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高渗盐水雾化吸入治疗儿童支原体肺炎继发哮喘发作及对其 T 淋巴细胞亚群及 Th1、Th2 型细胞因子的影响 *

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摘要 目的：探讨高渗盐水雾化吸入治疗儿童支原体肺炎继发哮喘发作的临床疗效及对其 T 淋巴细胞亚群及 Th1、Th2 型细胞因子的影响。**方法：**选取我院 2015 年 6 月到 2017 年 6 月间收治的支原体肺炎继发哮喘发作患儿 100 例为研究对象。随机分为对照组和观察组，各 50 例。两组均给予吸氧、抗生素、维持酸碱度、电解质平衡及相应症状等对症治疗，对照组给予生理盐水结合沙丁胺醇进行雾化治疗，观察组采用 3%高渗盐水结合沙丁胺醇进行雾化治疗，比较两组患儿发热、咳嗽、肺内啰音、咽部肿痒等症状消失时间及临床疗效；比较两组治疗前后 $CD3^+$、$CD4^+$、$CD8^+$、$CD4^+/CD8^+$、IFN-γ 及 IL-4 水平情况。**结果：**观察组患儿发热、咳嗽、肺内啰音、咽部肿痒等临床症状消失时间显著早于对照组，差异有统计学意义（$P<0.05$）；观察组总有效率 96.00%明显高于对照组 80.00%，差异有统计学意义（$P<0.05$）；两组患儿治疗前 $CD3^+$、$CD4^+$、$CD8^+$、$CD4^+/CD8^+$、IFN-γ 及 IL-4 水平比较差异无统计学意义（$P>0.05$）；治疗后 $CD3^+$、$CD4^+$、$CD4^+/CD8^+$ 及 IFN-γ 水平均明显升高，$CD8^+$ 及 IL-4 水平明显降低，差异均有统计学意义（均 $P<0.05$）；且观察组治疗后 $CD3^+$、$CD4^+$、$CD4^+/CD8^+$ 及 IFN-γ 水平均明显高于对照组，$CD8^+$ 及 IL-4 水平明显低于对照组，差异均有统计学意义（均 $P<0.05$）。**结论：**高渗盐水雾化吸入能够显著改善支原体肺炎继发哮喘发作患儿临床症状，提高 $CD3^+$、$CD4^+$、$CD4^+/CD8^+$ 及 Th1 水平，抑制 $CD8^+$ 及 Th2 水平，临床疗效确切，值得临床推广应用。

关键词：高渗盐水；儿童；支原体肺炎；哮喘发作；T 淋巴细胞亚群；Th1/Th2 细胞因子

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The Effect of Hypertonic Saline Inhalation on Secondary Asthma Attack in Children with Mycoplasma Pneumonia and Its Effect on T Lymphocyte Subsets and Th1 and Th2 Type Cytokines*

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ABSTRACT Objective: To investigate the clinical efficacy of hypertonic saline aerosol inhalation in the treatment of asthmatic attack secondary to Mycoplasma pneumonia in children and its influence on T lymphocyte subsets and Th1, Th2 cytokines. **Methods:** A total of 100 children with asthma secondary to Mycoplasma pneumonia admitted to our hospital from June 2015 to June 2017 were selected as subjects.They were randomly divided into the control group and the observation group, 50 cases in each group. The two groups were given the symptomatic treatment of oxygen inhalation, antibiotics, maintenance of acid-base, electrolyte balance and corresponding symptoms. The control group was given saline Combination salbutamol, the observation group was given 3% hypertonic saline Combination salbutamol. The symptoms of fever, cough, rale in the lungs, and swelling of the pharynx were compared in the two groups. The levels of $CD3^+$, $CD4^+$, $CD8^+$, $CD4^+/CD8^+$, IFN-γ and IL-4 were compared between the two groups before and after treatment. **Results:** The disappearance time of clinical symptoms such as fever, cough, pulmonary rales, pharyngeal swelling and itching in the observation group was significantly earlier than that in the control group, the difference was statistically significant ($P<0.05$). The total effective rate of the observation group was 96% significantly higher than that of the control group (80%), the difference was statistically significant($P<0.05$). There was no significant difference in the levels of $CD3^+$, $CD4^+$, $CD8^+$, $CD4^+/CD8^+$, IFN-γ and IL-4 before treatment in the two groups ($P>0.05$). After treatment, $CD3^+$, $CD4^+$, $CD4^+/CD8^+$ and IFN-γ were significantly increased, $CD8^+$ and IL-4 were significantly decreased, the differences were statistically significant ($P<0.05$); After treatment, the levels of $CD3^+$, $CD4^+$,$CD4^+/CD8^+$ and IFN-γ in the observation group were significantly higher than those in the control group, and the levels of $CD8^+$ and IL-4 were significantly lower than those in the control group, the differences were statistically significant ($P<0.05$). **Conclusion:** Atomization Iinhalation of hypertonic saline can significantly improve the clinical symptoms of Mycoplasma pneumoniae in children with asthma

