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麻杏石甘汤合玉屏风散对支原体肺炎患儿血清炎症因子、氧化应激及T淋巴细胞亚群的影响*

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摘要 目的:探讨麻杏石甘汤合玉屏风散对支原体肺炎患儿血清炎症因子、氧化应激及T淋巴细胞亚群的影响。**方法:**选取我院儿科门诊于2016年12月至2018年7月间收治的86例支原体肺炎患儿,按随机数字表法分为观察组(43例)和对照组(43例)。对照组采用常规治疗,观察组在对照组基础上联合使用麻杏石甘汤合玉屏风散治疗,两组均治疗14 d。比较两组患儿疗效及临床症状变化情况,检测并比较两组患儿血清炎症因子、氧化应激指标和T淋巴细胞亚群变化情况,观察两组患儿治疗过程中的不良反应发生情况。**结果:**观察组总有效率为93.02%(40/43),高于对照组的76.74%(33/43)(P<0.05)。观察组患儿体温恢复时间、啰音消失时间、咳嗽消失时间和X线检查恢复正常时间均明显短于对照组(P<0.05)。治疗14 d后,两组患儿血清白介素-2(IL-2)水平明显升高,而白介素-4(IL-4)、白介素-6(IL-6)和肿瘤坏死因子-α(TNF-α)水平明显降低(P<0.05);且与对照组比较,观察组患儿治疗14 d后的血清IL-2水平明显较高,而IL-4、IL-6和TNF-α水平明显较低(P<0.05)。与治疗前比较,治疗5 d后、治疗14 d后,两组患儿血浆丙二醛(MDA)降低,超氧化物歧化酶(SOD)水平升高(P<0.05);与对照组比较,观察组治疗5 d后的血浆MDA明显较低,而SOD水平明显较高(P<0.05)。治疗14 d后,两组患儿CD3⁺、CD4⁺、CD4^{+/}CD8⁺明显升高,且观察组高于对照组,而两组患儿CD8⁺明显降低,且观察组低于对照组(P<0.05)。两组不良反应比较差异无统计学意义(P>0.05)。**结论:**麻杏石甘汤合玉屏风散治疗支原体肺炎疗效显著,能够缓解临床症状、炎症反应,减轻患儿氧化应激状态,并可提高患儿免疫功能。

关键词:麻杏石甘汤;玉屏风散;支原体肺炎;炎症因子;氧化应激;T淋巴细胞亚群

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Effects of Maxing Shigan Decoction and Yupingfeng Powder on Serum Inflammatory Factor, Oxidative Stress and T Lymphocyte Subsets in Children with Mycoplasma Pneumonia*

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ABSTRACT Objective: To investigate the effects of Maxing Shigan Decoction and Yupingfeng Powder on serum inflammatory factors, oxidative stress and T lymphocyte subsets in children with mycoplasma pneumonia. **Methods:** 86 children with mycoplasma pneumonia who were admitted to pediatric clinic from our hospital from December 2016 to July 2018 were selected. All the children were randomly divided into observation group (43 cases) and control group (43 cases) according to random number table method. The control group was treated with routine treatment, while the observation group was treated with Maxing Shigan Decoction and Yupingfeng Powder on the basis of the control group. Both groups were treated for 14 days. The curative effect and clinical symptoms of the two groups were compared. The changes of serum inflammatory factors, oxidative stress index and T lymphocyte subsets were detected and compared between the two groups. The occurrence of adverse reactions during the treatment of two groups of children were observed. **Results:** The total effective rate of the observation group was 93.02%(40/43), which was significantly higher than that of the control group 76.74%(33/43)(P<0.05). The recovery time of body temperature, rale disappearance time, cough disappearance time and X-ray examination in the observation group were significantly shorter than those in the control group (P<0.05). After 14 days of treatment, the level of serum interleukin-2 (IL-2) increased significantly in both groups. The levels of interleukin-4 (IL-4), interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α) decreased significantly (P<0.05). Compared with the control group, the level of serum IL-2 in the observation group was significantly higher after 14 days of treatment, while the levels of IL-4, IL-6 and TNF-α were significantly lower (P<0.05). Compared with before treatment, after 5 days of treatment and 14 days of treatment, the plasma malondialdehyde (MDA) decreased, and

