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阿奇霉素联合辛伐他汀对慢性阻塞性肺疾病合并肺动脉高压患者肺功能的影响 *

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摘要 目的:探讨阿奇霉素联合辛伐他汀治疗慢性阻塞性肺疾病合并肺动脉高压的临床疗效及对患者肺功能的影响。**方法:**选取2013年6月-2016年3月我院收治的慢性阻塞性肺疾病合并肺动脉高压患者107例,根据治疗方法不同分为对照组(49例)与实验组(58例)。对照组患者采用阿奇霉素治疗,实验组患者在对照组基础上给予辛伐他汀治疗。观察并比较两组患者的临床疗效、不良反应以及肺功能指标的变化情况。**结果:**实验组患者治疗有效率(87.93%)高于对照组(73.47%),差异具有统计学意义($P < 0.05$)。与治疗前比较,两组患者治疗后1s用力呼吸容积(FEV1)、用力肺活量(FVC)及FEV1/FVC水平均升高,差异具有统计学意义($P < 0.05$);与对照组比较,实验组患者治疗后1s用力呼吸容积(FEV1)、用力肺活量(FVC)及FEV1/FVC水平较高,差异具有统计学意义($P < 0.05$)。治疗后,两组患者血清总胆固醇(TC)及三酰甘油(TG)水平均降低,差异具有统计学意义($P < 0.05$);与对照组比较,实验组患者治疗后血清总胆固醇(TC)及三酰甘油(TG)水平较低,差异具有统计学意义($P < 0.05$)。两组患者不良反应发生率比较,差异无统计学意义($P > 0.05$)。**结论:**阿奇霉素联合辛伐他汀治疗慢性阻塞性肺疾病合并肺动脉高压的临床效果显著,不仅能够改善患者肺功能,降低血脂相关指标水平,并且安全性较高,值得临床推广应用。

关键词:慢性阻塞性肺疾病;肺动脉高压;阿奇霉素;辛伐他汀

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Efficacy of Azithromycin Combined with Simvastatin in Treatment of COPD Complicated with Pulmonary Hypertension*

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ABSTRACT Objective: To investigate the clinical efficacy of azithromycin combined with simvastatin in the treatment of chronic obstructive pulmonary disease (COPD) and pulmonary hypertension and the effects on pulmonary function of patients. **Methods:** 107 cases with chronic obstructive pulmonary disease and pulmonary hypertension who were treated in our hospital from June 2013 to March 2016 were selected and according to the different treatment methods, the patients were divided into the control group (49 cases) and the experimental group (58 cases). The patients in the control group were treated with azithromycin, and the patients in the experimental group were treated with simvastatin on the basis of the control group. Then the clinical efficacy, the adverse reactions and the changes of pulmonary function indexes in the two groups were observed and compared before and after the treatment. **Results:** The clinical effective rate in the experimental group was 87.93%, which was higher than 73.47% in the control group, and the difference was statistically significant ($P < 0.05$). Compared with before treatment, the FEV1, FVC and FEV1/FVC in the two groups increased after the treatment, and the differences were statistically significant ($P < 0.05$); Compared with the control group, the FEV1, FVC and FEV1/FVC in the experimental group were higher, and the differences were statistically significant ($P < 0.05$); Compared with before treatment, the levels of TC and TG of patients in the two groups decreased, and the differences were statistically significant ($P < 0.05$); Compared with the control group, the levels of TC and TG of patients in the experiment group were lower, and the differences were statistically significant ($P < 0.05$). There was no significant difference about the incidence of adverse reactions between the two groups ($P > 0.05$). **Conclusion:** Azithromycin combined with simvastatin on the treatment of COPD and pulmonary hypertension is effective, which can improve the pulmonary functions, reduce the lipid indexes and it is safe and worthy of clinical application.

Key words: Chronic obstructive pulmonary disease; Pulmonary hypertension; Azithromycin; Simvastatin