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attacks, improve the levels of $CD3^+$, $CD4^+$, $CD4^+/CD8^+$ and Th1, and inhibit the level of $CD8^+$ and Th2, the clinical curative effect is exact, it is worthy of clinical application.

Key words: Hypertonic saline; Children; Mycoplasma pneumonia; Asthma attack; T lymphocyte subsets; Th1/Th2 cytokine

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前言

支气管哮喘是临床儿科常见的呼吸系统疾病类型之一,其病因较为复杂,肺炎支原体是诱发儿科呼吸系统疾病的一种非典型病原体,而肺炎支原体感染与支气管哮喘的发作有着密切的关系[1]。近年来,临床报道显示,肺炎支原体感染后继发支气管哮喘的发病率出现明显上升的趋势[2]。研究显示,该病是由多种免疫细胞,如 T 淋巴细胞亚群等参与的一种慢性气道炎性疾病,而 T 淋巴细胞在哮喘发病过程中起到重要的作用,此外,肺炎支原体感染继发哮喘患者机体外周血中 T 淋巴细胞亚群及辅助性 T 细胞 -1/-2 (Th1/Th2) 细胞因子存在异常紊乱现象[3-5]。临床报道显示, 雾化吸入高渗盐水通过其高渗透性的作用,能够有效改善呼吸道黏膜流变学特性,对于呼吸道炎症具有显著的疗效[6,7]。目前,临床上关于高渗盐水雾化吸入治疗肺炎支原体感染继发哮喘的报道甚少。因此,本研究旨在探讨高渗盐水雾化吸入治疗支原体肺炎继发哮喘的临床效果及对 T 淋巴细胞亚群与 Th1、Th2 型细胞因子的影响。现报道如下。

1 资料与方法

1.1 一般资料

选取我院 2015 年 6 月到 2017 年 6 月间收治的支原体肺炎继发哮喘发作患儿 100 例为研究对象。所有患儿经临床确诊符合中华医学会感染病学科分会制定的支原体感染型肺炎[8]及儿童支气管哮喘防治指南中关于儿童哮喘的诊断标准[9]。纳入标准:① 年龄 3～13 岁,实验室血特异性诊断为肺炎支原体抗体(MP-IgM)阳性;② 肺部 CT 或胸部 X 线片明显可见支气管肺炎病灶,未现肺部扩张;③ 患儿咳嗽时间持续 4 周以上,以干咳为主,夜间或清晨加重。排除标准:① 其他因素引发的哮喘,合并支气管肺部发育不良、先天性心脏病、肿瘤、肺结核者;② 合并心力或呼吸衰竭、胸腔积液或气胸、严重肝肾等脏器功能障碍或不全者;③ 合并精神疾病、依从性差以及不愿参与本次研究治疗者。本次研究经院伦理会批准同意,所有患者均知情并签署同意书。采用随机数字分组法将符合上述纳入排除标准的 100 例患儿分为观察组和对照组, 各 50 例。观察组中男 26 例、女 24 例;年龄 3～13 岁,平均年龄(5.64± 1.33)岁;病程 20 d～3 个月,平均病程(1.79± 0.66)月。对照组中男 24 例、女 26 例,年龄 3～12 岁,平均年龄(5.47± 1.42)岁,病程 22d～3 个月,平均病程(1.82± 0.71)月。两组患儿临床一般资料比较无统计学差异(P>0.05),具可比性。