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superoxide dismutase (SOD) increased in both groups ($P<0.05$). Compared with the control group, the level of plasma MDA in the observation group was significantly lower after 5 days of treatment. The SOD level was significantly higher ($P<0.05$). After 14 days of treatment, the levels of CD3⁺, CD4⁺, CD4⁺/CD8⁺ in the two groups increased significantly, and those in the observation group were higher than those in the control group. The levels of CD8⁺ in the two groups were significantly lower, and that in the observation group was lower than that in the control group ($P<0.05$). There was no significant difference in adverse reactions between the two groups ($P>0.05$). **Conclusion:** Maxing Shigan Decoction and Yupingfeng Powder are effective in treating mycoplasma pneumonia. They can quickly relieve clinical symptoms and inflammatory reaction, alleviate oxidative stress and improve immune function of children.

Key words: Maxing Shigan Decoction; Yupingfeng Powder; Mycoplasma pneumonia; Inflammatory factors; Oxidative stress; T lymphocyte subsets

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前言

支原体肺炎是由肺炎支原体引起的肺炎,该类肺炎在小区获得性肺炎中的占比约为20%~45%,是较常见的一种急性呼吸系统感染性疾病^[1]。肺炎支原体为非细胞依赖生长的一种最小微生物,主要通过飞沫传播,其可吸附于肺部的纤毛上皮细胞受体,进一步造成细胞损伤^[2,3]。支原体肺炎患儿因其自身器官系统发育不成熟,易发生肺外并发症,严重者可导致全身多器官衰竭^[4]。目前认为,支原体肺炎对患儿的损伤因素主要包括炎性损伤、氧化应激和继发性免疫损伤等^[5,6]。临床中治疗支原体肺炎多采用大环内酯类抗菌药物(如阿奇霉素),但仍有部分患儿疗效欠佳^[7]。本研究在常规治疗基础上,采用麻杏石甘汤合玉屏风散对支原体肺炎患儿进行治疗,并探讨其对血清炎症因子、氧化应激及T淋巴细胞亚群的影响,以期为临床治疗小儿支原体肺炎的用药提供参考。

1 资料与方法

1.1 一般资料

选取2016年12月至2018年7月间我院儿科门诊接收的支原体肺炎患儿86例,纳入标准:(1)均符合《诸福棠实用儿科学》中的相关标准^[8],血清支原体抗体检测呈阳性,中医辨证为“痰热闭肺证”;(2)符合上述痰热闭肺型支原体肺炎的相关诊断标准;(3)患儿均处于急性发作期;(4)患儿家长均签署知情同意书。排除标准:(1)合并支气管哮喘、肺结核等呼吸系统疾病的患儿;(2)伴有心、肝、肾等器官功能严重异常的患儿;(3)对本研究所用药物过敏的患儿;(4)治疗前一周内使用过其他药物治疗的患儿。按随机数字表法分为观察组(43例)和对照组(43例),其中观察组患儿男23例,女20例,年龄1~10岁,平均年龄(5.31 ± 2.23)岁,平均病程(2.96 ± 0.72)d,平均体温(39.36 ± 0.42)℃;对照组患儿男22例,女21例,年龄1~9岁,平均年龄(5.57 ± 2.14)岁,平均病程(3.08 ± 0.83)d,平均体温(39.47 ± 0.51)℃,两组患儿一般资料比较无差异($P>0.05$),临床基线资料具有可比性。

1.2 治疗方法

对照组患儿给予退热、止咳、化痰等对症治疗,同时给予阿奇霉素(上海上药新亚药业有限公司,国药准字:H20030249,规格:0.125g)缓慢静脉滴注治疗,用量为10mg/kg,1次/d,连用3~5d。待患儿病情稳定后,改为同剂量的阿奇霉素(重庆科

