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润肺健脾益肾汤对小儿过敏性咳嗽淋巴细胞亚群绝对计数的影响 *

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摘要 目的：探讨润肺健脾益肾汤对小儿过敏性咳嗽淋巴细胞亚群绝对计数的影响。**方法：**选择自 2017 年 5 月至 2019 年 1 月在盘锦辽油宝石花医院（我院）儿科就诊的过敏性咳嗽患儿 128 例，根据随机数字表法把患儿分为中药组与对照组，各 64 例，对照组给予沙丁胺醇治疗，观察组在对照组治疗对的基础上给予润肺健脾益肾汤治疗，两组都治疗观察 14 d，记录淋巴细胞亚群绝对计数变化情况。**结果：**治疗后中药组的总有效率为 98.3%，显著高于对照组的 88.3%(P<0.05)。两组治疗后的 1s 用力呼气容积(Forced expiratory volume in one second，FEV1)和 1s 用力呼气容积肺活量(Forced vital capacity，FVC)值都显著高于治疗前(P<0.05)，中药组也显著高于对照组(P<0.05)。两组治疗后的血清白细胞介素（interleukine，IL）-4、IL-13 水平都显著低于治疗前(P<0.05)，中药组也显著低于对照组(P<0.05)。两组治疗后的 $CD4^+$T 淋巴细胞绝对计数显著高于治疗前(P<0.05)，中药组也显著高于对照组(P<0.05)，两组治疗前后 $CD8^+$T 淋巴细胞绝对计数比较无差异(P>0.05)。**结论：**润肺健脾益肾汤治疗小儿过敏性咳嗽能提高 $CD4^+$T 淋巴细胞亚群绝对计数水平，抑制炎症因子的表达，从而改善患儿的肺功能，提高治疗效果。

关键词：润肺健脾益肾汤；小儿；过敏性咳嗽；淋巴细胞亚群绝对计数；炎症因子

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Effects of Runfei Jianpi Yishen Decoction on Absolute Count of Lymphocyte Subsets in Children with Allergic Cough*

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ABSTRACT Objective: To investigate the effects of Runfei Jianpi Yishen Decoction on the absolute count of lymphocyte subsets in children with allergic cough. **Methods:** From May 2017 to January 2019, A total of 128 children with allergic cough who were admitted to Panjin Liaoyou Gemstone Flower Hospital were enrolled and were equally divided into the Chinese medicine group and the control group accorded to the random number table. The control group were given salbutamol treatment, the observation group were given the treatment of Runfei Jianpi Yishen Decoction on the basis of the treatment group of the control group. Two groups were treated for 14 days, and the absolute counts of lymphocyte subsets were recorded. **Results:** The total effective rate of the Chinese medicine group after treatment were significantly higher than that of the control group (98.3% vs. 88.3%, P<0.05). The FEV1 and FVC values were significantly higher in the two groups after treatment (P<0.05), and the Chinese medicine group also significantly higher than the control group (P<0.05). The levels of IL-4 and IL-13 in the two groups were significantly lower than those before treatment (P<0.05), and the Chinese medicine group was also significantly lower than the control group (P<0.05). The absolute counts of $CD4^+$T lymphocytes after treatment were significantly higher than those before treatment (P<0.05), and the Chinese medicine group was also significantly higher than the control group (P<0.05). There was no difference in the absolute counts of $CD8^+$T lymphocytes between the two groups before and after treatment (P>0.05). **Conclusion:** Runfei Jianpi Yishen Decoction can improve the absolute count of $CD4^+$T lymphocyte subsets and inhibit the expression of inflammatory factors, thus improve the lung function and improving the therapeutic effect.

Key words: Runfei Jianpi Yishen Decoction; Pediatric; Allergic cough; Absolute counting of lymphocyte subsets; Inflammatory factors

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前言

过敏性咳嗽是一类与接触过敏原相关的咳嗽，该病的发病机制及病因尚不完全清楚，但是具有发病人数多、病情反复等特点[1]。过敏性咳嗽多发病于小儿，在临床上主要表现为呼吸不畅、气息喘促、发热等，长期发病可对患儿的身心健康造成严重负面影响[2]。过敏性咳嗽主要针状是咳嗽，与哮喘、上呼吸道感染、支气管炎的针状相似，和容易被误诊[3,4]。西医治疗该病的药物比较多，能够改善气道高反应性，缓解临床病症，但远期疗效欠佳，且停药后患儿容易复发[5]。中医认为该病辩证为肺、脾、肾等脏阳气虚损为主，在治疗上需要润肺健脾益肾。免疫球蛋白E(Immunoglobulin E，IgE)由白介素(Interleuki，IL)-4 产生，作为变态反应性疾病的重要指标参与免疫反应 [6-9]。同时 IL-4 和 IL-13 与过敏性咳嗽的发生发展密切相关[10,11]。而淋巴细胞亚群在过敏性咳嗽气道炎症中可发挥最终效应作用[12,13]。本文具体探讨了润肺健脾益肾汤对小儿过敏性咳嗽淋巴细胞亚群绝对计数的影响，以明确中药的应用价值与机制。现总结报道如下。