1.2 治疗方法

基础性治疗:所有患儿均给予吸氧、抗生素、维持酸碱度、电解质平衡及相应症状等对症治疗。观察组采用硫酸沙丁胺醇+3%高渗盐水进行治疗, 吸入用硫酸沙丁胺醇溶液(Glaxo Wellcome Operations,批准文号 H20140029,规格 5 mg× 20 mL),取 0.5 mL 溶入到 3%的高渗盐水 (取 10% NaCl 0.6 mL 加入 1.4 mL 注射用水中)2 mL 中,面罩雾化吸入治疗,每次治疗 30 min 后给予人工拍背排痰,4 次 /d, 连续治疗 2 周。对照组取 0.5 mL 硫酸沙丁胺醇溶液, 溶入到 2 mL 注射用生理盐水中,进行面罩雾化吸入治疗,其他同观察组。压缩式雾化吸入器(四川大爱科技公司生产,型号:405D-1 型)。

1.3 T 淋巴细胞亚群、Th1 及 Th2 细胞因子检测方法

分别于治疗前及治疗 3 个月后取患儿外周静脉血 5 mL,密封,常温下静止 60 min 后,2500 rpm 离心 15 min(贝克曼库尔特公司生产 Microfuge 20R 型离心机), 取上清液。采用 Attune® NxT 声波聚焦流式细胞仪 (赛默飞世尔科技生产)以及配套试剂对患儿血清 $CD3^+$、$CD4^+$、$CD8^+$ 进行检测分析;采用双抗夹心酶联免疫法(ELISA)法对血清干扰素(IFN)-γ 及白细胞介素(IL)-4 水平进行检测,ELISA 试剂盒购自默沙克生物,操作步骤严格按照说明书进行。

1.4 观察指标及疗效评价

比较两组患儿发热、咳嗽、肺内啰音、咽部肿痒等症状消失时间, 临床疗效, 治疗前、后 $CD3^+$、$CD4^+$、$CD8^+$、$CD4^+/CD8^+$、IFN-γ 及 IL-4 水平情况。疗效评价:患儿治疗后临床症状消失、CT 及 X 线片复查炎症消失或病灶减少 80%以上为治愈;临床症状基本消失、CT 及 X 线片复查炎症病灶范围减少 50%～79%为显效;临床症状好转、CT 及 X 线片复查炎症病灶范围减少 30%～49%为有效;临床症状、CT 及 X 线片复查结果与治疗前比较无变化或加重为无效,总有效率 =(治愈 + 显效 + 有效)/总例数× 100%。

1.5 统计学方法

数据采用 SPSS20.0 统计学软件进行分析处理, 对于符合正态分布的计量资料以($\bar{x}\pm s$)表示,采用独立样本 t 检验,计数资料以例数或(%)表示,采用 x^2 检验;比较结果以 P<0.05 表示差异有统计学意义。

2 结果

2.1 两组患儿临床症状消失时间比较

观察组患儿发热、咳嗽、肺内啰音、咽部肿痒等临床症状消失时间显著短于对照组,差异有统计学意义(P<0.05)。见表 1。

2.2 两组患儿临床疗效情况比较

观察组治愈 16 例、显效 27 例、有效 5 例、总有效 48 例,总有效率 96.00%;对照组治愈 9 例、显效 22 例、有效 9 例、总有效 40 例,总有效率 80.00%,观察组总有效率明显高于对照组,差异具有统计学意义(P<0.05)。见表 2。

2.3 两组患儿治疗前后 T 淋巴细胞亚群变化情况比较

两组患儿治疗前 $CD3^+$、$CD4^+$、$CD8^+$ 及 $CD4^+/CD8^+$ 水平比较差异无统计学意义 (P>0.05); 治疗后 $CD3^+$、$CD4^+$ 及 $CD4^+/CD8^+$ 水平均明显升高,$CD8^+$ 水平明显降低,差异均有统

计学意义（均 $P<0.05$）；且观察组治疗后 $CD3^+$、$CD4^+$ 及 $CD4^+/CD8^+$ 水平均明显高于对照组，$CD8^+$ 水平明显低于对照组，差异均有统计学意义（均 $P<0.05$）。见表 3。