瑞制药有限公司,国药准字:H20058150,规格:0.125g)口服,1次/d,连用4d后停用4d,再连续口服4d。观察组在对照组基础上加用麻杏石甘汤合玉屏风散治疗,方剂组成:麻黄、苦杏仁、甘草各3g,石膏12g,黄芪9g,白术、防风各6g;咽喉肿痛者,加芦根、射干;喘息痰鸣者,加枳壳、葶苈子。以上药物加水浸泡30min,清水煎煮。若患儿年龄为1~3岁,则每次服用100mL;若患儿年龄为4~6岁,则每次服用150mL;若患儿年龄为7~10岁,则每次服用200mL,2次/d,早晚温服,中药口服自治疗第1d开始。两组患儿均治疗14d。

1.3 观察指标

(1)临床症状:记录两组体温恢复时间、啰音消失时间、咳嗽消失时间和X线检查恢复正常时间。(2)炎症因子:分别于治疗前、治疗14d后抽取两组患儿的空腹静脉血5mL,3000r/min离心10min,取上层清液保存待测。血清白介素-2(Interleukin - 2, IL-2)、白介素-4(Interleukin - 4, IL-4)、白介素-6(Interleukin - 6, IL-6)和肿瘤坏死因子- α (Tumor necrosis factor- α , TNF- α)水平均采用酶联免疫吸附试验测定(采用上海盖宁生物科技有限公司的试剂盒),操作均按照说明书进行。(3)氧化应激指标:分别于治疗前、治疗5d后和治疗14d后采患儿的血浆样本,采用比色法测定丙二醛(Malondialdehyde, MDA)水平,采用酶速率法测定超氧化物歧化酶(Superoxide dismutase, SOD)水平,试剂盒均由南京建成生物工程研究所提供。(4)T淋巴细胞亚群:分别于治疗前和治疗14d后采用流式细胞仪检测两组患儿外周血CD3⁺、CD4⁺、CD8⁺细胞数,并计算CD4⁺/CD8⁺。(5)不良反应:记录并分析两组患儿用药过程中的不良反应发生情况。

1.4 疗效判定标准^[9]

治疗14d后根据患儿的临床症状及X线检查结果判定疗效。痊愈:临床症状消失,体温恢复正常,X线检查肺部病变吸收超过95%;显效:临床症状明显减轻,体温恢复正常,X线检查肺部病变吸收90%~94%;有效:临床症状有所好转,体温基本恢复正常,X线检查肺部病变吸收80%~89%;无效:临床症状未发生明显改变,甚至病情加重。总有效率=100%-无效率。

1.5 统计学方法

采用SPSS 22.0软件对数据进行统计分析,以均数±标准差($\bar{x}\pm s$)的形式表示计量资料,采用t检验,以[n(%)]的形式表示计数资料,采用 χ^2 检验,当 $P<0.05$ 时则差异有统计学意义。

2 结果

2.1 两组疗效比较

观察组总有效率高于对照组($P<0.05$)。见表1。

表1 两组疗效比较[n(%)]

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

| Groups | n | Recovery | Excellent | Valid | Invalid | Total effective rate |
|-------------------|----|-----------|-----------|-----------|-----------|----------------------|
| Control group | 43 | 12(27.91) | 16(37.21) | 12(27.91) | 3(6.98) | 40(93.02) |
| Observation group | 43 | 9(20.93) | 11(25.58) | 13(30.23) | 10(23.26) | 33(76.74) |
| χ^2 | - | | | | | 4.440 |
| P | - | | | | | 0.035 |

2.2 两组临床症状变化情况比较

观察组患儿啰音消失时间、体温恢复时间、咳嗽消失时间

表2 两组临床症状变化情况比较($\bar{x}\pm s$)

