doi: 10.13241/j.cnki.pmb.2018.23.030

# 蓝芩口服液联合阿奇霉素对支原体肺炎患儿免疫功能、血清β防御素-2、D-二聚体的影响*

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**摘要 目的：**探究蓝芩口服液联合阿奇霉素治疗支原体肺炎患儿的临床疗效及对其免疫功能、血清β防御素-2、D-二聚体水平的影响。**方法：**选取2014年1月至2016年6月扬州大学附属医院收治的支原体肺炎患儿80例，根据随机数字法将其分为对照组和治疗组。对照组以阿奇霉素常规治疗，治疗组在阿奇霉素常规治疗基础上服用蓝芩口服液。治疗1周后，评价两组患者的临床症状，检测和比较两组免疫功能及血清β防御素-2、D-二聚体水平的变化。**结果：**治疗后，治疗组总有效率为95%，显著高于对照组(80%，P<0.05)。两组患儿治疗后血液中的白细胞计数均显著下降(P<0.05)，且治疗组患儿治疗前后白细胞计数下调幅度显著高于对照组(P<0.05)。两组患儿治疗后血清$CD_3^+$、$CD_4^+$、$CD_4^+/CD_8^+$、NK细胞水平均较治疗前显著升高(P<0.05)，且治疗组患儿治疗前后以上指标水平变化幅度均明显高于对照组(P<0.05)。治疗后，治疗组与对照组患儿血清β防御素-2水平分别上调至(562.86± 45.38)pg/mL及(607.37± 47.26)pg/mL，血清D-二聚体浓度分别下调至(83.28± 10.46)pg/mL及(125.94± 14.83)pg/mL，治疗组以上指标的变化均显著高于对照组(P<0.05)。**结论：**蓝芩口服液联合阿奇霉素治疗支原体肺炎患儿的疗效明显优于阿奇霉素常规治疗，且能显著改善患者的免疫功能，降低患儿血清中D-二聚体的水平、升高β防御素-2的水平。

**关键词：**蓝芩口服液；支原体肺炎；阿奇霉素；免疫功能；β防御素-2；D-二聚体

**中图分类号：**R563.15 **文献标识码：**A **文章编号：**1673-6273(2018)23-4527-04

# Effects of Lanqin Oral Liquid Combined with Azithromycin on the Immune Function, Serum β Defensin-2 and D-Dimer Levels of Children with Mycoplasma Pneumonia*

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**ABSTRACT Objective:** To investigate the clinical effect of lanqin oral solution combined with azithromycin on the immune function and serum β-defensin-2 and D-dimer levels of children with mycoplasma pneumonia. **Methods:** From January 2014 to June 2016, eighty cases of children with mycoplasma pneumonia in Yangzhou University Hospital were divided into the control group and the treatment group according to the random number method. The control group was treated with azithromycin and the treatment group was treated with lanling oral liquid combined with azithromycin. After one week of treatment, the clinical effect, immune function, levels of β-defensin-2 and D dimer were detected and compared betwen two groups. **Results:** After treatment, the total effective rate of treatment group was 95% , which was significantly higher than that of the control group (80%, P<0.05). After treatment, the white blood cell count in the both groups were significantly decreased (P<0.05), and the decline degree of white blood cell count in the treatment group was significantly higher than that in the control group (P<0.05). The levels of $CD_3^+$, $CD_4^+$, $CD_4^+/CD_8^+$ and NK cells in the serum of both groups were higher than those in the control group(P<0.05), and the serum levels of these indicators in the treatment group was higher than that in the control group(P<0.05). The serum β-defensin-2 levels in the treatment group and in the control group were increased to (607.37± 47.26) pg/mL and (562.86± 45.38) pg/mL, and the serum D-dimer levels were decreased to (83.28± 10.46) pg/ml and (125.94± 14.83) pg/mL. The reduction degree of treatment group was significantly higher than that of the control group (P<0.05). **Conclusion:** The effect of lanqin oral solution combined with azithromycin on the treatment of children with mycoplasma pneumonia was better than that of azithromycin alone, it could improve the immune function of patients and reduce the serum D-dimer level and increase the serum β defensin-2 level.

