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甲泼尼龙治疗重症社区获得性肺炎的疗效及其对血清炎症因子水平的影响

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[摘　要]　**目的：**探讨甲泼尼龙治疗重症社区获得性肺炎(severe community acquired pneumonia，SCAP)的疗效及其对血清炎症因子水平的影响。**方法：**将2014年2月至2018年2月北京朝阳急诊抢救中心收治的80例SCAP患者随机分为2组，对照组(40例)采用抗感染等基础治疗，观察组(40例)在对照组基础上增加甲泼尼龙治疗，均治疗1周。观察两组疗效、临床症状消失时间以及治疗前后血气指标和炎症因子的变化。**结果：**观察组治疗有效率高于对照组(90.00% vs 70.00%，P<0.05)；观察组发热[(2.01±0.19) d vs (3.14±0.25) d]，喘息[(3.26±0.39) d vs (5.24±0.69) d]，咳嗽咳痰[(5.13±0.92) d vs (6.35±0.25) d]，肺湿啰音[(3.76±0.52) d vs (5.37±0.63) d]持续时间短于对照组，差异有统计学意义(P<0.05)。两组治疗后动脉血氧饱和度(arterial oxygen saturation，O_2sat)、动脉血氧分压((arterial blood carbon dioxide partial pressure，PO_2)、动脉血pH值增高；动脉血二氧化碳分压(arterial blood carbon dioxide partial pressure，PCO_2)、血清肿瘤坏死因子-α(tumor necrosis factor-α，TNF-α)、白介素-8(interleukin-8，IL-8)、超敏C反应蛋白(hypersensitive C-reactive protein，hs-CRP)水平降低，差异有统计学意义(P<0.05)。观察组治疗后PCO_2[(43.15±4.33) mmHg vs (47.08±5.12) mmHg]，TNF-α[(2.26±0.35) ng/mL vs (3.69±1.25) ng/mL]，IL-8[(2.31±0.65) vs (4.32±1.76) ng/mL]，hs-CRP[(7.35±2.26) mg/L vs (14.15±5.32) mg/L]低于对照组，差异有统计学意义(P<0.05)。观察组O_2sat[(89.25±6.35)% vs (80.24±5.39)%]，PO_2[(65.34±7.95) mmHg vs (54.23±6.07) mmHg]，pH[(7.49±0.65) vs (7.31±0.52)]高于对照组，差异有统计学意义(P<0.05)。**结论：**甲泼尼龙可提高SCAP疗效，并有效降低血清炎症因子水平。

[关键词]　甲泼尼龙；重症社区获得性肺炎；炎症因子；肺炎；社区获得性肺炎；炎症因子

Effect of methylprednisolone on severe community-acquired pneumonia and its impact on the level of serum inflammatory factors

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Abstract　**Objective:** To investigate the therapeutic effect of methylprednisolone on severe community acquired pneumonia

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(SCAP) and its effect on serum inflammatory factors. **Methods:** Eighty patients with SCAP admitted to Beijing Chaoyang Emergency Rescue Center from February 2014 to February 2018 were randomly divided into 2 groups. The control group (40 cases) received basic treatment such as anti-infection. The observation group (40 cases) received methylprednisolone on the basis of basic treatment. All patients were treated for 1 week. The therapeutic effect, time of clinical symptom disappearance, changes of blood gas index and inflammatory factors before and after the treatment were observed. **Results:** The effective rate of the observation group was higher than that of the control group (90.00% vs 70.00%, $P<0.05$); fever [(2.01±0.19) d vs (3.14±0.25) d], wheezing [(3.26±0.39) d vs (5.24±0.69) d], lung moist rales [(3.76±0.52) d vs (5.37±0.63) d], duration of cough and expectoration [(5.13±0.92) d vs (6.35±0.25) d] in the observation group were shorter than those in the control group. The differences were statistically significant ($P<0.05$). After the treatment, arterial oxygen saturation (O_2sat), arterial oxygen partial pressure (PO_2), arterial pH increased; arterial carbon dioxide partial pressure (PCO_2) and levels of serum tumor necrosis factor-α (TNF-α), interleukin-8 (IL-8), and high-sensitivity C-reactive protein (hs-CRP) decreased. The differences were statistically significant ($P<0.05$). After the treatment, PCO_2 [(43.15±4.33) mmHg vs (47.08±5.12) mmHg] and levels of serum TNF-α [(2.26±0.35) ng/mL vs (3.69±1.25) ng/mL], IL-8 [(2.31±0.65) ng/mL vs (4.32±1.76) ng/mL] and Hs-CRP [(7.35±2.26) mg/L vs (14.15±5.32) mg/L] in the observation group were lower than those of the control group. The differences were statistically significant ($P<0.05$). O_2sat [(89.25±6.35)% vs (80.24±5.39)%], PO_2 [(65.34±7.95) mmHg vs (54.23±6.07) mmHg] and pH [(7.49±0.65) vs (7.31±0.52)] of the observation group was higher than those of the control group. The differences were statistically significant ($P<0.05$). **Conclusion:** Methylprednisolone can improve the therapeutic effect of SCAP and effectively reduce the level of serum inflammatory factors.