表 1 两组患儿临床症状消失时间比较（$\bar{x}\pm s$）

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

Groups	Cases	Fever(d)	Cough(d)	Intrapulmonary rales (d)	Swollen itching of the pharynx(d)
Control group	50	5.22± 1.41	9.67± 2.35	6.22± 1.45	5.44± 1.78
Observation group	50	4.53± 0.89	6.13± 1.83	4.34± 1.23	3.28± 1.26
t		2.897	8.404	6.991	7.003
P		0.005	0.000	0.000	0.000

表 2 两组患儿临床疗效情况比较[n(%)]

Table 2 Comparison of clinical efficacy between two groups of children [n (%)]

Groups	Cases	Cure	Obvious effect	Effective	Invalid	Total effective rate
Control group	50	9(18.00)	22(44.00)	9(18.00)	10(20.00)	40(80.00)
Observation group	50	16(32.00)	27(54.00)	5(10.00)	2(4.00)	48(96.00)
x^2						6.061
P						0.014

表 3 两组患儿治疗前后 T 淋巴细胞亚群变化情况比较（$\bar{x}\pm s$）

Table 3 Comparison of T lymphocyte subsets before and after treatment in two groups of children（$\bar{x}\pm s$）

Groups	Cases	$CD3^+$(%)		$CD4^+$(%)		$CD8^+$(%)		$CD4^+/CD8^+$	
		Before surgery	After surgery	Before surgery	After surgery	Before surgery	After surgery	Before surgery	After surgery
Control group	50	59.23± 5.12	63.45± 5.38◆	31.46± 3.78	35.35± 3.88◆	24.56± 3.44	22.33± 1.22◆	1.50± 0.34	1.67± 0.29◆
Observation group	50	59.43± 5.24	68.78± 6.22◆	31.97± 3.54	42.64± 3.57◆	24.67± 3.46	19.12± 1.04◆	1.48± 0.36	1.79± 0.26◆
t		0.193	4.582	0.696	9.776	0.159	14.158	0.286	2.178
P		0.847	0.000	0.488	0.000	0.973	0.000	0.776	0.032

Note: compared with before treatment, ◆$P<0.05$.

2.4 两组患儿治疗前、后 Th1 及 Th2 细胞因子变化情况比较

两组患儿治疗前 IFN-γ 及 IL-4 表达水平比较差异无统计学意义（$P>0.05$）；治疗后 IFN-γ 表达水平显著升高，IL-4 表达水平显著降低，差异均有统计学意义（均 $P<0.05$）；观察组治疗后 IFN-γ 表达水平显著高于对照组，IL-4 表达水平显著低于对照组，差异均有统计学意义（均 $P<0.05$）。见表 4。

表 4 两组患儿治疗前后 Th1 及 Th2 细胞因子变化情况比较（$\bar{x}\pm s$）

Table 4 Comparison of Th1 and Th2 cytokines before and after treatment in two groups of children（$\bar{x}\pm s$）

Groups	Cases	IFN-γ(ng/L)		IL-4(ng/L)	
		Before surgery	After surgery	Before surgery	After surgery
Control group	50	679.53± 45.67	767.13± 105.28◆	108.66± 15.74	90.55± 13.58◆
Observation group	50	677.36± 47.68	1021.34± 166.78◆	107.68± 16.27	56.77± 13.46◆
t		0.232	14.022	0.306	17.048
P		0.817	0.000	0.760	0.000

Note: compared with before treatment, ◆$P<0.05$.

3 讨论

哮喘是世界范围内的一种高发慢性病，据相关报道，哮喘在全球范围内的临床发病率达到 3%左右，且随着近年环境的不断恶化，其发病率呈现出不断上升的趋势[10-12]。其致病因素较为复杂，包括过敏源、空气污染以及呼吸道病原菌感染等多种

