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乙酰半胱氨酸辅助治疗小儿支原体肺炎的疗效及对 CD 分子含量的影响 *

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摘要 目的：探讨乙酰半胱氨酸辅助治疗小儿支原体肺炎的疗效及对 CD 分子含量的影响。**方法：**选择 2019 年 1 月至 2019 年 12 月我院收治的 90 例支原体肺炎患儿，通过随机数表法分为观察组和对照组，每组 45 例。对照组给予常规处理，观察组在对照组基础上，联合吸入乙酰半胱氨酸溶液治疗，两组均连续治疗 5 d。比较两组临床疗效、症状消失时间、住院时间、治疗前后、白细胞计数(WBC)、C 反应蛋白(CRP)、CD_3^+、CD_4^+、CD_4^+/CD_8^+ 的变化及不良反应的发生情况。**结果：**治疗后，观察组临床疗效总有效率为 93.33%，明显高于对照组(77.78%，$P<0.05$)；观察组咳嗽及肺啰音消失时间、住院时间明显短于对照组[(5.24± 1.07)d vs (6.59± 1.16)d，(5.53± 0.76)d vs (6.75± 1.04)d，(7.01± 1.40)d vs (8.11± 1.36)d]($P<0.05$)；观察组白细胞计数(WBC)、C 反应蛋白(CRP)明显低于对照组[(5.06± 0.72)× 10^9/L vs(7.34± 1.30)× 10^9/L，(1.86± 0.20)mg/L vs (4.63± 0.61)mg/L]，CD_3^+、CD_4^+、CD_4^+/CD_8^+ 明显高于对照组[(64.81± 5.63)% vs(58.03± 4.27)%，(36.86± 3.09)% vs(29.17± 2.64)%，(1.32± 0.18)% vs(1.20± 0.12)%]($P<0.05$)。两组治疗期间均未见明显不良反应。**结论：**乙酰半胱氨酸辅助治疗小儿支原体肺炎效果明显，其有助于促进疾病恢复，且安全性好，其内在机制可能和调节 CD 分子含量、修复免疫紊乱等相关。

关键词：小儿支原体肺炎；乙酰半胱氨酸；阿奇霉素；红霉素；CD 分子含量

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Clinical efficacy of Acetylcysteine Adjuvant Therapy Mycoplasma Pneumonia in the Treatment of Children and Its Effect on the Content of CD Molecular*

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ABSTRACT Objective: To study the clinical efficacy of acetylcysteine adjuvant therapy mycoplasma pneumonia in the treatment of children and its effect on the content of CD molecular. **Methods:** 90 children with mycoplasma pneumonia who received therapy from January 2019 to December 2019 in our hospital were selected, according to the random number table, they were divided into the observation group and the control group, each group had 45 cases. The control group was given routine treatment, on the basis of the control group, the observation group was combined with acetylcysteine solution inhalation, they were treated for 5 days. The clinical efficacy, symptoms disappear time, hospital stay, the changes of the white blood cell count (WBC), C reactive protein (CRP), CD_3^+, CD_4^+ and CD_4^+/CD_8^+ before and after treatment, and the occurrence of adverse reactions were compared between the two groups. **Results:** After treatment, the total effective rate in the observation group was 93.33%, which was significantly higher than that of the control group 77.78%($P<0.05$); the disappearance time of cough, pulmonary rales and hospital stay in the observation group were significantly shorter than that of the control group[(5.24± 1.07)d vs (6.59± 1.16)d, (5.53± 0.76)d vs (6.75± 1.04)d, (7.01± 1.40)d vs (8.11± 1.36)d]($P<0.05$); the leukocyte count (WBC), C-reactive protein (CRP) in the observation group were significantly lower than that of the control group[(5.06± 0.72)× 10^9/L vs (7.34± 1.30)× 10^9/L, (1.86± 0.20)mg/L vs (4.63± 0.61)mg/L], the CD_3^+, CD_4^+ and CD_4^+/CD_8^+ were significantly higher than that of the control group[(64.81± 5.63)% vs (58.03± 4.27)% ,(36.86± 3.09)% vs (29.17± 2.64)%, (1.32± 0.18)% vs (1.20± 0.12)%]($P<0.05$). There were no obvious adverse reactions in the two groups during the treatment. **Conclusion:** Acetylcysteine adjuvant therapy is effective for mycoplasma pneumonia in children, it can promote disease recovery with high safety, the internal mechanism may be related to the regulation of CD molecular content, repair of the immune function and so on.