Keywords methylprednisolone; severe community acquired pneumonia; inflammatory factors; pneumonia; community acquired pneumonia; inflammatory factors

社区获得性肺炎(community acquired pneumonia，CAP)是常见的呼吸系统疾病。重症肺炎可引起持续低氧血症甚至急性呼吸衰竭、脓毒症休克、多脏器功能障碍等严重后果[1]。抗感染治疗是重症社区获得性肺炎(severe community acquired pneumonia，SCAP)的主要治疗手段，但是单纯抗感染疗效欠佳，不能有效抑制和逆转低氧血症。炎症反应是CAP的主要病理生理机制，如何有效控制炎症反应水平是治疗SCAP的关键。甲泼尼龙是人工合成的糖皮质激素，具有多种生物学效应，包括免疫抑制、抗过敏和抗炎，在感染性疾病、免疫性疾病等多种疾病治疗中均有广泛的应用[2-3]。本研究拟探讨甲泼尼龙治疗SCAP的疗效及其对血清炎症因子水平的影响。

1 对象与方法

1.1 对象

选择2014年2月至2018年2月北京朝阳急诊抢救中心收治的80例SCAP患者，采用随机数字表法将患者分为2组：观察组40例，男21例，女19例，年龄65~76(70.26±2.35)岁；对照组40例，男22例，女18例，年龄65~77(71.31±3.29)岁。两组患者性别、年龄比较差异无统计学意义($P>0.05$)。纳入标准：1)典型症状和体征，影像学检查提示肺部实变，病原菌培养证实感染，符合中华医学会SCAP诊断标准[4]；2)向患者告知本研究目的、内容，患者同意参与并签署同意书；3)能配合完成治疗。排除标准：1)入组前接受抗感染、激素治疗者；2)合并肝肾功能不全，其他部位感染者；3)中途退出者；4)对本研究药物过敏者。本研究获得北京朝阳急诊抢救中心伦理委员会批准。

1.2 方法

对照组：常规吸氧、雾化吸入、排痰仪排痰、抗感染、加强营养等基础治疗，必要时机械通气。持续治疗7 d。

观察组：在对照组基础上增加注射用甲泼尼龙琥珀酸钠(辉瑞制药有限公司，产品批号170124)80~240 mg + 5%葡萄糖注射液100 mL，分2~3次静脉滴注。持续治疗7 d。

1.3 观察指标

1)疗效[5]。治愈：临床症状和体征消失，外周血象、病原学检查恢复正常，胸部X射线片提示肺实变征象消失。显效：临床症状和体征明显好转，外周血象下降、病原学检查正常，胸部X射线片提示肺实变征象明显减轻。有效：临床症状和体征有所缓解，外周血象有所下降，胸部X射线片提示肺实变征象有所减轻。无效：用药3 d后上述项目无改善，甚至加重。2)观察两组发热、喘息、咳嗽咳痰、肺湿啰音等消失时间差异。3)治疗前后采用肝素化注射器抽取动脉血，采用美国雅培(Abbott)公司i-STAT微量血气分析仪检测动脉血氧饱和度(arterial oxygen saturation，O_2sat)、动脉血二氧化碳分压(arterial blood carbon dioxide partial pressure，PCO_2)、动脉血氧分压(arterial partial pressure of oxygen，PO_2)、动脉血pH值。4)炎症因子指标：治疗前后分别采集空腹静脉血2~3 mL，酶联免疫吸附试验测定血清肿瘤坏死因子-α(tumor necrosis factor-α，TNF-α)、白介素-8(interleukin-8，IL-8)、超敏C反应蛋白(hypersensitive C-reactive protein，hs-CRP)水平。