1 资料与方法

1.1 研究对象

选择 2017 年 5 月 -2019 年 1 月在我院治疗的过敏性咳嗽患儿 128 例，纳入标准：年龄 6-12 岁，符合过敏性咳嗽的诊断标准；病程≥ 1 个月；胸部 X 线检查未见异常；患儿及家属知情同意，依从性较好；本院伦理委员会批准了此次研究。排除标准：合并先天性免疫缺陷者；资料不全者；心、肝、肾及其他系统疾病者；支气管扩张、肺结核等结构性肺病者；临床资料缺乏者。

根据随机数字表法把患儿分为中药组与对照组各 64 例，两组的一般资料差异无统计学意义(P>0.05)。见表 1。

表 1 两组一般资料对比

Table 1 Comparison of general data between the two groups

Groups	n	Male /Female	Age(old)	Height(cm)	Weight(kg)	Course of disease (month)
Chinese medicine group	60	32/28	9.44± 2.58	134.20± 14.58	27.39± 5.33	12.48± 4.59
Control group	60	35/25	9.42± 1.98	133.09± 15.88	27.10± 7.19	13.20± 5.01

1.2 治疗方法

对照组：给予沙丁胺醇治疗，选择沙丁胺醇 (国药准字 H11021384，北京海德润医药集团有限公司)0.1 mg/kg+ 生理盐水雾化吸入给药，10 min/ 次，2 次 /d，治疗观察 14 d。

观察组：联合润肺健脾益肾汤治疗，组方：黄精 15 g，黄芩、橘红、石菖蒲各 6 g，熟地黄、菟丝子、杜仲、五味子、防风、沙参各 10 g，水复煎取 100 mL 并真空分装，每次口服 20-30 mL，2 次 /d，也治疗观察 14 d。

1.3 观察指标

(1)疗效判定：显效：相关临床症状完全消失，且在停药后无反复与加重；有效：相关临床症状减轻明显，停药后偶尔反复；无效：上述指标均未实现甚或恶化。(显效 + 有效)/ 组内例数× 100 %= 总有效率。(2)在治疗前后记录两组患儿的 1 s 用力呼气容积(Forced expiratory volume in one second，FEV1)和 1 s 用力呼气容积肺活量(Forced vital capacity，FVC)。(3)在治疗前后抽取患儿的空腹静脉血 4 mL(避免溶血)，室温静置 2 h，分为两份。其中第一份以 2000 r/min 离心 15 min(离心半径为 10 cm)留取血清，采用酶联免疫法检测血清 IL-4、IL-13 水平。第二份取全血组织，采用流式细胞测仪测定淋巴细胞亚群绝对计数 -$CD4^+$、$CD8^+$ 淋巴细胞水平。

1.4 统计方法

采用 SPSS22.00，肺功能、淋巴细胞绝对计数等计量数据用($\bar{x}$± s)表示，采用独立样本 t 检验与配对 t 检验；治疗效率等计数数据用%表示，采用 x^2 分析，P<0.05 有统计学意义。

2 结果

2.1 总有效率对比

治疗后中药组的总有效率为 98.3%，显著高于对照组的 88.3%(P<0.05)。见表 2。

表 2 两组总有效率对比(例，%)

Table 2 Comparison of total efficiency between the two groups (n, %)

Groups	n	Excellence	Effective	Invalid	Total effective rate
Chinese medicine group	60	55	4	1	59(98.3%)*
Control group	60	40	13	7	53(88.3%)

Note: compared with the control group, *P<0.05.

2.2 肺功能变化对比

两组治疗后的 FVC 与 FEV1 值都显著高于治疗前(P<0.05)，且中药组高于对照组(P<0.05)。见表 3。

2.3 血清 IL-4、IL-13 变化对比

两组治疗后的血清 IL-4、IL-13 水平都显著低于治疗前(P<0.05)，且中药组低于对照组(P<0.05)。见表 4。

2.4 淋巴细胞亚群绝对计数变化对比

两组治疗后的 $CD4^+$T 淋巴细胞绝对计数显著高于治疗前(P<0.05)，且中药组高于对照组(P<0.05)，两组治疗前后 $CD8^+$T 淋巴细胞绝对计数无差异(P>0.05)。见表 5。

表 3 肺功能变化对比(L)

Table 3 Comparison of lung function changes (L)

Groups	n	FVC		FEV1	
		Pretherapy	Post-treatment	Pretherapy	Post-treatment
Chinese medicine group	60	3.11± 0.24	3.89± 0.22*#	1.63± 0.21	1.98± 0.23*#
Control group	60	3.08± 0.13	3.51± 0.18*	1.65± 0.19	1.83± 0.15*

Note: Compared with before treatment, *P<0.05; compared with the control group, #P<0.05, the same below.