Key words: Mycoplasma pneumonia in children; Acetylcysteine; Azithromycin; Erythromycin; CD molecular content

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前言

支原体肺炎是儿童中较为常见的一种疾病，在住院儿童社区获得性肺炎中所占比例为 10%~40%，患儿发病后病症可急可缓，症状以发热、咳嗽等为主，病情较为复杂，对患儿的健康、生长发育质量等均可带来诸多不良影响[1,2]。研究认为在支原体感染病进展成为支原体肺炎的过程中，抗感染的 T、B 细胞均可被激活，主要表现为细胞表面的 CD 分子含量出现相应的改变，并启动一系列的免疫抵抗反应，是疾病发生、发展的关键环节[3,4]。

临床上针对小儿支原体肺炎的治疗首选大环内酯类抗菌药物，其中最为常用的是阿奇霉素、红霉素，均具有较好的抗感染效果[5,6]。但除常规的抗感染和对症治疗之外，积极抑制气道高反应、促进痰液排出、保证呼吸道通畅也是治疗中的重要环节[7,8]。乙酰半胱氨酸是一种新型的粘液溶解剂，祛痰效果明显，主要适用于以粘稠分泌物过多为主要症状的呼吸系统疾病中，例如支气管扩张症、慢性阻塞性肺疾病等患者[9,10]。近年来，有研究显示乙酰半胱氨酸可减少机械通气患儿发生呼吸机相关性肺炎的机率[11,12]。本研究将乙酰半胱氨酸辅助用于治疗小儿支原体肺炎，旨在探讨其疗效及可能机制。

1 资料与方法

1.1 一般资料

选择我院儿科 2019 年 1 月至 2019 年 12 月收治的 90 例支原体肺炎患儿，纳入标准[13]，(1)符合《儿童肺炎支原体肺炎诊治专家共识(2015 年版)》中诊断标准，有发热、咳嗽等临床症状，酶联免疫吸附法(ELISA)S/CO＞1.1，并肺部 X 线片、实验室检查、核酸诊断检查确诊；(2)年龄 1~12 岁；(3)患儿家属研究知情同意书。排除标准[14]，(1)由于病毒性肺炎、细菌性肺炎、肺炎衣原体肺炎、肺结核、支气管异物等所致的肺炎症状；(2)合并哮喘、其余自身免疫系统疾病、重要脏器功能障碍、精神疾病者；(3)近 1 个月内使用过免疫抑制剂、激素类药物；(4)胸腔积液受累面积＞1/4；(5)依从性差，无法按医嘱服药。将 90 例支原体肺炎患儿通过随机数表法分为观察组 45 例和对照组 45 例，一般资料见表 1(P＞0.05)。

表 1 两组一般资料比较[$\bar{x}\pm s$，n(%)]

Table 1 Comparison of the general information between two groups[$\bar{x}\pm s$, n(%)]

Groups	Sex(M/F)	Age(years)	Weight(kg)	Course of disease (d)	Temperature(℃)	Pulmonary rales
Observation group(n=45)	29/16	3.66± 0.72	15.75± 3.12	3.43± 0.74	38.67± 0.70	40(88.89)
Control group(n=45)	27/18	3.70± 0.67	15.49± 3.46	3.50± 0.61	38.71± 0.68	41(91.11)

1.2 治疗方法

对照组给予常规处理，包括退热、止咳、镇静、休息、保持呼吸道通畅、保持足够的水分及营养等；给予注射用阿奇霉素(规格 0.125 g，厂家：东北制药集团沈阳第一制药有限公司，国药准字 H20000197)或注射用乳糖红霉素(规格 0.25 g，厂家：美罗药业股份有限公司，国药准字 H21021678)治疗，阿奇霉素剂量 10 mg/kg/d，1 次 /d，红霉素剂量 20 mg/kg，分 2 次滴注完毕，2 次 /d；并给予氨溴特罗口服液(规格 100 mL，厂家：海南舍画阁药业有限公司，国药准字 H20183185)，体重 4~8 kg 的患儿，每次剂量 2.5 mL；体重 8~12 kg 的患儿，每次剂量 5 mL；体重 12~16 kg，每次剂量 7.5 mL；的患儿体重＞16 kg 的患儿，每次剂量 10 mL；2 次 /d；观察组在对照组基础上，联合吸入用乙酰半胱氨酸溶液(规格 3 mL:0.3 g，厂家，ZAMBON S.p.A，进口药品注册证号 H20150548)治疗，剂量 3 mL 雾化吸入，1 次 /d；均连续治疗 5 d。

1.3 观察指标

1.3.1 疗效评价标准 显效：患儿的体温恢复正常，且无咳嗽、咽痛、头痛等临床症状，肺啰音消失；有效：患儿的体温正常，咳嗽、咽痛、头痛等临床症状有所改善，肺啰音基本消失；无效：患儿病情和体征无转变。临床总有效率 = 显效率 + 有效率[15]。

