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益肺汤联合糖皮质激素治疗小儿难治性支气管肺炎的临床疗效及对患儿免疫功能影响*

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摘要 目的：探究益肺汤联合糖皮质激素治疗小儿难治性支气管肺炎中的临床效果及对患儿免疫功能的影响。**方法：**选择 2015 年 1 月至 2017 年 1 月于我院进行治疗的 288 例难治性支气管肺炎患儿为研究对象，按照随机数字表法将其均分为实验组与对照组，每组各 144 例患儿。对照组患儿在常规治疗的基础上加用糖皮质激素吸入治疗，实验组患儿在对照组基础上增加益肺汤进行治疗，治疗时间均为 7 d，对比两组患儿治疗有效率、临床指标(咳嗽、气喘、肺部湿罗音)改善时间、治疗前后外周血 T 淋巴细胞亚群指标及血清白介素 -8(Interleukine-8，IL-8)、肿瘤坏死因子 -α(Tumor necrosis factor-α，TNF-α)水平的变化。**结果：**(1)治疗后，实验组患儿的治疗有效率为 96.53%(139/144)，显著高于对照组患儿(89.58%，P<0.05)；(2)实验组患儿止咳、止喘、肺部湿罗音消失时间均短于对照组(P<0.05)；(3)实验组患儿治疗后 $CD4^+$ 高于对照组，$CD8^+$、血清 IL-8、TNF-α 水平均显著低于对照组(P<0.05)。**结论：**益肺汤联合糖皮质激素能够显著改善小儿难治性支气管肺炎临床症状，同时加快其症状转归，增强其免疫功能。

关键词：益肺汤；糖皮质激素；难治性支气管肺炎；免疫功能

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Efficacy of Yifei Decoction Combined with Glucocorticoid in the Treatment of Refractory Bronchopneum in Children and Its Effect on the Immune Function*

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ABSTRACT Objective: To explore the clinical effect of Yifei Decoction combined with glucocorticoid in the treatment of children with refractory bronchopneumonia and its influence on the immune function. **Methods:** 288 cases of patients with refractory bronchial pneumonia who were treated in our hospital from January 2015 to January 2017 were selected as the research objects. They were divided into the experimental group and the control group according to the random number table method. There were 144 children in each group. The control group was treated with glucocorticoid inhalation on the basis of routine treatment. The experimental group was treated with glucocorticoid inhalation. On the basis of control group, Yifei Decoction was added for 7 days. The treatment efficiency, improvement time of clinical indicators (cough, asthma, lung moist rale) and T lymphocyte subsets, IL-8 and TNF-α levels in the peripheral blood were compared between the two groups before and after treatment. **Results:** (1) After treatment, the treatment efficiency of experimental group was 96.53%(139/144), which was significantly higher than that of the control group (89.58%, P<0.05); (2) The disappearance time of cough, asthma and moist rales in the lung of the experimental group was shorter than that of the control group (P<0.05); (3) After treatment, the $CD4^+$ in the experimental group was higher than that in the control group, and the $CD8^+$, serum IL-8 and TNF-α levels were significantly lower than those in the control group (P<0.05). **Conclusion:** Yifei Decoction combined with glucocorticoid can significantly improve the clinical symptoms of children with refractory bronchopneumonia, accelerate the recovery of symptoms and enhance the immune function.

Key words: Yifei Decoction; Glucocorticoid; Refractory bronchopneumonia; Immune function

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前言

支气管肺炎是一类以发热、咳嗽、气急、肺部湿罗音等为典型临床症状的气道炎症，也是儿童尤其是婴幼儿最常见的感染性疾。，近些年，随着我国空气污染的加重，此类疾病的发病率有逐年上升趋势，已经成为儿童住院的最主要原因[1]。支气管肺

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炎好发于 2 岁以内儿童，多于冬春季节或气候骤变时出现，临床研究显示儿童气管、支气管管腔较成年人狭窄，纤毛摆动力较弱，其肺组织发育尚不成熟，因而在炎性刺激下分泌的黏液更易于堵塞气道，引发咳嗽、气喘等症状。且由于儿童免疫机能发育尚不完善，出现支气管肺炎后病情多发展较为迅速，炎症易于扩散、融合并蔓延至肺部，增加治疗难度[2,3]。

