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阿奇霉素联合糖皮质激素治疗重症支原体肺炎患儿的临床效果分析 *

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摘要 目的:分析阿奇霉素联合糖皮质激素治疗重症支原体肺炎患儿的临床效果及安全性。**方法:**选择 112 例重症支原体肺炎患儿并通过抽签法分为对照组与观察组,每组各 56 例。对照组予以阿奇霉素治疗,观察组在对照组基础上加用糖皮质激素治疗。观察并比较两组患儿治疗前后血沉(ESR)、血清乳酸脱氢酶(LDH)、同工酶 MB(CK-MB)、肌酸激酶(CK)、谷草转氨酶(AST)、C 反应蛋白(CRP)、白细胞介素 -6(IL-6)、肿瘤坏死因子 -α(TNF-α)水平、$CD4^+$ 及 $CD8^+$,临床疗效及不良反应的发生情况。**结果:**观察组有效率为 96.4%,显著高于对照组(82.1%),差异有统计学意义(P<0.05)。治疗后,两组 ESR、血清 LDH、CK-MB、CK、AST、CRP、IL-6、TNF-α 水平及 $CD8^+$ 均较治疗前显著降低,且观察组以上指标均明显低于对照组;两组 $CD4^+$ 均较治疗前明显上升,且观察组显著高于对照组,差异均有统计学意义(P<0.05)。观察组退热、咳嗽缓解、肺部湿啰音消失时间均明显短于对照组(P<0.05)。两组不良反应的发生情况比较差异无统计学意义(P>0.05)。**结论:**阿奇霉素联合糖皮质激素治疗小儿重症支原体肺炎的临床效果明显优于单用阿奇霉素治疗,可有效减轻心肌损伤和炎症反应,并提高患儿免疫功能,且安全性高。

关键词:重症支原体肺炎;阿奇霉素;糖皮质激素

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Analysis of Clinical Efficacy of Azithromycin Combined Glucocorticoids in Treatment of Severe Pneumonia Mycoplasma*

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ABSTRACT Objective: To analyze the influences of azithromycinantibiotic combined glucocorticoids on the levels of erythrocyte sedimentation rate (ESR), serum lactate dehydrogenase (LDH) and inflammatory cytokines levels as well as the clinical effect of severe pneumonia mycoplasma. **Methods:** 112 children with severe pneumonia mycoplasma who were treated in our hospital were selected and randomly divided into the control group and the observation group with 56 cases in each group. The patients in the control group were treated with azithromycinantibiotic, while the patients in the observation group were treated with glucocorticoid on the basis of the control group. Then the levels of ESR, LDH, isoenzyme MB (CK-MB), creatine kinase (CK), aspertate aminotransferase (AST), c-reactive protein (CRP), interleukin 6 (IL-6), tumor necrosis factor-α (TNF-α), $CD4^+$ and $CD8^+$, the clinical efficacy and adverse reactions between two groups were observed and compared before and after the treatment. **Results:** The effective rate in the observation group was higher than that of the control group, and the difference was statistically significant (P<0.05). After treatment, the levels of ESR, LDH, CK-MB, CK, AST, CRP, IL-6, TNF-α and $CD8^+$ in the two groups decreased, which were lower in the observation group than those of the control group (P<0.05). After treatment, the levels of $CD4^+$ in both groups increased, which was higher in the observation group than that of the control group (P<0.05). The disappearance time of fever, cough relief, lung rale of observation group were shorter than those of the control group(P<0.05). There was no statistically significant difference in the adverse reactions between the two groups (P>0.05). **Conclusion:** Azithromycin combined with glucocorticoids was more effective than azithromycin alone in the treatment of severe mycoplasma pneumonia with high safety, which could obviously relieve the myocardial injury and inflammatory response, enhance the immune function.

Key words: Severe mycoplasma pneumonia; Azithromycin; Glucocorticoids

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前言

小儿支原体肺炎是的一种肺部炎症性疾病,是因感染肺炎支原体所致,咳嗽、发热是其主要临床症状,部分患儿可出现呼吸困难、气促等[1]。其中,重症支原体肺炎发病急,进展快,容易使患儿出现全身炎症反应及大量胸腔积液等,严重影响患儿的生长发育[2]。目前,小儿重症支原体肺炎的临床治疗仍以大环酯类抗生素为主,但可产生一定的耐药性,且疗效欠佳[3]。糖皮质

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激素的抗菌谱比较广泛，且安全性高，现已逐步用于治疗支原体肺炎。相关研究显示重症支原体肺炎患者血沉(ESR)、乳酸脱氢酶(LDH)明显上升，能够直观反映病情进展[4]。因此，本研究主要探讨了阿奇霉素联合糖皮质激素对重症支原体肺炎患儿ESR、LDH水平及临床疗效的影响，以期为临床治疗提供参考依据。