1.3.2 症状消失时间、住院时间 包括退热时间、咳嗽消失时间、肺啰音消失时间、胸部 X 线阴影消失时间。

1.3.3 实验室指标 在治疗前后患儿空腹状态下抽取静脉血 5 毫升，血液在转速为 3000 r/min 的状态下进行离心 10 分钟，完成后收集血清液，使用迈瑞公司生产的全自动血细胞分析仪 6900 型检测白细胞计数(WBC)、C 反应蛋白(CRP)。

1.3.4 CD 分子含量 留取上述血液样本 3 毫升，使用美国 BD 公司生产的 Calibur 型流式细胞仪检测 CD 分子含量，指标包括 CD_3^+、CD_4^+、CD_4^+/CD_8^+。

1.3.5 观察两组不良反应的发生情况 包括消化道不良反应、头晕头痛、皮疹等。

1.4 统计学分析

数据以 spss18.0 软件包处理，计量资料用($\bar{x}\pm s$)表示，组间比较采用 t 检验，计数资料采用 x^2 检验比较，以 P<0.05 表示差异具有统计学意义。

2 结果

2.1 两组临床疗效的比较

治疗后，观察组患儿的临床疗效为 93.33%，明显高于对照组患儿(77.78%，P＜0.05)，见表 2。

2.2 两组症状消失时间、住院时间的比较

两组退热时间比较差异无统计学意义(P＞0.05)，观察组患儿的咳嗽、肺啰音消失时间、住院时间均短于对照组(P＜0.05)，见表 3。

2.3 两组治疗前后实验室指标的比较

两组患儿治疗后 WBC、CRP 的指标水平均低于治疗前，且观察组以上指标均低于对照组(P＜0.05)，见表 4。

2.4 两组治疗前后 CD 分子含量的比较

治疗后，两组 CD_3^+、CD_4^+、CD_4^+/CD_8^+ 含量值均升高 (P＜0.05)，且观察组 CD_3^+、CD_4^+、CD_4^+/CD_8^+含量值均高于对照组(P＜

表 2 两组临床疗效比较[例(%)]

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

Groups	Markedly effective	Valid	Invalid	Total effective rate
Observation group(n=45)	27(60.00)	15(33.33)	3(6.67)	42(93.33)*
Control group(n=45)	20(44.44)	15(33.33)	10(22.22)	35(77.78)

Note: Vs the control group, *P<0.05.

表 3 两组症状消失时间、住院时间的比较($\bar{x}\pm s$,d)

Table 3 Comparison of the symptoms disappear time and hospital stay between two groups($\bar{x}\pm s$, d)

Groups	Antipyretic time	Cough disappear time	Pulmonary rales disappear time	Hospital stay
Observation group(n=45)	3.14± 0.58	5.24± 1.07*	5.53± 0.76*	7.01± 1.40*
Control group(n=45)	3.19± 0.51	6.59± 1.16	6.75± 1.04	8.11± 1.36

Note: Vs the control group, *P<0.05.

表 4 两组治疗前后实验室指标比较($\bar{x}\pm s$)

Table 4 Comparison of the laboratory index between two groups before and after treatment($\bar{x}\pm s$)

Groups		WBC(× 10^9/L)	CRP(mg/L)
Observation group(n=45)	Before treatment	14.27± 2.39	26.64± 2.45
	After treatment	5.06± 0.72*#	1.86± 0.20*#
Control group(n=45)	Before treatment	14.40± 2.11	26.51± 2.67
	After treatment	7.34± 1.30*	4.63± 0.61*

Note: Vs the before treatment, *P<0.05; vs the control group, #P<0.05.

表 5 两组治疗前后 CD 分子含量比较($\bar{x}\pm s$)

Table 5 Comparison of the CD molecular content between two groups before and after treatment($\bar{x}\pm s$)

Groups		CD_3^+(%)	CD_4^+(%)	CD_4^+/CD^{8+}
Observation group(n=45)	Before treatment	52.52± 4.69	25.17± 2.86	1.03± 0.16
	After treatment	64.81± 5.63*#	36.86± 3.09*#	1.32± 0.18*#
Control group(n=45)	Before treatment	51.09± 5.11	25.30± 2.42	1.05± 0.14
	After treatment	58.03± 4.27*	29.17± 2.64*	1.20± 0.12*

Note: Vs the before treatment, *P<0.05; vs the control group, #P<0.05.