因素,其中由肺炎支原体感染诱发哮喘是儿童时期常见的呼吸道疾病类型之一[13-15]。目前,临床上对于支原体肺炎诱发哮喘的发病机制主要为呼吸道炎症及高反应机制和免疫学机制[16]。哮喘患者本身就存在呼吸道高反应性,支原体肺炎感染后可造成呼吸道上皮组织及细胞结构的破坏,进而影响其正常功能,引起呼吸道慢性炎性反应,而呼吸道炎症反应是导致呼吸道高反应性的病理基础[17,18]。而人体呼吸道系统一旦感染肺炎支原体后,在机体补体及抗体的调节下,机体的免疫系统会立即变得具有趋化性,大量的白细胞及淋巴细胞便会出现,随后体内便会产生大量的免疫球蛋白及炎性因子,但当机体免疫功能低下或出现异常而不能完全消化这种刺激时,会导致相关细胞分泌出现紊乱,进而造成机体的相关功能障碍,导致哮喘发作[19,20]。目前,临床上针对支原体肺炎继发哮喘的治疗主要以氧疗、抗生素、糖皮质激素及对症治疗以改善患者临床症状的综合性治疗为主[21]。研究报道显示[22],高渗盐水具有较强的渗透性水化作用,通过雾化吸入高渗盐水能够有效改善呼吸道上皮黏液的流动性,促进呼吸道纤毛的摆动,从而增强呼吸道黏液的清除能力,此外,雾化吸入高渗盐水还能增强咳嗽诱导排痰的作用,进而改善患者肺部功能[23]。本研究结果显示,高渗盐水雾化吸入组患儿临床症状的改善情况及其临床疗效均显著优于对照组。结果提示,雾化吸入高渗盐水对改善支原体肺炎继发哮喘患儿的临床症状具有显著的效果。

相关研究表明,T 淋巴细胞亚群表达水平在支原体肺炎的诊断及预后中具有重要的意义[24]。T 淋巴细胞是由骨髓淋巴干细胞分化、发育而来,是白细胞的重要组成部分,存在于机体外周血液中,参与机体免疫应答,起到调节免疫功能的作用。T 淋巴细胞在数量在机体中相对稳定,正常情况下,其各亚群中 $CD3^+$、$CD4^+$ 及 $CD8^+$ 等细胞因子数量及比例均维持在一定范围内,对维持其他淋巴细胞正常功能起到调控或者辅助调控的作用,其平衡关系情况反应了机体免疫功能的状态。$CD3^+$ 代表机体总的 T 淋巴细胞数量,机体 $CD3^+$ 数量越多,表示机体参与免疫应答的免疫细胞数量及免疫活性越强。$CD4^+$ 活化后主要分化成辅助及调节性型 T 淋巴细胞,即 Th 细胞,主要起到辅助调节 $CD8^+$ 及 B 淋巴细胞的免疫应答功能的作用。而 Th 细胞主要分为 Th1 及 Th2,正常情况下,Th1/Th2 处于动态平衡。Th1 细胞的作用为介导细胞免疫应答,主要通过分泌 IFN-γ、TNF-β、IL-2 等促炎症递质,增强杀伤毒性炎症细胞作用;Th2 细胞的作用为介导体液免疫应答,通过分泌 IL-4、5、6 等炎性细胞因子,从而促进体液内抗体的产生。因此,Th1、Th2 表达水平变化过程反应了机体的免疫状态。本研究结果显示,观察组患儿治疗后 $CD3^+$、$CD4^+$、$CD4^+/CD8^+$ 及 IFN-γ 水平均明显高于对照组,$CD8^+$ 及 IL4 水平明显低于对照组。结果提示,雾化吸入高渗盐水能够有效提高支原体肺炎继发哮喘患儿 $CD3^+$、$CD4^+$、$CD4^+/CD8^+$ 及 IFN-γ 水平,抑制 $CD8^+$ 及 IL4 水平,起到增强患者免疫应答功能的作用。

综上所述,高渗盐水雾化吸入能够显著改善支原体肺炎激发哮喘发作患儿临床症状,提高 $CD3^+$、$CD4^+$、$CD4^+/CD8^+$ 及 Th1 水平,抑制 $CD8^+$ 及 Th1 水平,临床疗效确切,同时,由于本研究条件的局限性,针对高渗盐水雾化吸入对 T 淋巴细胞亚群的影响机制有待进一步研究。

参考文献(References)

[1] Kassisse E, García H, Prada L, et al. Prevalence of Mycoplasma pneumoniae infection in pediatric patients with acute asthmaexacerbation. [J]. Arch Argent Pediatr, 2018, 116(3): 179-185

[2] Duenas Meza E, Jaramillo CA, Correa E, et al. Virus and Mycoplasma pneumoniae prevalence in a selected pediatric population with acute asthma exacerbation[J]. J Asthma, 2016, 53(3): 253-260