1 资料与方法

1.1 一般资料

选择2014年6月~2016年6月于我院就诊的112例小儿重症支原体肺炎，所有患儿均经临床确诊为支原体肺炎，且符合重症支原体肺炎的诊断标准[5](出现① ~⑤ 中任1项，且满足⑥ ~⑩ 中任3项)：① 需予以机械通气；② 感染性休克，需血管升压类药物；③ 意识或定向障碍；④ 氧合指数在250 mmHg以下；⑤ 低血压，需予以强力液体复苏；⑥ 多肺叶可见浸润现象；⑦ 呼吸频率在30次/分以上；⑧ 体温在36℃以上；⑨ 血小板在10× 10^9/L以下；⑩ 白细胞在4× 10^9/L以下。纳入无其他急慢性疾病史、未接受任何相关治疗者。排除肺结核、其他病原菌引起的肺炎、肝肾功能显著障碍、过敏体质者。本研究家属已签署知情同意书，且经过医院伦理委员会的许可，按抽签法分作对照组和观察组，各56例。对照组有29例男性，有27例女性；年龄3~10岁，平均(6.41± 0.27)岁；病程3~15d，平均(7.61± 0.53)d。观察组有24例男性，有32例女性；年龄2~9岁，平均(5.23± 0.45)岁；病程2~13d，平均(6.28± 0.23)d。两组一般资料比较差异均无统计学意义(P>0.05)，具有可比性。

1.2 治疗方法

两组患儿均予以吸氧、祛痰、平喘、止咳、降温、维持电解质平衡、营养心肌、保护肝功能等基础治疗。对照组予以静脉滴注10 mg/kg阿奇霉素(湖北潜江制药股份有限公司，规格0.25 g，国药准字H20020342，批号140525)，每天1次。观察组在对照组基础加用糖皮质激素治疗，静脉滴注1 mg/kg·d甲泼尼龙琥珀酸钠 (国药集团容生制药有限公司，规格0.5 g，国药准字H20010098，批号140521)，两组均连续治疗7 d。

1.3 临床疗效评估

痊愈：体征及症状全部消退，实验室及胸部X线平片未见异常；显效：体征及症状显著缓解，实验室指标显著改善，胸部X线平片提示肺部纹理、阴影显著减轻；好转：体征及症状有一定缓解，部分实验室指标异常，胸部X线平片提示肺部纹理、阴影有减轻；无效：体征及症状缓解不明显，实验室指标无减轻，胸部X线平片提示肺部纹理及阴影增粗。有效=痊愈+显效+好转[6]。记录两组患儿退热时间、咳嗽缓解时间、肺部湿啰音消失时间。定期检测两组患儿血尿常规、肝肾功能等，并记录其用药期间的不良反应。

1.4 指标检测

采集两组患儿治疗前后空腹外周静脉血2 mL，肝素抗凝后常规分离血清，保存待检。① ESR予以全自动血沉仪检测；② 予以酶联免疫吸附法检测LDH、同工酶MB(CK-MB)、肌酸激酶(CK)、谷草转氨酶(AST)；③ 予以免疫荧光法检测C反应蛋白(CRP)、白细胞介素-6(IL-6)、肿瘤坏死因子-α(TNF-α)；④ 予以流式细胞仪检测$CD4^+$、$CD8^+$值。

1.5 统计学分析

选择spss18.0行数据统计，计量资料以均数± 标准差($\bar{x}\pm s$)表示，用t检验，计数资料以[(n)%]表示，用x^2检验，以P<0.05为差异有统计学意义。

2 结果

2.1 两组患儿临床疗效的比较

观察组有效率为96.4%，显著高于对照组(82.1%)，差异有统计学意义(P<0.05)，见表1。

表1 两组患儿临床疗效比较

Table 1 Comparison of the clinical efficacy between two groups

Groups	Recovery	Markedly	Better	Invalid	Effective rate
Control group (n=56)	26	11	9	10	82.1%
Observation group(n=56)	34	14	6	2	96.4%#

Note: Compared with control group, #P<0.05.

2.2 两组患儿治疗前后ESR水平的比较

治疗前，两组ESR水平比较差异无统计学意义(P>0.05)；治疗后，两组ESR水平均较治疗前显著降低，且观察组明显低于对照组，差异有统计学意义(P<0.05)，见表2。

表2 两组患儿治疗前后ESR水平的比较($\bar{x}\pm s$)

Table 2 Comparison of the ESR before and after treatment between two groups

Groups	Time	ESR(mm/h)
Control group (n=56)	Before treatment	50.49± 5.67
	After treatment	37.85± 4.20△
Observation group(n=56)	Before treatment	51.68± 6.23
	After treatment	26.43± 3.61△#

Note：Compared with before treatment, △ P<0.05; Compared with control group, #P<0.05.