**Key words:** Lanqin oral liquid; Mycoplasma pneumonia; Azithromycin; Immune function; β defensin-2; D-dimer

**Chinese Library Classification(CLC): R563.15 Document code: A**

**Article ID: 1673-6273(2018)23-4527-04**

* 基金项目：江苏省自然科学基金项目(BK20130432)

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(收稿日期：2018-08-06 接受日期：2018-08-30)

## 前言

支原体肺炎是儿童和青少年在春初及冬天寒冷季节最容易患的肺部炎症疾病[1],为临床呼吸内科常见病,具有发病急、病程长、范围广等特点[2,3],严重影响患儿的健康成长与日常生活。若临床医治不及时,将会严重损害患儿呼吸系统,进而诱使心、脑、胃、肝、肾等各个器官发生病变[4-6],威胁患儿的生命。另外,该病的治疗与住院费用也给家庭带来了严重的经济负担[8]。因此,开发能缩短病程、廉价而高效的治疗方法仍然是小儿支原体肺炎研究的热点问题。目前,临床上用于治疗小儿支原体肺炎的药物主要为大环内酯类抗生素,如阿奇霉素、红霉素等[9,10]。研究表明蓝芩口服液对于呼吸道感染疾病具有良好的治疗作用[11]。本研究选取 2014 年 1 月至 2016 年 6 月扬州大学附属医院收治的支原体肺炎患儿 80 例, 观察蓝芩口服液联合阿奇霉素对支原体肺炎患儿临床疗效及对患儿免疫功能、血清中β 防御素 -2、D- 二聚体水平的影响,且将与阿奇霉素常规治疗进行对比,旨在为进一步推广中西药结合治疗支原体肺炎患儿提供参考依据。

## 1 资料与方法

### 1.1 一般资料

选择 2014 年 1 月至 2016 年 6 月来扬州大学附属医院就诊的支原体肺炎患儿 80 例, 经过临床医师检查发现各患者均出现不同程度的咳嗽、发热、呼吸音粗等临床症状,X 射线全胸片检查发现各患儿肺部纹理不同程度的增多且出现紊乱,两侧或单侧下肺出现斑片状的模糊阴影,符合支原体肺炎的诊断标准[12]。纳入标准的患儿均无先天性呼吸系统疾病,无心、脑、肝、肾等重要器官的器质性病变,也无其他感染性疾病。

将纳入标准的 80 例患儿按照随机数字法分为对照组和治疗组,每组 40 例,治疗组中,男性 21 例,女性 19 例,年龄 2～11 岁,平均年龄(6.2± 2.5)岁,病程 1~8 天,平均病程(2.9± 0.6)天,体温 37.2~39.4 ℃,平均体温(37.7± 1.5)℃,单侧感染 28 例,双侧感染 12 例;对照组中,男性 20 例,女性 20 例,年龄 1～12 岁,平均年龄(6.4± 2.7)岁,病程 1~9 天,平均病程(2.8± 0.7)天,体温 37.1~39.5 ℃,平均(37.8± 1.4)℃,单侧感染 27 例,双侧感染 13 例。两组患儿的性别、年龄、病程、病情、体温等一般资料比较差异均无统计学意义(P>0.05),具有临床可比性。本研究中所有患儿家长均签署知情同意书,且本研究经扬州大学附属医院伦理委员会批准。

### 1.2 治疗方法

对照组 40 例患儿采用阿奇霉素进行常规治疗[13],将每 250 mg 乳糖酸阿奇霉素充分溶解于 250 mL 5%的葡萄糖溶液中,按照患儿体重换算, 以每天 10 mg/kg 的剂量进行静脉滴注给药,治疗 7 天后观察疗效。实验组 40 例患儿在采用阿奇霉素进行常规治疗的同时,加用蓝芩口服液进行治疗[11],一次 1 支,一日 3 次,治疗 7 天后观察疗效。