现阶段抗生素在支气管肺炎中应用频率越来越高，但部分患儿在接受正规抗炎治疗后，其肺部湿罗音仍难以消失，甚至有些患儿还会遗留肺不张、局限性支气管闭塞等后遗症，严重影响了其生活质量[4]。糖皮质激素在支气管肺炎治疗中的效果已经过临床验证，益肺汤属于祖国传统医学方剂，具有清热化痰、养阴益肺的功效[5]，本主要探讨了益肺汤联合糖皮质激素治疗小儿难治性支气管肺炎的临床效果及对患儿免疫功能的影响，结果报道如下。

1 资料与方法

1.1 一般资料

研究时间为 2015 年 1 月至 2017 年 1 月，将 288 例难治性支气管肺炎患儿按随机数字表法分为两组。对照组 144 例，男 80 例，女 64 例，年龄 2-11 岁，平均年龄(6.13± 1.01)岁，实验组 144 例，男 79 例，女 65 例，年龄 2-12 岁，平均年龄(6.19± 0.97)岁，两组一般资料比较无统计学差异(P>0.05)，具有可比性。

纳入标准：(1) 所有患儿均符合难治性支气管炎诊断标准[6]；(2)患儿病历资料齐全；(3)本研究经医院伦理学会批准实施。

排除标准：(1)合并肺部恶性病变者；(2)对本研究应用药物过敏者；(3)近期接受激素治疗者；(4)合并其他器质性疾病如冠心病、肾衰竭者。

1.2 治疗方法

两组患儿均接受相同的基础护理及治疗，包括营养支持、维持呼吸道通畅、吸氧、应用抗菌药物、气道管理等，对照组患儿在基础治疗的基础上加用糖皮质激素(布地奈德混悬液)吸入治疗，使用剂量为 1 mg/ 次，2 次 / 日，连续治疗 7 d；实验组患儿在对照组患儿基础上加用益肺汤进行治疗，服用剂量为 1 剂 /日，连续治疗 7 d。

1.3 观察指标及评测标准

1.3.1 治疗有效率 比较两组临床治疗效果，评价标准[7,8]：显效：咳嗽、气喘症状完全消失，偶尔发作已无需药物即可缓解，肺部湿罗音消失；有效：咳嗽、气喘症状较治疗前有明显好转，肺部湿罗音明显减轻；无效：咳嗽、哮喘症状改善不明显甚至有加重，肺部湿罗音无明显改观。

1.3.2 临床指标改善时间对比 对两组患儿临床症状诸如咳嗽、气喘、肺部湿罗音的消失时间进行记录和比较。

1.3.3 干预前后外周血 T 淋巴细胞亚群比较 采集两组患儿治疗前后空腹静脉血 5 mL，使用 ACEA 公司生产的 Quanreon 流式细胞仪对干预前后两组患儿 $CD4^+$ 及 $CD8^+$ 细胞比率进行检测对比。

1.3.4 血清炎性因子水平 采集两组患儿干预前后空腹静脉血 5 mL，于离心机离心后留置血清待用，置于低温条件下保存，待标本收集完毕后统一使用酶联免疫吸附法(ELISA)对干预前后血清 IL-8 及 TNF-α 水平进行检测对比。试剂盒由上海恒远生物科技有限公司提供。

1.4 统计学分析

采用 SPSS16.0 进行数据分析，计数资料以率(%)表示，组间比较行卡方检验，计量资料以($\bar{x}$± s)表示，组间比较行 t 检验，以 P<0.05 为差异有统计学意义。

2 结果

2.1 两组治疗有效率的比较

治疗后，实验组患儿治疗有效率为 96.53%，显著高于对照组(89.58%，P<0.05)，见表 1。

表 1 两组患儿治疗有效率对比[例(%)]