1.4 统计学处理

采用SPSS 25.0统计学软件进行数据分析。Kolmogorov-Smirnov法检验血气指标和炎症因子等计量资料是否符合正态分布，符合正态分布的计量资料以均数±标准差($\bar{x}\pm s$)表示，采用t检验比较。计数资料以例(%)形式表示，采用χ^2检验比较。所有统计均采用双侧检验，P<0.05为差异有统计学意义。

2 结果

2.1 疗效比较

观察组治愈19例，显效12例，有效5例，有效率90.00%；对照组治疗有效率70.00%，观察组治疗有效率高于对照组，差异有统计学意义(P<0.05，表1)。

2.2 临床症状比较

观察组治疗后发热、喘息、咳嗽咳痰症状、肺湿啰音持续时间短于对照组，差异有统计学意义(P<0.05，表2)。

2.3 血气指标比较

两组治疗前O_2sat，PCO_2，PO_2和pH比较差异均无统计学意义(P>0.05)；治疗后两组O_2sat，PO_2，PH增高，PCO_2降低，差异有统计学意义(P<0.05)。观察组治疗后PCO_2低于对照组，O_2sat，PO_2，PH高于对照组，差异有统计学意义(P<0.05，表3)。

2.4 炎症因子指标比较

两组治疗前血清TNF-α，IL-8，hs-CRP水平比较差异均无统计学意义(P>0.05)；治疗后两组血清TNF-α，IL-8，hs-CRP水平均降低，差异有统计学意义(P<0.05)。观察组治疗后血清TNF-α，IL-8，hs-CRP水平低于对照组，差异有统计学意义(P<0.05，表4)。

表1 两组疗效比较(n=40)

Table 1 Comparison of efficacy between the 2 groups (n=40)

组别	治愈/[例(%)]	显效/[例(%)]	有效/[例(%)]	无效/[例(%)]	有效率/[例(%)]
观察组	19 (47.50)	12 (30.00)	5 (12.50)	4 (10.00)	36 (90.00)
对照组	10 (25.00)	11 (27.50)	7 (17.50)	12 (30.00)	28 (70.00)
χ^2	—	—	—	—	5.000
P	—	—	—	—	0.025

表2 两组临床症状和体征差异(n=40，$\bar{x}\pm s$)

Table 2 Difference of clinical symptoms and signs between the 2 groups (n=40, $\bar{x}\pm s$)

组别	发热	喘息	肺湿啰音	咳嗽、咳痰
观察组	2.01 ± 0.19	3.26 ± 0.39	3.76 ± 0.52	5.13 ± 0.92
对照组	3.14 ± 0.25	5.24 ± 0.69	5.37 ± 0.63	6.35 ± 0.25
t	22.760	15.800	12.465	8.093
P	0.001	0.001	0.001	0.001

表3 两组治疗期间O_2sat，PCO_2，PO_2和pH的差异(n=40，$\bar{x} \pm s$)

Table 3 Differences of O_2sat, PCO_2, PO_2 and pH between the 2 groups during the treatment (n=40, $\bar{x} \pm s$)

组别	O_2sat/%		PCO_2/mmHg	
	治疗前	治疗后	治疗前	治疗后
观察组	52.31 ± 6.59	89.25 ± 6.35*	58.25 ± 6.23	43.15 ± 4.33*
对照组	52.16 ± 6.42	80.24 ± 5.39*	58.39 ± 6.29	47.08 ± 5.12*
t	0.103	6.842	0.100	3.707
P	0.918	0.001	0.921	0.001

组别	PO_2/mmHg		pH	
	治疗前	治疗后	治疗前	治疗后
观察组	41.25 ± 5.16	65.34 ± 7.95*	7.15 ± 0.53	7.49 ± 0.65*
对照组	41.39 ± 5.19	54.23 ± 6.07*	7.13 ± 0.52	7.31 ± 0.52*
t	0.121	7.025	0.170	1.368
P	0.904	0.001	0.865	0.175

1 mmHg=0.133 kPa。与治疗前比较，*P<0.05。

1 mmHg=0.133 kPa. Compared with before treatment, *P<0.05.