### 1.3 指标观察

两组患儿在治疗前后分别抽取静脉血 4 mL 于 5 mL 无抗凝剂的试管中,取其中 2 mL 全血,利用全自动生化仪,测定其中白细胞计数。其余的 2 mL 室温下静置 2 h 后, 置于离心机中,4 ℃于 3000 rpm 下离心 10 min,吸取上清液,采用流式细胞仪检测血清中 $CD_3^+$、$CD_4^+$、$CD_8^+$、NK 细胞水平,采用免疫散射比浊法测定血清中 D- 二聚体的水平,采用酶联免疫检测法,根据β 防御素 -2 试剂盒(南京建成生物有限公司,南京,中国)说明书中的实验操作,测定其血清浓度。

### 1.4 疗效评价

疗效评价标准分为显效、有效、无效。患儿的咳嗽、发热及呼吸音粗等临床症状消退,X 射线全胸片检查肺部正常, 且白细胞计数 (临床上正常人血液中白细胞计数的标准为(3.5~9.5) × $10^9$/L)及体温恢复到正常范围,则判定为显效;若患儿的临床症状、白细胞计数、体温向正常范围靠近,X 射线全胸片检查肺部阴影面积减少,则说明该患儿被有效治疗后病情好转;若患儿的以上症状均无明显改善或加重,则判定为无效。

### 1.5 统计学分析

采用 SPSS17.0 软件进行统计学分析, 计量资料数据以平均值± 标准差(Mean± s) 表示,多组间比较采用 One-way ANOVA 检验中的 Dunnett 检验;计数资料以百分比(%)表示,采用卡方检验,以 P<0.05 为差异具有统计学意义。

## 2 结果

### 2.1 两组患儿疗效比较结果

治疗组 40 例患者中,29 例显效,9 例好转,1 例无效,临床总有效率可达 95%;对照组 40 例患者,22 例显效,10 例好转,8 例无效,临床总有效率为 80%,明显低于治疗组(P<0.05),详细结果见表 1。

表 1 两组治疗效果的比较[例(%)]

Table 1 Comparison of the clinical effect between two groups[n(%)]

| Groups | n | Effective | Improve | Invalid | Always effective |
|---|---|---|---|---|---|
| Treatment group | 40 | 29(72.5) | 9(22.5) | 2(5) | 38(95) |
| Control group | 40 | 22(55) | 10(25) | 8(20) | 32(80) |
| P | | 0.009 | 0.152 | 0.011 | 0.012 |

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

### 2.2 两组患者治疗前后外周血白细胞计数的比较

治疗前,两组患儿外周血白细胞计数比较差异无统计学意义(P >0.05),有临床可比性。治疗后,两组患儿外周血白细胞计数均较治疗前显著减少(P<0.05),且治疗组患儿治疗前后外周血白细胞计数变化幅度显著高于对照组(P<0.05)。详细数据见表 2。

表 2 两组患者治疗前后外周血血液白细胞计数($10^9$/L)的比较

Table 2 Comparison of the blood white blood cell count ($10^9$/L) between two groups before and after treatment

| Groups | n | Before treatment | After treatment | Difference | #P |
|---|---|---|---|---|---|
| Treatment group | 40 | 25.41± 2.79 | 5.84± 0.74*# | 19.57± 1.58* | 0.001 |
| Control group | 40 | 24.85± 2.66 | 9.73± 1.03# | 15.12± 1.39 | 0.001 |
| *P | | 0.318 | 0.007 | 0.009 | |

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

### 2.3 两组患儿治疗前后血清中 $CD_3^+$、$CD_4^+$、$CD_8^+$、NK 细胞水平的比较

治疗前，两组患儿血清 $CD_3^+$、$CD_4^+$、$CD_8^+$、$CD_4^+/CD_8^+$、NK 细胞水平比较差异无统计学意义(P>0.05)；治疗后，两组患儿血清 $CD_3^+$、$CD_4^+$、$CD_4^+/CD_8^+$、NK 细胞水平均较治疗前显著升高(P<0.05)，且治疗组患儿治疗前后血清 $CD_3^+$、$CD_4^+$、$CD_4^+/CD_8^+$、NK 细胞水平变化幅度均明显高于对照组血液中。详细数据见表 3。