Table 1 Comparison of the effective rates between two groups of children

Groups	Cases	Obvious effect	Effective	Invalid	Effective rate
Experience group	144	130(90.28)	9(6.25)	5(3.47)	139(96.53)
Control group	144	114(79.17)	15(10.42)	15(10.42)	129(89.58)
x^2	-	-	-	-	5.373
P	-	-	-	-	0.020

2.2 两组临床指标改善时间的比较

实验组患儿止咳、止喘、肺部湿罗音消失时间均显著短于对照组(P<0.05)，见表 2。

表 2 两组患儿临床指标改善时间对比($\bar{x}$± s，天)

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

Groups	Cases	Relieve a cough	Antiasthmatic	Pulmonary wet rales disappear
Experience group	144	3.16± 1.21	2.13± 0.17	3.89± 0.46
Control group	144	3.69± 1.63	2.98± 0.31	4.61± 1.31
t	-	-3.133	-28.850	-6.223
P	-	0.002	<0.001	<0.001

2.3 两组干预前后外周血 T 淋巴细胞亚群的比较

干预前，两组患儿 $CD4^+$ 及 $CD8^+$ 水平对比差异无统计学意义(P>0.05)，两组患儿干预后 $CD4^+$ 细胞水平均较干预前显著上升，而 $CD8^+$ 细胞水平下降，且实验组患儿 $CD4^+$ 高于对照组，$CD8^+$ 低于对照组(P<0.05)，见表 3。

表 3 两组患儿干预前后外周血 T 淋巴细胞亚群比较($\bar{x}\pm s$, %)

Table 3 Comparison of the T lymphocyte subsets in peripheral blood between two groups before and after intervention

Groups	Cases	$CD4^+$		$CD8^+$	
		Pre intervention	Dry prognosis	Pre intervention	Dry prognosis
Experience group	144	29.26± 3.12	38.98± 4.16	29.61± 2.61	23.09± 2.68
Control group	144	29.18± 3.61	32.01± 2.69	29.43± 2.11	27.69± 1.61
t	-	0.201	16.883	0.644	-14.656
P	-	0.841	<0.001	0.520	<0.001

2.4 两组干预前后血清炎性因子水平的比较

干预前，两组患儿血清 IL-8 及 TNF-α 水平对比差异无统计学意义(P>0.05)，两组患儿干预后血清 IL-8 及 TNF-α 水平均较治疗前显著下降(P<0.05)，且实验组患儿上述指标均低于对照组(P<0.05)，见表 4。

表 4 两组患儿干预前后血清炎性因子水平对比($\bar{x}\pm s$，ng/L)

Table 4 Comparison of serum inflammatory factors levels between two groups before and after intervention($\bar{x}\pm s$, ng/L)

Groups	Cases	IL-8		TNF-α	
		Pre intervention	Dry prognosis	Pre intervention	Dry prognosis
Experience group	144	31.98± 4.11	14.61± 3.01	38.09± 1.21	26.01± 0.38
Control group	144	32.06± 4.09	20.16± 2.98	37.96± 2.04	30.96± 0.81
t	-	-0.168	-15.724	0.658	-66.390
P	-	0.868	<0.001	0.511	<0.001

3 讨论

小儿身体机能发育尚不完善，生理构造尚不成熟，在面对病原菌侵袭时更易出现各类病症，影响其正常生长发育[9,10]。支气管肺炎是小儿常见疾病之一，好发于冬春季节，以病毒感染最为常见[11]。流调学显示全球 5 岁以下儿童 2010 年死亡例数为 760 万，死于肺炎者占 18.0%，其中支气管肺炎占据较大比例，已经成为医学界面临重难点之一[12,13]。临床研究显示支气管肺炎的发病多因病原菌侵入气道，引起肺泡壁充血、水肿、炎性渗出，进而导致患儿出现呼吸不畅、肺泡萎缩等症状，影响气体交换，同时血氧浓度的降低还会引发二氧化碳滞留，导致呼吸衰竭，危及患儿生命，因而早期的干预及治疗具有重要意义[14,15]。支气管肺炎的治疗手段包括气道清理、吸氧、抗菌治疗等，但部分支气管肺炎患儿接受治疗后，病情变化并不明显，且随着病情的发展，支气管肺炎会演变为难治性支气管肺炎，治疗难度明显增加[16]。

