearance time of fever	Disappearance time of wheeze	Disappearance time of lung rale
Control group(n=90)	8.41±1.05	5.87±0.79	7.05±0.79	6.41±0.74
Experimental group (n=90)	6.09±1.21	3.23±0.68	4.28±0.54	4.81±0.56
t	13.738	24.028	27.462	16.356
P	0.000	0.000	0.000	0.000

2.2 两组疗效比较

治疗 3 周后实验组的临床总有效率为 91.11%(82/90),高于对照组的 78.89%(71/90)(P<0.05);见表 2。

2.3 两组 T 淋巴细胞亚群比较

两组治疗前 $CD3^+$、$CD8^+$、$CD4^+$、$CD4^+/CD8^+$ 比较无显著差异(P>0.05);与治疗前相比,治疗 3 周后两组 $CD8^+$ 降低,且实验组低于对照组 (P<0.05),$CD4^+$、$CD3^+$、$CD4^+/CD8^+$ 均升高,且实验组高于对照组(P<0.05);见表 3。

表 2 两组疗效比较【例(%)】

Table 2 Comparison of curative effect between the two groups [n(%)]

Groups	Remarkable effect	Effective	Invalid	Total effective rate
Control group(n=90)	29(32.22)	42(46.67)	19(21.11)	71(78.89)
Experimental group (n=90)	36(40.00)	46(51.11)	8(8.89)	82(91.11)
χ^2		-		5.272
P		-		0.022

表 3 两组 T 淋巴细胞亚群比较($\bar{x}\pm s$)

Table 3 Comparison of T lymphocyte subsets between the two groups($\bar{x}\pm s$)

Groups	$CD3^+$(%)		$CD4^+$(%)		$CD8^+$(%)		$CD4^+/CD8^+$	
	Before treatment	3 weeks after treatment	Before treatment	3 weeks after treatment	Before treatment	3 weeks after treatment	Before treatment	3 weeks after treatment
Control group(n=90)	36.78±5.37	41.42±6.33*	31.56±5.39	35.96±5.32*	30.53±4.65	26.51±3.84*	1.03±0.18	1.36±0.22*
Experimental group (n=90)	36.02±6.38	46.73±5.41*	31.91±6.35	40.39±6.35*	30.96±5.72	21.82±2.54*	1.03±0.21	1.85±0.11*
t	0.865	6.050	0.399	5.073	0.553	9.664	0.000	15.991
P	0.388	0.000	0.691	0.000	0.581	0.000	1.000	0.000

Note: Compared with before treatment,*P<0.05.

2.4 两组炎性因子水平比较

两组治疗前血清炎性因子水平比较无显著差异(P>0.05)；两组治疗 3 周后血清 TNF-α、IL-10、IL-6 水平较治疗前均下降,且实验组低于对照组(P<0.05)；见表 4。

表 4 两组炎性因子水平比较($\bar{x}\pm s$)

Table 4 Comparison of inflammatory factors between the two groups($\bar{x}\pm s$)

Groups	IL-6(pg/mL)		TNF-α(pg/mL)		IL-10(pg/mL)	
	Before treatment	3 weeks after treatment	Before treatment	3 weeks after treatment	Before treatment	3 weeks after treatment
Control group(n=90)	6.82±1.23	4.53±0.78*	18.63±2.57	14.65±2.42*	14.92±2.52	11.52±1.21*
Experimental group (n=90)	6.51±1.02	3.12±0.63*	18.82±2.32	8.01±1.32*	15.07±2.61	7.68±1.13*
t	1.840	13.341	0.934	18.967	0.392	22.004
P	0.067	0.000	0.342	0.000	0.695	0.000

Note:Compared with before treatment, *P<0.05.