2.3 两组患儿治疗前后心肌酶水平的比较

治疗前，两组血清心肌酶(LDH、CK、CK-MB、AST)水平比较差异均无统计学意义(P>0.05)；治疗后，两组血清 LDH、CK、CK-MB、AST 水平均较治疗前显著降低，且观察组以上指标均明显低于对照组，差异有统计学意义(P<0.05)，见表 3。

表 3 比较两组患儿治疗前后血清心肌酶水平的变化($\bar{x}\pm s$)

Table 3 Comparison of the serum myocardial enzymes levels between two groups before and after treatment($\bar{x}\pm s$)

Groups	Time	LDH(U/L)	CK(U/L)	CK-MB(U/L)	AST(U/L)
Control group (n=56)	Before treatment	321.40± 70.42	258.73± 42.61	52.93± 9.60	98.73± 17.43
	After treatment	180.64± 36.50$^{\triangle}$	141.62± 26.80$^{\triangle}$	30.78± 5.11$^{\triangle}$	42.78± 11.46$^{\triangle}$
Observation group (n=56)	Before treatment	324.97± 68.53	260.92± 43.11	54.35± 9.21	96.30± 16.72
	After treatment	152.77± 33.49$^{\triangle\#}$	124.78± 17.85$^{\triangle\#}$	24.62± 4.51$^{\triangle}$	36.41± 9.10$^{\triangle\#}$

Note: Compared with before treatment, $^{\triangle}$P<0.05; Compared with control group, $^{\#}$P<0.05.

2.4 两组患儿治疗前后炎性因子水平的比较

治疗前，两组血清 CRP、IL-6、TNF-α 水平比较差异均无统计学意义(P>0.05)；治疗后，两组血清 CRP、IL-6、TNF-α 水平均较治疗前显著降低，且观察组明显低于对照组，差异有统计学意义(P<0.05)，见表 4。

表 4 两组患儿治疗前后血清炎性因子水平的比较($\bar{x}\pm s$)

Table 4 Comparison of the serum inflammatory factors levels between two groups before and after treatment($\bar{x}\pm s$)

Groups	Time	CRP(mg/L)	IL-6(ng/L)	TNF-α(ng/L)
Control group (n=56)	Before treatment	65.47± 9.85	17.96± 2.35	65.43± 5.97
	After treatment	30.58± 4.61$^{\triangle}$	13.60± 1.70$^{\triangle}$	34.29± 4.62$^{\triangle}$
Observation group(n=56)	Before treatment	67.12± 9.43	18.75± 2.81	63.81± 6.30
	After treatment	17.85± 3.20$^{\triangle\#}$	10.24± 1.48$^{\triangle\#}$	24.51± 3.80$^{\triangle\#}$

Note: Compared with before treatment, $^{\triangle}$P<0.05; Compared with control group, $^{\#}$P<0.05.

2.5 两组患儿治疗前后免疫功能的比较

治疗前，两组 $CD4^+$、$CD8^+$、$CD4^+/CD8^+$ 水平比较差异均无统计学意义(P>0.05)；治疗后，两组 $CD4^+$、$CD4^+/CD8^+$ 均明显高于治疗前，且观察组明显高于对照组，$CD8^+$ 水平显著低于治疗前，且观察组明显低于对照组，差异有统计学意义(P<0.05)，见表 5。

表 5 两组患儿治疗前后 $CD4^+$、$CD8^+$、$CD4^+/CD8^+$ 水平的比较($\bar{x}\pm s$)

Table 5 Comparison of the $CD4^+$, $CD8^+$ and $CD4^+/CD8^+$ levels between two groups before and after treatment($\bar{x}\pm s$)

Groups	Time	$CD4^+$(%)	$CD8^+$(%)	$CD4^+/CD8^+$
Control group (n=56)	Before treatment	30.23± 2.39	26.98± 1.85	1.19± 0.23
	After treatment	33.67± 4.20$^{\triangle}$	24.60± 2.11$^{\triangle}$	1.42± 0.25$^{\triangle}$
Observation group(n=56)	Before treatment	29.14± 3.85	27.84± 1.76	1.26± 0.18
	After treatment	35.94± 4.27$^{\triangle\#}$	21.53± 1.42$^{\triangle\#}$	1.63± 0.29$^{\triangle\#}$

Note：Compared with before treatment, $^{\triangle}$P<0.05; Compared with control group, $^{\#}$P<0.05.