糖皮质激素对支气管肺炎的治疗效果已经经过多项临床验证[17]，相关研究将 100 例喘息性支气管炎患儿按照病情进行分组的方式，就吸入型糖皮质激素在治疗婴幼儿喘息性支气管炎中的疗效进行了探究，结果显示所有接受糖皮质激素雾化吸入治疗患儿临床症状评分均明显降低，轻、中度患儿治疗 24 h 内临床症状评分下降明显，重度患儿在治疗 72 h 后也出现下降，提示糖皮质激素能够显著缓解支气管肺炎患儿临床症状[18,19]。此外，β2- 受体激动剂联合糖皮质激素在治疗小儿支气管哮喘合并肺炎中具有较好的疗效，接受联合治疗的观察组患儿治疗总有效率高达 97.5%，治疗后患儿肺功能指标第一秒用力呼气容积(Forced expiratory volume in first second, FEV1)及 FEV1% 均得到明显提升，且远期随访显示联合治疗的观察组患儿复发率仅为 5.0%，提示糖皮质激素能够较好的缓解患儿症状，改善其肺功能[20,21]。

祖国传统医学认为肺主气，司呼吸，为机体清浊气交换之地，同时肺气需要肾的滋养，因而主张调和肾肺精气，来维持个体的正常呼吸，支气管肺炎患儿病理病因多为肺肾两虚，因而主张通过补益肾脾作为治疗的切入点[22,23]。益肺汤是由金银花、麦冬、川穹、黄芩等药物组成，具有养阴益肺、清热化痰的功效。既往研究显示加用益肺汤的患者治疗后第 1 秒用力呼气量、最大吸气压、最大呼气压等治疗均明显改善，且患者的动脉血氧分压(Arterial partial pressure of oxygen，PaO_2)、动脉血二氧化碳分压(Partial pressure of carbon dioxide in artery，$PaCO_2$)显著优于对照组，提示益肺汤能够改善患者血气、肺功能相关指标[24,25]。此外，加用益肺汤的患者干预后 FEV1 及 FEV1%明显改善，且患者免疫球蛋白 E(Immunoglobulin E，IgE)较治疗前有所下降，免疫球蛋白 A(Immunoglobulin A，IgA)较治疗前有所提升，提示益肺汤能够改善患者临床症状，调节患者免疫状态，有利于改善其预后[26,27]。

本研究作业探讨了益肺汤联合糖皮质激素在治疗小儿难

治性支气管肺炎中的临床效果，结果显示加用益肺汤的患儿治疗有效率明显高于单纯应用糖皮质激素治疗，且患者的临床症状改善时间明显缩短，外周血 T 淋巴细胞亚群指标改善也较明显，血清 IL-8、TNF-α 水平明显下降。分析原因可能在于糖皮质激素能够显著降低气道炎性反应，显著缓解患者的临床症状，同时雾化吸入的方式能够直接作用于呼吸道，减少了药物经肝代谢引发的不良反应。也有研究指出，糖皮质激素的应用容易损伤气道黏膜细胞，长期应用容易引发患者全身反应，尤其是对小儿来说，耐受性更低，因而联合治疗的方式安全性更高[28]。本研究选择的益肺汤中含有多种中药材，具有润肺止咳、补肾益肺的功效，如金银花能够解热清毒、宣散风热，麦冬能够养阴生津、补益肾脾，川穹能够调理气血、通达血脉，多味药物联用一方面能够缓解患者临床症状，同时还能够改善患者的免疫机能，提高其对病原菌的抵抗能力，加快其病情转归[29,30]。

总之，益肺汤联合糖皮质激素能够显著改善小儿难治性支气管肺炎临床症状，同时加快其症状转归，增强其免疫功能。

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