[3] Li W, Liu YJ, Zhao XL, et al. Th1/Th2 Cytokine Profile and Its Diagnostic Value in Mycoplasma pneumoniae Pneumonia [J]. Iran J Pediatr, 2016, 26(1): e3807

[4] 彭丽琨,张翠香,陈泽莹,等.支气管哮喘患儿体内体液免疫及细胞免疫功能变化分析[J].医学综述, 2017, 23(9): 1847-1850

[5] Zhao JL, Wang X, Wang YS. Relationships between Th1/Th2 cytokine profiles and chest radiographic manifestations in childhood Mycoplasma pneumoniae pneumonia[J]. Ther Clin Risk Manag, 2016, 11 (12): 1683-1692

[6] Jochmann A, Artusio L, Robson K, et al. Infection and inflammation in induced sputum from preschool children with chronic airways diseases[J]. Pediatr Pulmonol, 2016, 51(8): 778-786

[7] Ma Q, Xiao P, Sun L, et al. Liver kinase B1/adenosine monophosphate-activated protein kinase signaling axis induces p21/WAF1 expression in a p53-dependent manner [J]. Oncol Lett, 2018, 16 (1): 1291-1297

[8] 中华医学会儿科学分会呼吸学组.儿童肺炎支原体肺炎诊治专家共识(2015 年版)[J].中华实用儿科临床杂志, 2015, 30(17): 1304-1308

[9] 中华医学会儿科学分会呼吸学组.儿童支气管哮喘诊断与防治指南(2016 年版)[J].中华儿科杂志, 2016, 54(3): 167-181

[10] Mclean W, Gillis J, Waller R. The BC Community Pharmacy Asthma Study: A study of clinical, economic and holistic outcomes influenced by an asthma care protocol provided by specially trained community pharmacists in British Columbia [J]. Can Respir J, 2003, 10 (4): 195-202

[11] Morales DR, Dreischulte T, Lipworth BJ, et al. Respiratory effect of beta-blocker eye drops in asthma: population-based study and meta-analysis of clinical trials [J]. Br J Clin Pharmacol, 2016, 82(3): 814-822

[12] Han RF, Li HY, Wang JW, et al. Study on clinical effect and immunologic mechanism of infants capillary bronchitis secondary bronchial asthma treated with bacterial lysates Broncho-Vaxom [J]. Eur Rev Med Pharmacol Sci, 2016, 20(10): 2151-2155

[13] Shao L, Cong Z, Li X, et al. Changes in levels of IL-9, IL-17, IFN-γ, dendritic cell numbers and TLR expression in peripheral blood in asthmatic children with Mycoplasma pneumoniae infection [J]. Int J Clin Exp Pathol, 2015, 8(5): 5263-5272

[14] Jobin MS, Moisan J, Bolduc Y, et al. Factors associated with the appropriate use of asthma drugs[J]. Can Respir J, 2011, 18(2): 97-104

[15] Flor-Escriche X, Méndez-Gómez J, Poblet-Cortés R, et al. Quality of life and associated factors in asthma in a Primary Care Center. Application of the reduced version of the Asthma Quality of Life Questionnaire[J]. Semergen, 2016, 42(8): 538-546

[16] Ding S, Wang X, Chen W, et al. Decreased Interleukin-10 Responses in Children with Severe Mycoplasma pneumoniae Pneumonia [J]. PloS One, 2016, 11(1): e014397

(下转第 2739 页)

437-441

[16] Tomer, Tarcic, Ohad, et al. Mutant p53 Prolongs NF-kappa B Activation and Promotes Chronic;Inflammation and Inflammation-Associated Colorectal Cancer[J]. Cancer Cell, 2013, 23(5): 634-646

[17] López I, L P O, Tucci P, et al. Different mutation profiles associated to P53 accumulation in colorectal cancer [J]. Gene, 2012, 499(1): 81-87

[18] Tavana O, Gu W. The Hunger Games: p53 regulates metabolism upon serine starvation[J]. Cell Metabolism, 2013, 17(2): 159-161

[19] Homayounfar R, Jedditehrani M, Cheraghpour M, et al. Relationship of p53 accumulation in peripheral tissues of high-fat diet-induced obese rats with decrease in metabolic and oncogenic signaling of insulin [J]. General & Comparative Endocrinology, 2015, 214(1473): 134-139