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前言

慢性阻塞性肺疾病(Chronic obstructive pulmonary disease, COPD)是指气道壁与肺实质慢性炎症性病变,主要临床特征为外周血炎症细胞增加,急性反应蛋白含量增加等^[1]。慢性阻塞性肺疾病是我国呼吸系统的常见病,具有不可逆性发展的特点,急性加重期常引起通气及换气功能障碍加重,引发呼吸衰竭^[2]。其中肺动脉高压(Pulmonary arterial hypertension, PAH)是慢性阻塞性肺疾病患者较为严重的并发症,也是一组以肺血管阻力持续增高为特征的临床病理生理综合征^[3]。因此,早期有效控制肺动脉压有助于改善慢性阻塞性肺疾病合并肺动脉高压患者的预后。阿奇霉素作为大环内酯类抗菌药物通过发挥抗菌杀菌,免疫调节与消炎的作用,从而显著降低慢性阻塞性肺疾病患者急性加重发生风险,并改善肺功能状况^[4]。辛伐他汀作为他汀类药物通过选择作用于羟甲基戊二酰辅酶A(3-hydroxy-3-methylglutaryl-coenzyme A, HMG-CoA)还原酶,从而发挥保护血管和降脂的作用^[5]。因此,本研究主要探讨了阿奇霉素联合辛伐他汀治疗慢性阻塞性肺疾病合并肺动脉高压的临床疗效。

1 资料与方法

1.1 临床资料

选取2013年6月-2016年3月我院收治的慢性阻塞性肺疾病合并肺动脉高压患者107例,根据治疗方法不同分为对照组(49例)与实验组(58例)。两组患者一般资料比较差异无统计学意义($P>0.05$)。其中,对照组包括男29例、女20例;年龄60-84岁,平均年龄(69.8 ± 3.9)岁;平均病程(12.81 ± 2.68)年;心功能分级:Ⅱ级14例、Ⅲ级23例、Ⅳ级12例。实验组包括男35例、女23例;年龄60-84岁,平均年龄(69.66 ± 3.43)岁;平均病程(13.10 ± 2.47)年;心功能分级:Ⅱ级18例、Ⅲ级29例、Ⅳ级11例。

1.2 纳入及排除标准

纳入标准:均符合慢性阻塞性肺疾病与肺动脉高压的诊断标准^[6],静息条件下右心导管测定平均动脉压(mean arterial pressure, MAP) ≥ 25 mmHg,或运动条件下MAP ≥ 30 mmHg,自愿参加本研究,患者或者其家属签署知情同意书。排除标准:

合并恶性肿瘤、自身免疫性疾病、肝肾功能障碍、药物过敏史、全身感染性疾病、原发性肺动脉高压、哮喘、过敏性鼻炎、肺血栓栓塞与精神性疾病等患者。近期未出现急性肺部感染或慢性阻塞性肺疾病急性发作期患者。

1.3 治疗方法

对照组患者口服阿奇霉素分散片(上海天龙药业有限公司,国药准字H20010725)0.25 g/次,每日一次,实验组患者在对照组患者的基础上口服辛伐他汀片(山西云鹏制药有限公司,国药准字H20083593)20 mg/次,每日一次。6个月为1个疗程,两组均治疗1个疗程。

1.4 观察指标及检测方法

1.4.1 肺功能检测 治疗前后采用全套肺功能分析仪(美国森迪公司)测定所有患者的肺功能状态,包括FEV₁、FVC、FEV₁%pre和FEV₁/FVC等指标。

1.4.2 血脂水平检测 采用日立7600全自动生化分析仪及其配套的试剂盒检测血清总胆固醇(total cholesterol, TC)与三酰甘油(triacylglycerol, TG)水平,上述指标的检测严格参照光学浊度法标准进行测定。

1.5 疗效评价

显效:治疗后咳、痰、喘等症状明显缓解或消失,肺部听诊较前明显改善,胸片肺纹理好转,意识清,无发热,血象下降至正常;有效:治疗后咳、痰、喘等症状轻度缓解,肺部听诊稍有改善;无效:临床症状、体征及影像学检查无好转或较前加重或需气管插管治疗。记录两组患者不良反应。

1.6 统计学分析

采用SPSS18.0软件处理数据,计量资料以($\bar{x}\pm s$)表示,行t检验,计数资料以率(%)表示,应用 χ^2 检验, $P<0.05$ 为差异具有统计学意义。

2 结果

2.1 两组患者的临床疗效比较

对照组治疗有效率为73.47%(36/49),实验组治疗有效率为87.93%(51/58);实验组患者治疗有效率高于对照组,差异具有统计学意义($P<0.05$)。两组患者不良反应发生率比较,差异无统计学意义($P>0.05$)。见表1。

表1 两组临床疗效对比(例,%)

Table 1 Comparison of the clinical efficacy between two groups(n,%)

Groups	n	Excellence	Effective	Invalid	Clinical efficacy rate
Control group	49	17(34.69%)	19(38.78%)	13(26.53%)	73.47%(36/49)
Experimental group	58	27(46.55%)	25(43.10%)	7(12.07%)	87.93%(51/58)*