Table 2 Comparison of clinical symptom changes between the two groups($\bar{x}\pm s$)

| Groups | n | Temperature recovery time(d) | Rales vanishing time(d) | Cough resolution time(d) | X-ray examination normal time(d) |
|-------------------|----|------------------------------|-------------------------|--------------------------|----------------------------------|
| Control group | 43 | 4.48±1.13 | 8.55±2.36 | 12.31±3.41 | 11.62±2.28 |
| Observation group | 43 | 2.94±0.72 | 5.83±1.75 | 8.29±2.62 | 8.46±1.84 |
| t | | 7.537 | 6.071 | 6.130 | 7.073 |
| P | | 0.000 | 0.000 | 0.000 | 0.000 |

2.3 两组血清炎症因子变化情况比较

两组患儿治疗前血清 IL-2、IL-4、IL-6 和 TNF- α 水平比较差异无统计学意义($P>0.05$)；治疗 14 d 后，两组患儿血清 IL-2 水平明显升高，而 IL-4、IL-6 和 TNF- α 水平明显降低($P<0.05$)；

且与对照组比较，观察组患儿治疗 14 d 后的血清 IL-2 水平明显较高，而 IL-4、IL-6 和 TNF- α 水平明显较低($P<0.05$)。见表 3。

表3 两组血清炎症因子变化情况比较($\bar{x}\pm s$)

Table 3 Comparison of serum inflammatory factors between the two groups($\bar{x}\pm s$)

| Groups | n | IL-2(mg/L) | | IL-4(ng/L) | | IL-6(ng/L) | | TNF- α (mg/L) | |
|-------------------|----|------------------|-------------------------|------------------|-------------------------|------------------|-------------------------|----------------------|-------------------------|
| | | Before treatment | After 14 d of treatment | Before treatment | After 14 d of treatment | Before treatment | After 14 d of treatment | Before treatment | After 14 d of treatment |
| Control group | 43 | 3.23±0.57 | 6.46±1.52* | 47.06±12.32 | 33.52±7.74* | 17.52±4.88 | 12.06±1.57* | 2.66±0.67 | 1.34±0.49* |
| Observation group | 43 | 3.32±0.64 | 8.35±1.26* | 46.63±13.52 | 26.18±8.35* | 17.39±5.07 | 8.37±1.46* | 2.61±0.71 | 0.79±0.23* |
| t | - | 0.689 | 6.277 | 0.154 | 4.227 | 0.121 | 11.286 | 0.336 | 6.663 |
| P | - | 0.493 | 0.000 | 0.878 | 0.000 | 0.904 | 0.000 | 0.738 | 0.000 |

Note: compare with before treatment, * $P<0.05$.

2.4 两组氧化应激指标变化情况比较

两组患儿治疗前的血浆 MDA、SOD 水平比较差异无统计学意义($P>0.05$)；与治疗前比较，治疗 5 d 后、治疗 14 d 后，两组患儿血浆 MDA 降低，SOD 水平升高($P<0.05$)；与对照组比较，观察组治疗 5 d 后的血浆 MDA 明显较低，而 SOD 水平明显较高($P<0.05$)；而两组治疗 14 d 后的血浆 MDA、SOD 水平比较差异无统计学意义($P>0.05$)。见表 4。

2.5 两组 T 淋巴细胞亚群变化情况比较

两组患儿治疗前的 CD4 $^{+}$ 、CD3 $^{+}$ 、CD8 $^{+}$ 、CD4 $^{+}$ /CD8 $^{+}$ 比较差

异无统计学意义 ($P>0.05$)；治疗 14 d 后，两组患儿 CD4 $^{+}$ 、CD3 $^{+}$ 、CD4 $^{+}$ /CD8 $^{+}$ 明显升高，且观察组高于对照组($P<0.05$)；治疗 14 d 后，两组患儿 CD8 $^{+}$ 明显降低，且观察组低于对照组($P<0.05$)。见表 5。