2.5 两组不良反应发生情况

两组不良反应总发生率对比未见差异(P>0.05)；见表 5。

表 5 两组不良反应发生率比较【例(%)】

Table 5 Comparison of the incidence of adverse reactions between the two groups [n(%)]

Groups	Diarrhea	Vomit	Nausea	Total incidence rate
Control group(n=90)	2(2.22)	3(3.33)	1(1.11)	6(6.67)
Experimental group (n=90)	3(3.33)	5(5.56)	1(1.11)	9(10.00)
χ^2				0.655
P				0.418

3 讨论

RRTI 可累及上、下呼吸道,是儿科常见病,冬春季节气候变化剧烈时极易反复发作,既往研究认为该病与病毒、细菌、支原体等致病因素有关[13-15]。患儿由于年龄尚幼,脏腑娇嫩,行气未充,免疫系统通常尚未完全成型,当遭受病毒等外来物质侵入时,免疫屏障受损,引起机体炎症因子大量分泌,使得感染迅速蔓延,加之部分患儿无法正确诉说病情,在一定程度上加大了治疗难度[16,17]。既往研究表明[18],RRTI 受病毒感染后,辅助性 T 细胞遭到侵犯,$CD4^+$ 分化受阻, 同时病毒破坏免疫气管,导致总 T 淋巴细胞减少,免疫功能下降甚至被抑制,从而导致呼吸道感染反复发生,引起恶性循环,而 T 淋巴细胞亚群失调可

引起机体细胞因子的改变,在炎症的启动和扩大中发挥重要作用[19,20]。TNF-α 是一种可以促进中性粒细胞吞噬作用的细胞因子,其分泌上调时可引起发热症状,同时还参与某些自身免疫疾病的病理性损伤。IL-6、IL-10 均可诱导炎性反应,促进其他炎症因子的分泌[21,22]。

目前临床上多采用抗病毒、免疫促进剂等药物进行治疗,重组人干扰素 α-1b 是人工合成的广谱强效抗病毒药,雾化吸入使药物直接作用于患处,帮助患儿达到有效的血药浓度[23]。由于 RRTI 发病机制复杂,单一的抗感染并不能达到很好的理想预期效果,且反复治疗还增加了医疗成本和社会负担。近年来研究发现[24],中医药在 RRTI 的治疗中发挥重要作用,陈垣等学者采用补中益气汤治疗 RRTI 患儿,发现其在改善患儿的细胞免疫功能和提高临床疗效方面效果显著。钱钻好等人[25]在小儿上呼吸道感染的治疗中,采用玉屏风颗粒联合葡萄糖酸锌治疗的方法,临床效果较好。故本研究尝试将玉屏风颗粒应用于 RRTI 患儿的治疗中,分析结果如下。

本次研究结果显示,玉屏风颗粒联合重组人干扰素 α-1b 雾化吸入治疗 RRTI 患儿,可在一定程度上提高治疗效果,有效改善临床症状。这可能是由于重组人干扰素 α-1b 属于免疫调节剂,可诱导 B 细胞增殖、分化,进而产生抗体,调节 T 淋巴细胞活性,达到抗病毒、增强免疫的效果[26]。穆丹等学者[27]认为,重组人干扰素 α-1b 可充分发挥免疫调节作用,增强细胞活性,提升机体免疫力。同时,该药通过雾化吸入方式治疗,直接作用于患处,激活黏膜下血管,进一步纠正免疫紊乱状态。玉屏风颗粒主要由防风、白术、黄芪精制而成,其中防风可扶正驱邪、祛风解表、益气固卫;白术亦具有健脾益气之功效;黄芪更是补益气血之要药,可扶正驱邪、益气固表、健脾利湿,以上药物共同发挥解表驱邪、扶正固本的功效,联合重组人干扰素 α-1b 发挥协同作用,进一步改善患者临床症状[28]。研究亦表明,在常规西药治疗 RRTI 的基础上辅以玉屏风颗粒可发挥益肺健脾、利咽解毒、益气祛风功效[29]。随着 RRTI 的进展,机体逐渐产生免疫紊乱、炎性因子水平失衡等反应,其造成的负反馈可严重加剧病情,甚者导致患儿死亡。本次研究结果中玉屏风颗粒联合重组人干扰素 α-1b 雾化吸入治疗在改善 RRTI 患儿炎性因子、T 细胞亚群水平方面效果显著。药理研究证实[30],防风可抑制病菌生长、抵抗炎症;白术有增强细胞免疫和体液免疫,促进巨噬细胞吞噬功能的作用;黄芪对干扰素系统有明显的刺激作用,能抗病毒感染,可调节、促进机体的体液免疫和细胞免疫。上述诸药的药理作用是治疗 RRTI 的基础与依据。另两组不良反应发生率对比无明显差异,可见玉屏风颗粒联合重组人干扰素 α-1b 雾化吸入治疗安全可靠。