2.6 两组患儿体征及症状消失时间的比较

观察组退热时间、咳嗽缓解时间、肺部湿啰音消失时间均明显短于对照组，差异有统计学意义(P<0.05)，见表 6。

表 6 两组患儿体征及症状消失时间的比较($\bar{x}\pm s$)

Table 6 Comparison of the disappearance time of signs and symptoms between two groups($\bar{x}\pm s$)

Groups	Antifebrile time(d)	Cough relief time (d)	Lung wet then disappear time(d)
Control group (n=56)	3.46± 1.12	5.49± 1.36	5.89± 1.39
Observation group(n=56)	1.54± 0.40$^{\#}$	4.11± 1.20$^{\#}$	4.51± 1.17$^{\#}$

Note: Compared with control group, $^{\#}$P<0.05.

2.7 两组患儿不良反应发生情况的比较

对照组有 3 例患儿出现腹痛，5 例恶心呕吐；观察组各有 2 例胃肠道反应及皮疹，两组不良反应的发生率比较差异无统计学意义(P>0.05)。

3 讨论

支原体肺炎是小儿呼吸道的常见疾病，肺炎支原体可经鼻腔、口部分泌物由空气传播，存在散发性，临床症状轻重不一，其中重症支原体肺炎具有治疗难度高、病情重、反复发作等特点[7]。肺炎支原体是一种介于细菌和病毒的微生物，可独立生存，对抗生素的敏感性比较高，由于其不存在细胞壁，因此青霉素等旨在破坏细胞壁成分的抗生素对其无效，大环酯类抗生素是其首选药物[8]。阿奇霉素是大环酯类的新型药物，组织渗透性比较好，可经血液循环进入机体组织器官的单核细胞、巨噬细胞等[9]。同时，阿奇霉素可于溶酶内蓄留，从而直接作用于感染病灶，使细菌转肽作用受到抑制，从而干扰其蛋白质的生成，其半衰期比较长，能够维持一个有效的药物浓度[10]。目前，随着此类药物的广泛应用，支原体的耐药性明显增加，影响了临床效果。

有研究报道在大环酯类抗生素药物治疗基础上使用糖皮质激素能够显著提高小儿支原体肺炎的临床效果[11]。糖皮质激素是临床常用免疫调节剂，可起到免疫调节、抗过敏、抗炎等多种药物学作用[12]。本结果显示联合糖皮质激素治疗者有效率显著高于阿奇霉素治疗者，与临床研究报道结果相似，进一步证实二者联合治疗的可行性。ESR 作为一种疾病活动及炎症感染的典型标志物，能够直观反映疾病的动态变化、发展程度等[13]，重症支原体肺炎患儿 ESR 显著高于普通支原体患儿。本研究结果显示联合糖皮质激素治疗者 ESR 显著降低，说明两者联合治疗能够利于病情的控制。临床研究显示小儿重症支原体肺炎由于酸中毒、低氧血症等导致体内生成过多的氧自由基，与病原体释放的酶类、毒素等一起作用于心肌细胞，导致心肌损伤[14]。LDH、CK、CK-MB、AST 是常见的心肌酶，当心肌受到损伤时可导致系列心肌酶释放入血，造成心肌酶浓度增加[15]。本结果显示联合糖皮质激素治疗后 LDH、CK、CK-MB、AST 水平显著降低，说明两者联合治疗可使心肌损伤减轻，避免病情进一步恶化，促进患儿的恢复。

机体感染肺炎时，支原体通过气道进入肺部，对肺泡处的巨噬细胞产生刺激，生成 CRP、IL-6、TNF-α 等炎性细胞因子，再刺激肺部多种细胞因子，诱导外周循环的炎症细胞，使其进入肺泡与肺间质，进而生成大量细胞因子与炎症介质，进一步的加重机体炎症反应[16,17]。梅玉霞研究发现阿奇霉素治疗基础上加用糖皮质激素治疗重症支原体肺炎可使炎症因子水平显著降低，本结果也证实此结果[18]。另有学者报道免疫功能紊乱是支原体肺炎的主要发病机制，支原体能够导致 T 淋巴细胞亚群的正常比例受到破坏，诱导细胞因子的生成减少、紊乱[19]。$CD4^+$ 作为一种辅助性 T 淋巴细胞，可介导淋巴细胞的应答反应；$CD8^+$ 可导致靶抗原杀伤，若两者动态平衡受到破坏可引起病理性的免疫损伤 [20]。本结果显示联合糖皮质激素治疗后 $CD4^+$、$CD4^+/CD8^+$ 显著上升，且 $CD8^+$ 明显降低，说明两者联合治疗能够纠正机体的免疫功能紊乱。且经两者联合治疗后患儿的体征及症状消失时间明显缩短，且无明显不良反应，说明两者联合治疗可促进患儿临床表现的改善，从而减轻其痛苦，增加患儿的耐受性。

综上所述，阿奇霉素联合糖皮质激素治疗小儿重症支原体肺炎的临床效果明显优于单用阿奇霉素治疗，可有效减轻心肌损伤和炎症反应，并提高患儿免疫功能，且安全性高。

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