表 3 两组患儿治疗前后血清 $CD_3^+$、$CD_4^+$、$CD_8^+$、NK 细胞水平的比较

Table 3 Comparison of the $CD_3^+$, $CD_4^+$, $CD_8^+$ and NK cell levels in serum between two groups before and after treatment

| Groups | n | Times | $CD_3^+$ | $CD_4^+$ | $CD_8^+$ | $CD_4^+/CD_8^+$ | NK |
|---|---|---|---|---|---|---|---|
| Treatment group | 40 | Before treatment | 57.08± 5.83 | 33.56± 3.27 | 27.53± 2.46 | 1.22± 0.12 | 8.53± 0.96 |
| | | After treatment | 70.45± 6.65# | 40.62± 3.82# | 25.11± 2.31# | 1.62± 0.14#* | 14.26± 1.34#* |
| | | P | 0.002 | 0.007 | 0.031 | 0.005 | 0.004 |
| Control group | 40 | Before treatment | 56.69± 5.72 | 33.48± 3.53 | 27.46± 2.61 | 1.22± 0.13 | 8.48± 1.04 |
| | | After treatment | 67.42± 6.17# | 37.23± 3.92# | 26.61± 2.53 | 1.40± 0.14# | 11.25± 1.18# |
| | | P | 0.011 | 0.019 | 0.063 | 0.015 | 0.008 |

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

### 2.4 两组患者治疗前后血清 β 防御素 -2 水平比较

治疗前，两组患儿血清β 防御素 -2 水平分别为(406.58± 36.41)pg/mL 及(411.26± 38.02)pg/mL，差异无统计学意义(P>0.05)；治疗后，治疗组与对照组患儿血清β 防御素 -2 浓度分别上调至(562.86± 45.38)pg/mL 及(607.37± 47.26)pg/mL，治疗组的上调幅度显著高于对照组(P <0.05)，详细数据见表 4。

表 4 两组患者治疗前后血清 β 防御素 -2(pg/mL)含量的比较

Table 4 Comparison of the serum levels of β-defensin-2 (pg/mL) between two groups before and after treatment

| Groups | n | Before treatment | After treatment | Difference | #P |
|---|---|---|---|---|---|
| therapy group | 40 | 406.58± 36.41 | 607.37± 47.26*# | 196.11± 20.37* | 0.001 |
| Control group | 40 | 411.26± 38.02 | 562.86± 45.38# | 156.28± 18.43 | 0.003 |
| *P | | 0.372 | 0.017 | 0.006 | |

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

### 2.5 两组患者治疗前后血清 D- 二聚体水平的比较

治疗前，治疗组与对照组患儿血清 D- 二聚体浓度分别为(271.63± 37.29)pg/mL 及(274.82± 35.41)pg/mL，差异无统计学意义(P>0.05)；治疗后，治疗组与对照组患儿血清β 防御素 -2 浓度分别下调至(83.28± 10.46)pg/mL 及(125.94± 14.83)pg/mL，治疗组的下调幅度显著高于对照组(P<0.05)。

表 5 两组患者治疗前后血清 D- 二聚体含量的比较(ng/mL，n=60)

Table 5 Comparison of the serum D-dimer levelsbetween two groups before and after treatment(ng/mL, n=60)

| Groups | n | Before treatment | After treatment | Difference | P |
|---|---|---|---|---|---|
| therapy group | 40 | 271.63± 37.29 | 83.28± 10.46*# | 191.54± 20.62* | 0.001 |
| Control group | 40 | 274.82± 35.41 | 125.94± 14.83# | 145.69± 17.58 | 0.006 |
| P | | 0.347 | 0.005 | 0.008 | |