综上所述,玉屏风颗粒联合重组人干扰素 α-1b 雾化吸入治疗 RRTI 患儿,可迅速改善患儿临床症状,改善其炎性因子、T 细胞亚群水平,且不增加不良反应发生率,疗效显著。

参 考 文 献(References)

[1] Mamaeva T, Mehlum CS, Davidsen JR. Recurrent respiratory papillomatosis with lower airway involvement in a young woman[J]. Eur Clin Respir J, 2020, 7(1): 1740567

[2] Jaber R. Respiratory and allergic diseases: from upper respiratory tract infections to asthma[J]. Prim Care, 2002, 29(2): 231-261

[3] Morpeth SC, Munywoki P, Hammitt LL, et al. Impact of viral upper respiratory tract infection on the concentration of nasopharyngeal pneumococcal carriage among Kenyan children [J]. Sci Rep, 2018, 8 (1): 11030

[4] 徐燕玲, 霍莉莉, 武艺林, 等. 儿童反复呼吸道感染外治方案优化研究[J]. 中国中医药信息杂志, 2019, 26(8): 35-39

[5] Mant i S, Parisi GF, Papale M, et al. Bacteriotherapy with Streptococcus salivarius 24SMB and Streptococcus oralis 89a nasal spray for treatment of upper respiratory tract infections in children: a pilot study on short-term efficacy[J]. Ital J Pediatr, 2020, 46(1): 42

[6] Cobey S. Repeated Vaccination May Protect Children From Influenza Infection[J]. JAMA Netw Open, 2018, 1(6): e183730

[7] de Hoog MLA, Venekamp RP, Damoiseaux RAMJ, et al. Impact of Repeated Influenza Immunization on Respiratory Illness in Children With Preexisting Medical Conditions[J]. Ann Fam Med, 2019, 17(1): 7-13

[8] Green DS, Nunes AT, David-Ocampo V, et al. A Phase 1 trial of autologous monocytes stimulated ex vivo with Sylatron (Peginterferon alfa-2b) and Actimmune (Interferon gamma-1b) for intra-peritoneal administration in recurrent ovarian cancer [J]. J Transl Med, 2018, 16 (1): 196

[9] Abdolvahab MH, Fazeli A, Halim A, et al. Immunogenicity of Recombinant Human Interferon Beta-1b in Immune-Tolerant Transgenic Mice Corresponds with the Biophysical Characteristics of Aggregates[J]. J Interferon Cytokine Res, 2016, 36(4): 247-257

[10] 陈海燕, 林少娜, 甘影妃, 等. 玉屏风颗粒治疗慢性阻塞性肺疾病稳定期患者认知功能障碍的临床研究 [J]. 广州医科大学学报, 2019, 47(6): 105-107

[11] 贝政平, 李毅 王莹, 等. 儿科疾病诊断标准(第 2 版)(精)[M]. 北京: 科学出版社, 2007: 126

[12] 陈永红. 儿科疾病诊断与疗效标准 [M]. 上海: 上海中医药大学出版社, 2006: 54

[13] 王艳艳, 安淑华, 李芹, 等. 6 岁以下年幼儿哮喘发病的相关因素分析[J]. 疑难病杂志, 2019, 18(7): 710-714

[14] Dehn Lunn A. Reducing inappropriate antibiotic prescribing in upper respiratory tract infection in a primary care setting in Kolkata, India [J]. BMJ Open Qual, 2018, 7(4): e000217

[15] Okamoto M, Dapat CP, Sandagon AMD, et al. Molecular Characterization of Respiratory Syncytial Virus in Children With Repeated Infections With Subgroup B in the Philippines [J]. J Infect Dis, 2018, 218(7): 1045-1053