0.05),见表 5。

2.5 两组不良反应的发生情况

两组患儿在我院接受治疗期间均未出现明显的不良反应。

3 讨论

支原体肺炎是临床儿科中常见的疾病之一,基本每隔 3~7 年就会出现一次地域周期性的流行,该病的病原体主要为肺炎支原体,也是呼吸道感染中最常见的致病菌类型,多发于学龄前儿童。近年的流行病学显示其发病趋于低龄化,5 岁以下的儿童发病率也逐渐升高[16,17]。支原体肺炎的主要病理改变为支气管壁充血水肿、分泌物对气道有堵塞、肺不张等,严重者甚至可进展成闭塞性细支气管炎、坏死性肺炎等,威胁患儿的生命安全[18,19]。

支原体肺炎的发病机制较为复杂,涉及多因素、多环节[20,21]。肺炎支原体侵入到呼吸道后可粘附于上皮细胞表面,对粘膜纤毛的清除和吞噬细胞的吞噬产生抵抗作用,这一系列反应除诱发患儿出现呼吸系统症状之外,也会对其余系统产生影响,尤其是细胞免疫功能的紊乱,也参与着支原体肺炎患儿的发生、发展[22,23]。$CD3^+$ 是反映人体细胞免疫功能的重要指标,其表达降低提示细胞免疫功能的衰弱,机体容易遭受到感染[24]。CD_4^+、CD_4^+/CD_8^+ 是也是机体重要的免疫细胞因子,在反复出现慢性感染、急性感染的状态下,CD_4^+、CD_4^+/CD_8^+ 的表达可明显降低,导致细胞免疫功能出现障碍[25,26]。目前已有较多报道显示在支原体肺炎患儿中,CD_3^+、CD_4^+、CD_4^+/CD_8^+ 含量明显降低,而通过增加细胞免疫功能可增加机体对多种病原体的抗病能力[27,28]。

临床上针对支原体肺炎患儿的治疗首选抗感染治疗,其中阿奇霉素、红霉素是常用药物,主要是通过对病原体转肽中所依赖的 RNA 蛋白质合成过程产生阻断作用,继而抑制支原体繁殖,抗菌效果满意。但阿奇霉素和红霉素在抑制气道高反应、促进痰液排出方面效果欠佳,而增加此类手段在促进疾病早期恢复中也十分关键[29]。氨溴特罗是临床上常用的祛痰药,具有较好的痰液溶解效果和润滑呼吸道等效果,有助于促进肺表面

活性物质和呼吸液的分泌，并促进纤毛运动，适用于诸多急慢性呼吸道疾病、支气管分泌异常等的临床治疗。但也有报道显示支原体肺炎患儿单独使用氨溴特罗的祛痰效果仍有可提升的空间[30,31]。乙酰半胱氨酸是一类新型的痰液溶解剂，除具有祛痰效果之外，其也是一种富含巯基的抗氧化剂，有助于修复组织细胞损伤，临床上也已应用于诸多呼吸道疾病的治疗中，目前的临床研究也显示其联合氨溴特罗有助于提高祛痰效果[32,33]。此外，乙酰半胱氨酸对新生儿支气管肺炎的炎症因子具有调节作用，可缓解全身炎症反应所致的组织器官损伤[34]。近年来研究显示乙酰半胱氨酸除具有祛痰、抗氧化等作用之外，对免疫功能也具有调节效果[35]。

本研究结果显示联合乙酰半胱氨酸辅助治疗的患儿 CD_3^+、CD_4^+、CD_4^+/CD_8^+ 含量的升高程度均优于对照组，通过分析是由于乙酰半胱氨酸作为细胞内还原谷胱肽的前体，对机体大量活性氧的生产具有抑制作用，而在抑制氧化应激反应的同时，可减少炎症因子、趋化因子、粘附分子等物质的生成，发挥免疫保护作用，最终帮助细胞免疫功能紊乱的修复。谢梦莹[36]等研究也显示乙酰半胱氨酸对 NF-KB 的活化具有抑制作用，可抑制肺泡巨噬 T 细胞、中性粒细胞的生成，减少炎症介质的产生，并通过降低炎症因子水平的过程发挥调节 T 淋巴细胞亚群的作用，并改善免疫功能。因此，联合乙酰半胱氨酸治疗的患者 CD 含量水平值的变化程度更明显。此外，本研究结果显示联合乙酰半胱氨酸治疗的患儿临床疗效总有效率高达 93.33%，咳嗽、肺啰音消失时间和住院时间明显更短，实验室指标水平也改善得更明显，分析可能是由于乙酰半胱氨酸富含巯基，可和氧化基团之间相互结合，令痰液中糖蛋白多肽链的二硫键出现断裂，从而达到促进粘蛋白分解、降低痰液粘稠度的效果，且乙酰半胱氨酸还可通过抑制致病菌的粘附对已生成的生物细胞被膜产生破坏作用，降低炎症反应，并联合氨溴特罗的祛痰作用及阿奇霉素、红霉素的抗菌作用，联合用药发挥相互协同作用，进一步促进疾病的恢复，在提高机体抗病能力、缩短病程方面也具有积极意义。但本研究也存在着部分不足，例如样本量过少、研究时间过短等，此后仍需持续研究来验证本结论。

综上所述，乙酰半胱氨酸辅助治疗小儿支原体肺炎效果明显，其有助于促进疾病恢复，且安全性好，其内在机制可能和调节 CD 分子含量、修复免疫紊乱等相关。

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