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

## 3 讨论

支原体肺炎是由支原体经呼吸道进入机体肺部，刺激机体

内的单核细胞、淋巴细胞、巨噬细胞，释放多种细胞因子，引起机体正常生理功能失衡，最终诱发肺部的一系列炎症反应。近年来多项研究表明[14-16]支原体肺炎机体内免疫功能异常。机体内的细胞免疫的应答细胞主要为 T 细胞与 NK 细胞。T 细胞是由骨髓造血干细胞分化，迁移至胸腺发育而成。由于 T 细胞抗原受体与其表面 $CD_3$ 分子的结合物为 T 细胞活化所必需的物质，血液中 $CD_3^+$ 的水平可代表成熟 T 细胞的水平。根据 T 细胞表面糖蛋白 CD 分子表达产物的不同，可分为 $CD_4$ 和 $CD_8$，临床上常用 $CD4^+/CD8^+$ 来反应机体免疫功能的状态，$CD_4^+/CD_8^+$ 比值升高说明机体免疫功能增强，反之则说明减弱[17]。NK 细胞为大颗粒淋巴细胞，可直接溶解破坏肿瘤细胞与病毒感染细胞，是机体的第一道防御屏障，发挥着重要的免疫调节作用，因此机体内 NK 细胞数量在一定程度上反映了机体细胞免疫功能[18]。

β 防御素 -2 是由皮肤粘膜上皮细胞合成和分泌的具有特殊结构的内源性抗菌肽，对皮肤粘膜起着一定的保护作用。β 防御素 -2 可直接杀伤入侵机体的病原微生物，参与机体的免疫反应，减缓机体的炎症反应并加速创伤的修复[19,20]。有研究显示[21]肺炎患者血清β 防御素 -2 的浓度显著低于健康人，而治疗后，其血清浓度恢复正常水平。D- 二聚体是由交联纤维蛋白降解而来，可特异性代表纤维蛋白产生和纤溶发生的程度。当机体处于高凝血状态时，血浆 D- 二聚体水平将明显升高，而其含量的高低可反映血液凝血状态及纤溶活性的强弱[22,23]。因此，血浆 D- 二聚体水平的测定则可用于血栓性疾病的辅助诊断。有报道显示[24,25]血浆 D- 二聚体的水平在凝血功能异常的肺炎患者体内明显升高。

本研究以支原体肺炎患儿为研究对象观察蓝芩口服液联合阿奇霉素对其临床疗效及免疫功能、血清中β 防御素 -2、D- 二聚体水平的影响，研究结果显示蓝芩口服液联合阿奇霉素治疗的总有效率为 95%，显著高于阿奇霉素治疗的 80%。两组患儿治疗后外周血白细胞计数均显著下降，且治疗组患儿在治疗前后白细胞计数下调幅度显著高于对照组，说明蓝芩口服液联合阿奇霉素对支原体感染的肺炎具有一定的治疗作用，且效果好于阿奇霉素单独治疗。两组患儿治疗后血清中 $CD_3^+$、$CD_4^+$、$CD_4^+/CD_8^+$、β 防御素 -2、NK 细胞水平均升高，而蓝芩口服液联合阿奇霉素治疗组患儿治疗前后血清中该指标水平变化幅度均高于对照组，说明蓝芩口服液联合阿奇霉素能改善患儿的免疫功能，效果优于阿奇霉素单独治疗。另外，两组患儿治疗后血清中 D- 二聚体浓度均下调，且蓝芩口服液联合阿奇霉素治疗组的下调幅度显著高于对照组，说明蓝芩口服液联合阿奇霉素能在一定程度上改善患儿的凝血状态。

综上所述，蓝芩口服液联合阿奇霉素治疗支原体肺炎患儿的疗效明显优于阿奇霉素常规治疗，且能显著改善患者的免疫功能，降低患儿血清中 D- 二聚体的水平、升高β 防御素 -2 的水平。由于血浆 D- 二聚体水平在反映患者凝血状态的灵敏度上有限，因此在后期实验中将进一步测定其他凝血功能相关指标，全面阐述蓝芩口服液联合阿奇霉素对支原体肺炎患儿凝血功能的影响。

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