[16] 周艳茹, 霍黎, 葛娇, 等. 细菌溶解产物联合匹多莫德对反复呼吸道感染儿童炎性因子水平及免疫功能的影响[J]. 现代生物医学进展, 2017, 17(28): 5528-5531

[17] Hansen TE, Evjenth B, Holt J. Lower respiratory tract infections appear to be the most important risk factor for current asthma in subarctic schoolchildren[J]. Acta Paediatr, 2019, 108(5): 911-919

[18] 宫铁锋, 方彬, 任会利, 等. 甘露聚糖肽联合匹多莫德对反复呼吸道感染患儿炎症指标、免疫功能的影响及安全性分析[J]. 国际检验医学杂志, 2019, 40(16): 1963-1967

[19] To KKW, Lu L, Fong CHY, et al. Rhinovirus respiratory tract infection in hospitalized adult patients is associated with TH2 response irrespective of asthma[J]. J Infect, 2018, 76(5): 465-474

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Death Risk in Patients With AcuteExacerbation of Chronic Obstructive Pulmonary Disease Using Vital Signs and Admission History: Retrospective Cohort Study [J]. JMIR Med Inform, 2019, 7 (4): e13085

[14] 周少珠, 叶旭军, 杨静, 等. 沙丁胺醇、布地奈德不同雾化吸入联合头孢哌酮钠舒巴坦钠对 AECOPD 患者血气指标和肺功能的影响[J].现代生物医学进展, 2020, 20(8): 1468-1472

[15] Chen PK, Hsiao YH, Pan SW, et al. Independent factors associate with hospital mortality in patients with acuteexacerbation of chronic obstructive pulmonary disease requiring intensive care unit admission: Focusing on the eosinophil-to-neutrophil ratio [J]. PLoS One, 2019, 14(7): e0218932

[16] Liu S, Chen J, Zuo J, et al. Comparative effectiveness of six Chinese herb formulas for acuteexacerbation of chronic obstructive pulmonary disease: a systematic review and network meta-analysis [J]. BMC Complement Altern Med, 2019, 19(1): 226

[17] 吴明, 刘钦华, 郭永明, 等. 福州市 40 岁及以上人群慢性阻塞性肺疾病流行病学调查分析[J]. 国际呼吸杂志, 2020, 40(2): 107-113

[18] Goto T, Shimada YJ, Faridi MK, et al. Incidence of Acute Cardiovascular Event After Acute Exacerbation of COPD [J]. J Gen Intern Med, 2018, 33(9): 1461-1468

[19] Dastan F, Salamzadeh J, Pourrashid MH, et al. Effects of High-Dose Vitamin D Replacement on the Serum Levels of Systemic Inflammatory Biomarkers in Patients with Acute Exacerbation of Chronic Obstructive Pulmonary Disease [J]. COPD, 2019, 16(3-4): 278-283

[20] Janaudis-Ferreira T, Tansey CM, Harrison SL, et al. A Qualitative Study to Inform a More Acceptable Pulmonary Rehabilitation Program after Acute Exacerbation of Chronic ObstructivePulmonary Disease[J]. Ann Am Thorac Soc, 2019, 16(9): 1158-1164

[21] Carrier M, Altman AD, Blais N, et al. Extended thromboprophylaxis with low-molecular weight heparin (LMWH) following abdominopelvic cancer surgery[J]. Am J Surg, 2019, 218(3): 537-550

[22] Felder S, Rasmussen MS, King R, et al. Prolonged thromboprophylaxis with low molecular weight heparin for abdominal or pelvic surgery [J]. Cochrane Database Syst Rev, 2019, 8(8): CD004318

[23] Lin A, Vazquez SR, Jones AE, et al. Description of anti-Xa monitoring practices during low molecular weightheparin use [J]. J Thromb Thrombolysis, 2019, 48(4): 623-628

[24] Monagle P, Lensing AWA, Thelen K, et al. Bodyweight-adjusted rivaroxaban for children with venous thromboembolism (EINSTEIN-Jr): results from three multicentre, single-arm, phase 2 studies [J]. Lancet Haematol, 2019, 6(10): e500-e509