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

2.2 两组患者治疗前后肺功能比较

与治疗前比较,两组患者治疗后FEV₁、FVC及FEV₁/FVC水平均升高,差异具有统计学意义($P<0.05$);与对照组比较,实验组患者治疗后FEV₁、FVC及FEV₁/FVC水平较高,差异具有统计学意义($P<0.05$)。见表2。

2.3 两组患者治疗前后血脂比较

与治疗前比较,治疗后两组患者TC及TG水平均降低,差异具有统计学意义($P<0.05$);与对照组比较,实验组患者治疗后TC及TG水平更低,差异具有统计学意义($P<0.05$)。(表3)。

表 2 两组患者治疗前后肺功能指标比较($\bar{x} \pm s$)

Table 2 Comparison of the pulmonary functions between two groups before and after treatment($\bar{x} \pm s$)

Groups	Time	FEV ₁ (L)	FVC(L)	FEV ₁ /FVC(%)
Control group (n=49)	Before treatment	0.86± 0.28	1.43± 0.57	47.75± 6.13
	After treatment	1.11± 0.35*	1.64± 0.48*	52.33± 6.15*
Experimental group (n=58)	Before treatment	0.84± 0.25	1.52± 0.63	47.32± 6.18
	After treatment	1.31± 0.33*#	2.05± 0.50*#	57.24± 6.39*#

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

表 3 两组患者治疗前后血脂相关指标比较

Table 3 Comparison of the lipid indexes between the two groups before and after the treatment

Groups	n	TC (mmol/l)		TG (mmol/l)	
		Before treatment	After treatment	Before treatment	After treatment
Experimental group	58	6.45± 1.01	4.22± 1.03*#	3.32± 0.42	1.64± 0.26*#
Control group	49	6.56± 1.02	5.84± 1.06*	3.19± 0.44	2.76± 0.04*

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

3 讨论

阿奇霉素属于大环内酯类抗菌药物,不但具有抗感染作用,而且具有免疫调节作用^[8]。相关研究表明,辛伐他汀在肺动脉高压的治疗中可通过选择性作用于 HMG-CoA 还原酶,从而显著降低胆固醇合成,发挥有效降脂与保护血管的药理作用^[9,10]。还有研究显示,辛伐他汀具有抗炎、抗氧化和改善肺功能的作用,还能通过重塑血管达到降低肺部血管重构的风险^[11,12]。本研究成果显示,与治疗前比较,两组患者治疗后 FEV₁,FVC 及 FEV₁/FVC 水平均升高(P<0.05);与对照组比较,实验组患者治疗后 FEV₁,FVC 及 FEV₁/FVC 水平较高(P<0.05)。结果说明,辛伐他汀联合阿奇霉素能够明显改善慢性阻塞性肺疾病合并肺动脉高压患者的肺功能指标。这是因为阿奇霉素通过发挥有效的抗菌杀菌作用,彻底清除感染等诱发因素,避免疾病进展^[13];同时,阿奇霉素通过清除肺实质的炎症病灶,进而发挥其改善肺功能的作用^[14]。相关研究表明,辛伐他汀不仅具有降脂作用,而且具有抗凝、抗血小板作用^[15]。还有研究显示,阿奇霉素联合辛伐他汀在改善慢性阻塞性肺疾病合并肺动脉高压患者肺通气功能与降血脂中作用显著,其疗效明显优于单纯采用阿奇霉素治疗^[16]。本研究成果显示,与治疗前比较,治疗后两组患者 TC 及 TG 水平均降低(P<0.05);与对照组比较,实验组患者治疗后 TC 及 TG 水平更低(P<0.05)。结果说明,与单纯阿奇霉素治疗患者比较,辛伐他汀联合阿奇霉素能够降低慢性阻塞性肺疾病合并肺动脉高压患者的血脂水平,提高临床疗效^[17]。此外,两组患者不良反应发生率无统计学差异(P>0.05)。说明辛伐他汀联合阿奇霉素治疗患者不增加药物不良反应的发生,提示辛伐他汀联合阿奇霉素治疗慢性阻塞性肺疾病合并肺动脉高压的安全性较高^[18,20]。

综上所述,阿奇霉素联合辛伐他汀治疗慢性阻塞性肺疾病合并肺动脉高压的临床效果显著,能够改善患者肺功能,降低血脂相关指标水平,并且安全性较高,值得临床推广应用。

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