2.6 两组不良反应发生情况比较

对照组出现 1 例呕吐，2 例恶心，1 例腹泻，不良反应发生率为 9.30%(4/43)；观察组出现 1 例皮疹、1 例腹泻、1 例恶心，不良反应发生率为 6.98%(3/43)，两组不良反应发生情况比较差异无统计学意义($\chi^2=0.156, P=0.693$)。

表 4 两组氧化应激指标变化情况比较($\bar{x} \pm s$)Table 4 Comparison of oxidative stress index changes between the two groups($\bar{x} \pm s$)

| Groups | n | MDA(nmol/mL) | | | SOD(Nu/mL) | | |
|-------------------|----|------------------|------------------------|-------------------------|------------------|------------------------|-------------------------|
| | | Before treatment | After 5 d of treatment | After 14 d of treatment | Before treatment | After 5 d of treatment | After 14 d of treatment |
| Control group | 43 | 11.62± 1.82 | 9.76± 1.73* | 7.52± 1.25** | 13.15± 2.72 | 15.37± 2.62* | 19.34± 3.31** |
| Observation group | 43 | 11.54± 1.93 | 8.23± 1.62* | 7.46± 1.18** | 13.08± 2.65 | 17.43± 2.58* | 19.52± 3.46** |
| t | - | 0.198 | 4.233 | 0.229 | 0.121 | 4.737 | 0.318 |
| P | - | 0.884 | 0.000 | 0.820 | 0.904 | 0.000 | 0.751 |

Notes: compare with before treatment, *P<0.05, compare with After 5d of treatment, **P<0.05.

表 5 两组 T 淋巴细胞亚群变化情况比较($\bar{x} \pm s$)Table 5 Comparison of T lymphocyte subsets between the two groups($\bar{x} \pm s$)

| Groups | n | CD3 ⁺ (%) | | CD4 ⁺ (%) | | CD8 ⁺ (%) | | CD4 ⁺ /CD8 ⁺ | |
|-------------------|----|----------------------|-------------------------|----------------------|-------------------------|----------------------|-------------------------|------------------------------------|-------------------------|
| | | Before treatment | After 14 d of treatment | Before treatment | After 14 d of treatment | Before treatment | After 14 d of treatment | Before treatment | After 14 d of treatment |
| Control group | 43 | 59.64± 4.29 | 64.73± 6.56* | 31.62± 3.48 | 35.38± 5.58* | 30.29± 3.84 | 27.31± 6.10* | 1.04± 0.17 | 1.30± 0.23* |
| Observation group | 43 | 60.04± 4.15 | 68.25± 7.71* | 31.09± 3.62 | 38.94± 5.92* | 30.72± 3.73 | 24.59± 6.27* | 1.01± 0.18 | 1.58± 0.26* |
| | 43 | - | 0.439 | 2.280 | 0.893 | 2.870 | 0.711 | 2.039 | 1.055 |
| | 43 | - | 0.661 | 0.025 | 0.374 | 0.005 | 0.478 | 0.045 | 0.293 |
| | | | | | | | | | 0.000 |

Note: compare with before treatment, *P<0.05.

3 讨论

肺炎支原体是一种原核细胞型微生物，其无细胞壁而含DNA 和 RNA。西医认为，肺炎支原体侵袭呼吸道粘膜后吸附于细胞膜受体表面，并通过独立完成自我复制而生存^[10]。肺炎支原体在持续的繁殖、复制过程中不断产生有毒物质，进一步导致组织细胞损伤，累及呼吸系统，若得不到及时有效的治疗，还将影响肺外器官的功能活动，危及患儿的生命健康^[11,12]。因此，缩短自然病程、提高治疗疗效成为支原体肺炎治疗的关键。阿奇霉素是目前治疗支原体肺炎患儿的首选药物，是一种半合成的十五元大环内酯类抗生素，该药生物利用度高，不良反应少，可通过阻断病原体中的 tRNA 移位达到杀灭病原体的作用^[13,14]。然而研究表明^[15,16]，单用阿奇霉素治疗可导致血药浓度降低，同时耐药菌株的出现也导致其对部分患儿的疗效不甚满意。