[25] Male C, Lensing AWA, Palumbo JS, et al. Rivaroxaban compared with standard anticoagulants for the treatment of acute venous thromboembolism in children: a randomised, controlled, phase 3 trial [J]. Lancet Haematol, 2020, 7(1): e18-e27

[26]Wingert NR, Arbo MD, Göethel G, et al. In vitro toxicity assessment of rivaroxaban degradation products and kinetic evaluation to decay process[J]. Drug Chem Toxicol, 2019, 42(5): 509-518

[27] Ding S, Wang L, Xie L, et al. Bioequivalence Study of 2 Formulations of Rivaroxaban, a Narrow-Therapeutic-Index Drug, in Healthy Chinese Subjects Under Fasting and Fed Conditions [J]. Clin Pharmacol Drug Dev, 2020, 9(3): 346-352

[28] Kale DP, Puri V, Kumar A, et al. The Role of Cocrystallization-Mediated Altered Crystallographic Properties on the Tabletability of Rivaroxaban and Malonic Acid[J]. Pharmaceutics, 2020, 12(6): E546

[29] Fronas SG, Dahm AEA, Wik HS, et al. Safety and feasibility of rivaroxaban in deferred workup of patients with suspected deep vein thrombosis[J]. Blood Adv, 2020, 4(11): 2468-2476

[30] Anwer MK, Mohammad M, Iqbal M, et al. Sustained release and enhanced oral bioavailability of rivaroxaban by PLGA nanoparticles with no food effect[J]. J Thromb Thrombolysis, 2020, 49(3): 404-412

(上接第 897 页)

[20] Miyauchi K. Helper T Cell Responses to Respiratory Viruses in the Lung: Development, Virus Suppression, and Pathogenesis [J]. Viral Immunol, 2017, 30(6): 421-430

[21] 任安义. 外周血炎症介质对支气管哮喘并发呼吸道感染的早期诊断意义[J]. 中国实验诊断学, 2017, 21(6): 1050-1052

[22] 黄邀. 小儿哮喘发作中相关炎症介质水平的变化及意义 [J]. 中国妇幼保健, 2017, 32(15): 3581-3583

[23] Kalal C, Shukla A, Mohanka R, et al. Sofosbuvir, pegylated interferon, and ribavirin for retreatment of hepatitis C virus genotype 1b following sofosbuvir and ledipasvir failure [J]. Hepatology, 2018, 67(5): 2049-2050

[24] 陈垣, 周静. 补中益气汤治疗反复呼吸道感染患儿的疗效及对免疫功能的影响[J]. 海南医学, 2020, 31(3): 354-356

[25] 钱钻好, 王荧荧, 傅元凤. 玉屏风颗粒联合葡萄糖酸锌治疗小儿反复呼吸道感染的临床效果[J]. 世界中医药, 2018, 13(9): 2233-2236

[26] Tamai H, Ida Y, Kawashima A, et al. Simeprevir-Based Triple Therapy with Reduced Doses of Pegylated Interferon α-2a Plus Ribavirin for Interferon Ineligible Patients with Genotype1bHepatitis C Virus[J]. Gut Liver, 2017, 11(4): 551-558

[27] 穆丹, 钟红平. 玉屏风散联合重组人干扰素 α-1b 雾化吸入治疗小儿反复呼吸道感染的研究 [J]. 现代中西医结合杂志, 2018, 27(32): 3558-3560, 3564

[28] 周逸珊, 李诚, 刘晓清, 等. 玉屏风颗粒联合布地奈德福莫特罗粉吸入剂治疗支气管哮喘的疗效观察 [J]. 广东医学, 2019, 40(24): 3446-3451

[29] 张昱, 陈继源, 王茂壮, 等. 玉屏风颗粒联合脾氨肽治疗反复下呼吸道感染患儿的疗效及对炎性因子、SAA 水平的影响 [J]. 贵州医药, 2020, 44(2): 234-236

[30] 郝文东, 郎华, 李晓婧, 等. 玉屏风颗粒联合厚朴排气合剂治疗气虚腑实型稳定期 COPD 疗效及对免疫功能、CX3 CL1 与 MFAP-4 的影响[J]. 现代中西医结合杂志, 2020, 29(9): 918-922