表4 两组治疗前后血清TNF-α，IL-8和hs-CRP水平的差异(n=40，$\bar{x} \pm s$)

Table 4 Differences of serum TNF-α, IL-8 and hs-CRP levels between the 2 groups before and after the treatment (n=40, $\bar{x} \pm s$)

组别	TNF-α/(ng·mL^{-1})		IL-8/(ng·mL^{-1})		hs-CRP/(mg·L^{-1})	
	治疗前	治疗后	治疗前	治疗后	治疗前	治疗后
观察组	6.35 ± 2.15	2.26 ± 0.35*	7.51 ± 2.69	2.31 ± 0.65*	25.15 ± 9.51	7.35 ± 2.26*
对照组	6.37 ± 2.41	3.69 ± 1.25*	7.63 ± 2.41	4.32 ± 1.76*	25.19 ± 9.66	14.15 ± 5.32*
t	0.039	7.113	0.210	6.776	0.019	7.440
P	0.969	0.001	0.834	0.001	0.985	0.001

与治疗前比较，*P<0.05。

Compared with before treatment, *P<0.05.

3 讨论

重症肺炎是导致全球中老年人死亡的常见原因之一[6]，其中SCAP发病率呈逐年升高趋势，严重威胁中老年患者健康。高龄、合并基础疾病、营养缺乏、重度贫血、反复呼吸道感染及侵入性操作等是社区重症肺炎的高危因素[7]。细菌是CAP的首位致病原，抗感染治疗是SCAP的治疗基础，但是单纯应用抗生素效果似乎并不显著，且存在耐药和耐药菌株感染风险。如何提高SCAP疗效是临床研究的重点。

近年来研究[8]发现：SCAP患者血清炎症因子水平普遍升高，在疾病早期即出现强烈炎症反应。大量炎性介质释放诱导的炎症级联反应参与全身多器官功能损害过程，炎性介质可诱导其他致病因子释放，导致以休克为主的恶性循环表现和全身炎症反应综合征。剧烈的炎症反应与SCAP患者预后密切相关。相关报道[9]显示：SCAP死亡患者血清降钙素、*D*-二聚体、C反应蛋白水平高于存活组，降钙素、*D*-二聚体、C反应蛋白水平与肺炎严重指数呈正相关。因此控制SCAP患者过度炎症反应是控制疾病进展的关键。

糖皮质激素是临床应用较广的非特异性抗炎药物，可降低全身炎症反应水平。SCAP患者多伴

肾上腺皮质功能不全，尤其是合并基础疾病的老年患者。肺炎治疗早期应用糖皮质激素可抑制全身炎症反应综合征进程，缓解咳嗽咳痰、喘息等临床症状，并可降低多脏器功能障碍风险。临床研究证实糖皮质激素治疗SCAP可降低血清炎症因子水平，改善临床症状，缩短住院时间，减少疾病复发，降低病死率[10-11]。甲泼尼龙是中效激素，可特异性强力亲和糖皮质激素受体，减少炎性细胞浸润，减少气道分泌物分泌，改善肺通气功能。甲泼尼龙无需肝脏转化，停药不良反应少，具有较高的安全性。本研究观察组在常规治疗基础上增加甲泼尼龙治疗，治疗有效率达90.00%，高于对照组，且发热、喘息、咳嗽咳痰等症状、肺湿啰音持续时间明显短于对照组，说明甲泼尼龙可提高SCAP治疗效果，显著改善临床症状。

本研究观察组治疗后血气指标优于对照组，分析原因为甲泼尼龙改善肺通气功能，减轻肺组织渗出和水肿，有效纠正了低氧血症，改善全身血液循环，进而提高动脉血氧含量。TNF-α，IL-8等炎症因子升高可诱导免疫细胞浸润，TNF-α可引发纤连蛋白蓄积，损伤肺血管[12]。hs-CRP是炎症反应敏感指标，参与气道炎症反应、全身炎症反应等几乎人体所有系统炎症反应。本研究治疗后观察组血清TNF-α，IL-8，hs-CRP水平低于对照组，说明甲泼尼龙可显著降低SCAP患者机体炎症反应，抑制炎症反应损伤。分析原因为甲泼尼龙可能通过激活淋巴细胞功能，抑制炎性细胞因子释放，发挥抗炎作用；其次甲泼尼龙通过与细胞内特异性受体结合，启动mRNA转录，致使酶蛋白合成，影响炎症反应信号通路发挥抗炎作用。

综上所述，本研究结果证实甲泼尼龙可提高SCAP疗效，有效改善患者临床症状，降低血清炎症因子水平，具有更高的应用价值。

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