表 4 血清 IL-4、IL-13 变化对比(ng/mL)

Table 4 Comparison of serum IL-4 and IL-13 levels(ng/mL)

Groups	n	IL-4		IL-13	
		Pretherapy	Post-treatment	Pretherapy	Post-treatment
Chinese medicine group	60	92.44± 8.44	13.02± 2.41*#	148.92± 14.29	47.29± 8.49*#
Control group	60	93.39± 5.55	34.92± 4.81*	149.02± 15.00	87.32± 14.88*

表 5 淋巴细胞亚群绝对计数变化对比(例,%)

Table 5 Comparison of absolute counts of lymphocyte subsets (n,%)

Groups	n	$CD4^+$		$CD8^+$	
		Pretherapy	Post-treatment	Pretherapy	Post-treatment
Chinese medicine group	60	36.40± 5.33	38.78± 2.48*#	34.10± 5.10	33.82± 5.82
Control group	60	33.20± 4.55	35.10± 3.11*	33.98± 4.11	33.10± 5.00

3 讨论

过敏性咳嗽大部分患儿在经过治疗后,病情可以得到有效的控制,但也有部分患儿疗效不佳[14,15]。中医认为该病属于"肺胀"、"喘证"等范畴,以肺脾肾虚为主,累及其他功能脏器[16]。特别是小儿机体生理特征为"肺脾肾常虚、脏腑娇嫩",肺卫不固、肺卫闭郁、失于宣肃、藩篱薄弱,易反复受到外邪侵袭所致肺卫闭郁[17]。西医治疗该病可减轻气道阻塞,缓解临床病症,但是停药后患儿病情容易复发[18]。在润肺健脾益肾汤中,黄精可健脾润肺益肾;黄芩、橘红能够起到养阴敛肺、固肾平喘的作用;熟地黄、菟丝子有补肾纳气的功效;杜仲、五味子能够祛风解表、止痛;防风、沙参可补肾宁心、益气生津;石菖蒲能够理气化痰。该药方联合起到了标本兼治的功效[19]。本研究治疗后中药组的总有效率显著高于对照组;两组治疗后的 FVC 与 FEV1 值都显著高于治疗前,且中药组也显著高于对照组,表明润肺健脾益肾汤中的应用能改善患儿的肺功能,从而提高治疗效果。

研究表明,过敏性咳嗽是一种慢性炎症性疾病,由多种炎症介质、细胞因子和酶共同作用发病[20,21]。其中 IL-4 能够促进 B 细胞增殖,并且促进 B 细胞产生 IgE,体内 IL-4 水平升高,会导致 IgE 水平增加,使机体产生致敏反应[22]。IL-13 是一种多功能免疫调节因子,也可诱导 IgE 的产生[23]。临床上通过检测 IL-4、IL-13 水平,以及结合其他的一些辅助检查手段,可早期诊断与鉴别哮喘或过敏性咳嗽,有助于患儿早期治疗。本研究显示两组治疗后的血清 IL-4、IL-13 水平都显著低于治疗前,中药组也显著低于对照组, 表明润肺健脾益肾汤中的应用能抑制 IL-4、IL-13 的表达。主要在于该药各组方具有抗炎、改善循环等作用,使小儿局部炎症控制能力得到提高。

淋巴细胞亚群是引起气变态反应、气道高反应性的关键细胞,也可反映气道炎症变化,血液中淋巴细胞亚群绝对计数与咳嗽的严重程度密切相关,也可能在过敏性咳嗽发病中发挥重要作用[24]。淋巴细胞亚群绝对计数与免疫细胞结合,产生致敏反应。当致敏原再次刺激后,机体释放炎症介质,发生过敏性咳嗽,可能进一步发展为哮喘[25-27]。中医认为肺、脾、肾作为水液代谢的重要场所,功能异常机体会出现水液代谢出现障碍,从而诱发咳嗽的发生,为此在临床上需要健脾固本、补肾纳气[28-30]。本研究显示 两组治疗后的 $CD4^+$T 淋巴细胞绝对计数显著高于治疗前,中药组也显著高于对照组,两组治疗前后 $CD8^+$T 淋巴细胞绝对计数对比差异无统计学意义,表明润肺健脾益肾汤能改善机体的免疫功能。本研究也存在不足之处,样本量少,未进行远期疗效、复发率的随访,将在后续研究中深入分析。

总之,润肺健脾益肾汤治疗小儿过敏性咳嗽能提高 $CD4^+$T 淋巴细胞亚群绝对计数水平,抑制炎症因子的表达,从而改善患儿的肺功能,提高治疗效果。

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