我国传统医学中，支原体肺炎属于“风温”、“肺热”、“肺炎喘嗽”等范畴，该病患儿温热内蕴、血气受阻、热瘀互结，中医辨证多为“痰热闭肺证”，其治则应以祛风清热、辛凉宣泄、清肺化痰为主^[17]。近年来诸多研究表明^[18-20]，支原体肺炎患儿在接受西医常规治疗的同时辅以中药方剂治疗，可以在一定程度上提升治疗效果。本研究中观察组总有效率高于对照组，同时观察组患儿啰音消失时间、体温恢复时间、咳嗽消失时间和 X 线检查恢复正常时间均明显短于对照组，说明麻杏石甘汤合玉屏风散辅助常规治疗可明显提高对支原体肺炎的疗效，加快患儿临床症状恢复。中医认为患儿发生支原体肺炎的外因包括寒温失调、风邪夹热等，而内因包括卫外不固、脏腑娇嫩、形气未充等。麻杏石甘汤为《伤寒论》中治疗肺热咳喘的经典方剂，方

中麻黄辛散具有极强的缓解支气管痉挛、宣肺止咳平喘作用；石膏药性寒凉，可抑制麻黄的温燥，有宣肺降逆之效；甘草解毒、调和药性；杏仁宣降肺气，可配合麻黄止咳平喘^[21]。现代药理学研究表明^[22]，麻杏石甘汤对呼吸系统具有较广泛的药理作用，可抗炎、抗菌、抗病毒，同时有解热、提高免疫力的作用。玉屏风散出自金元四大家之一朱丹溪的《丹溪心法》，是扶正固表的经典方剂，方中黄芪可固表止汗、补脾肺之气；白术健脾益气，与黄芪配伍则补益肺气之功愈强；防风祛风解表，可助黄芪、白术发散表邪^[23]。现代药理学研究证实^[24]，玉屏风散具有调节细胞因子、调节免疫功能、抗氧化等作用。麻杏石甘汤合玉屏风散治疗支原体肺炎标本兼顾，兼具辛凉宣肺、清热化痰以及益气固表、扶正祛邪之效。

本研究进一步观察了两组患儿血清炎症因子、氧化应激及 T 淋巴细胞亚群的变化情况，以探讨麻杏石甘汤合玉屏风散辅助治疗支原体肺炎可能的机制。支原体肺炎患儿体内以 IL-2、IL-4 为代表的抗炎症因子和以 IL-6、TNF-α 为代表的促炎症因子多存在表达异常，炎症反应是造成患儿组织损伤的主要原因^[25-27]。本研究中麻杏石甘汤合玉屏风散治疗支原体肺炎在缓解炎症反应方面具有更为显著的效果。机体内脂质经过氧化反应后最终可产生 MDA，其可反映脂质过氧化损伤的程度；经研究发现 SOD 是一种酶促防御系统，是抗氧化损害的主要防御屏障，其水平可反映机体细胞组织的抗损伤效应^[28,29]。本研究结果表明麻杏石甘汤合玉屏风散治疗支原体肺炎可以更为快速地减轻患儿机体氧化应激状态，从而减轻氧化应激损伤。另有研究发现^[30]，支原体肺炎患儿往往存在 T 淋巴细胞亚群比例失衡，免疫功能紊乱，机体免疫力降低的现象。本研究结果表明麻

杏石甘汤合玉屏风散治疗支原体肺炎对患儿的免疫功能有更好的恢复效果。此外,两组患儿不良反应发生率比较无明显差异,说明两种治疗方法均有较好的安全性。

综上所述,麻杏石甘汤合玉屏风散治疗支原体肺炎患儿疗效确切,其作用机制可能与该中药方剂可减轻患儿氧化应激状态、缓解炎症反应以及提高患儿免疫功能有关。

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