[20] Wang S J, Gu W. To be, or not to be: functional dilemma of p53 metabolic regulation [J]. Current Opinion in Oncology, 2014, 26(1): 78

[21] Kastenhuber E R , Lowe S W . Putting p53 in Context[J]. Cell, 2017, 170(6): 1062-1078

[22] Liu S,Tackmann N R,Yang J , et al. Disruption of the RP-MDM2-p53 pathway accelerates APC loss-induced colorectal tumorigenesis [J]. Oncogene, 2017, 36(10): 1374-1383

[23] Duffy M J , Synnott N C , Crown J . Mutant p53 as a target for cancer treatment [J]. European journal of cancer (Oxford, England: 1990), 2017, 83: 258-265

[24] Lerner L K, Francisco G, Soltys D T, et al. Predominant role of DNA polymerase eta and p53-dependent translesion synthesis in the survival of ultraviolet-irradiated human cells[J]. Nucleic Acids Research, 2017, 45(3): 1270-1280

[25] Tsai M H, Liu J F, Chiang Y C, et al. Artocarpin, an isoprenyl flavonoid, induces p53-dependent or independent apoptosis via ROS-mediated MAPKs and Akt activation in non-small cell lung cancer cells[J]. Oncotarget, 2017, 8(17): 28342-28358

[26] Kim E M, Jung C H, Kim J , et al. The p53/p21 complex regulates cancer cell invasion and apoptosis by targeting Bcl-2 family proteins [J]. Cancer Research, 2017, 77(11): 3092-3100

[27] Turkiew E, Falconer D, Reed N, et al. Deletion of Sarm1 gene is neuroprotective in two models of peripheral neuropathy[J]. Journal of the Peripheral Nervous System, 2017, 22(3): 162

[28] Liu Y, Chen X, Qin B , et al. Knocking Down Snrnp200 Initiates Demorphogenesis of Rod Photoreceptors in Zebrafish [J]. Journal of Ophthalmology, 2015, 2015(15): 1-7

[29] Wang Y J, Zhang Y K, Kathawala R , et al. Repositioning of Tyrosine Kinase Inhibitors as Antagonists of ATP-Binding Cassette Transporters in Anticancer Drug Resistance [J]. Cancers, 2014, 6 (4): 1925-1952

[30] Avi H, Ashok A, Ozgur G S, et al. Smoking and Male Infertility: An Evidence-Based Review [J]. The World Journal of Men's Health, 2015, 33(3): 143-145

(上接第 2729 页)

[17] Hu Y, Liu W, Huang C, et al. Home Dampness, Childhood Asthma, Hay Fever and Airway Symptoms in Shanghai, China: Associations, Dose-response Relationships and Lifestyle's Influences[J]. Indoor Air, 2014, 24(5): 450-463

[18] Parameswaran K, Knight AC, Keaney NP, et al. Ventilation and perfusion lung scintigraphy of allergen-induced airway responses in atopic asthmatic subjects[J]. Can Respir J, 2017, 14(5): 285-291

[19] Farne HA, Johnston SL. Immune mechanisms of respiratory viral infections in asthma[J]. Curr Opin Immunol, 2017, 9(48): 31-37

[20] Liu W, Liu S, Verma M, et al. Mechanism of Th2/Th17-predominant and Neutrophilic, Th2/Th17-low Subtypes of Asthma [J]. J Allergy Clin Immunol, 2017, 139(5): 1548-1558

[21] Coogan PF, Castro-Webb N, Yu J, et al. Active and Passive Smoking and the Incidence of Asthma in the Black Women's Health Study[J]. Am J Respir Crit Care Med, 2015, 191(2): 168-176

[22] Barben J, Kuehni C E. Hypertonic saline for acute viral bronchiolitis: take the evidence with a grain of salt [J]. Eur Respir J, 2014, 44(4): 827-830

[23] Corcoran TE, Godovchik JE, Donn KH, et al. Overnight delivery of hypertonic saline by nasal cannula aerosol for cystic fibrosis[J]. Pediatr Pulmonol, 2017, 52(9): 1142-1149

[24] Li P, Li Y, Shao G, et al. Comparison of immune responses to intranasal and intrapulmonary vaccination with the attenuated Mycoplasma hyopneumoniae 168 strain in pigs [J]. J Vet Med Sci, 2015, 77(5): 519-525