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舒利迭联合无创正压通气治疗 COPD 合并呼吸衰竭的临床疗效观察

楚文丽[1] 宋立强[2] 严蕊娜[1] 王惠芳[1] 牛攀霞[1] 周 立[1]

（1 西安医学院第二附属医院呼吸内科 陕西 西安 710038；2 西京医院呼吸内科 陕西 西安 710032）

摘要 目的：分析舒利迭联合无创正压通气治疗慢性阻塞性肺疾病(COPD)合并Ⅱ型呼吸衰竭的临床疗效。**方法：**选取于我院诊治的 COPD 合并Ⅱ型呼吸衰竭患者 120 例，随机均分为观察组和对照组。所有患者均予以常规、对症和支持治疗，在此基础上对照组予以无创正压通气(NIPPV)治疗，观察组在对照组的基础上加用舒利迭治疗。分析和比较两组患者治疗前后的动脉血气、炎性因子水平、肺功能和 CAPS 评分。**结果：**与治疗前相比，两组患者治疗后的 pH、PaO_2、SaO_2 水平均明显升高，$PaCO_2$ 明显降低，血清 IL-33、TNF-α、sICAM-1 水平均明显降低，FVC、PEFR、FEV1%、FEV1/FVC 水平均明显升高，CAPS 评分明显下降，且观察组的上述指标变化均较对照组更为明显(P＜0.05)。**结论：**舒利迭联合 NIPPV 能够较单用 NIPPV 更有效降低 COPD 合并Ⅱ型呼吸衰竭患者炎性因子水平，改善血气和肺功能。

关键词：慢性阻塞性肺疾病；Ⅱ型呼吸衰竭；舒利迭；无创正压通气；疗效

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Observation on the Clinical Effect of Seretide and Noninvasive Positive Pressure Ventilation on the COPD Combined with Respiratory Failure

CHU Wen-li[1], SONG Li-qiang[2], YAN Rui-na[1], WANG Hui-fang[1], NIU Pan-xia[1], ZHOU Li[1]

(1 Department of Respiration Medicine, The Second Affiliated Hospital of Xi'an Medical University, Xi'an, Shaanxi, 710038, China; 2 Department of Respiration Medicine, Xijing Hospital, Xi'an, Shaanxi, 710032, China)

ABSTRACT Objective: To analyze the clinical efficacy of Seretide combined with noninvasive positive pressure ventilation (NIPPV) in the treatment of chronic obstructive pulmonary disease (COPD) complicated with type 2 respiratory failure (RF). **Methods:** 120 patients of COPD complicated with type 2 RF were randomly divided into the observation group and the control group. All patients were treated with routine, symptomatic and supportive treatment, based on that NIPPV was used in the control group, and the observation group was treated with Seretide on the basis of NIPPV. The levels of arterial blood gas, inflammatory factors, pulmonary function and CAPS score before and after treatment were compared and analyzed. **Results:** After treatment, the pH, PaO_2 and SaO_2 of both groups were significantly increased, $PaCO_2$ levels weresignificantly decreased, serum IL-33, TNF-α and sICAM-1 levels were significantly decreased, FVC, PEFR, FEV1% and FEV1/FVC were significantly decreased, and the CAPS scores were significantly decreased; the changes of all the index mentioned above in the observation group were more statistically significant (P<0.05). **Conclusion:** Seretide combined with NIPPV could more effectively decrease the levels of inflammatory factors and improve the blood gas and lung function in the patients of COPD with type 2 respiratory failure.

Key words: Chronic obstructive pulmonary disease; Type 2 respiratory failure; Seretide; Noninvasive positive pressure ventilation; Efficacy

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前言

慢性阻塞性肺疾病(COPD)是一种常进行性加重并可引起显著全身效应的慢性气道炎症性疾病。随着我国步入老龄化社会，COPD 的患病率持续增长，已经成为危害人民身体健康最重要的慢性呼吸系统疾病[1,2]。由于呼吸系统感染、支气管痉挛等因素呼吸肌疲劳更易加重，COPD 急性加重会进一步加剧疾病进展，使肺功能明显下降，易致并发Ⅱ型呼吸衰竭[3,4]。COPD 并发呼吸衰竭发生时，机体处于缺氧状态，气道阻力升高，形成内源性呼气末正压，增加呼吸功耗，血氧分压进一步下降，增加患者死亡风险[5,6]。

无创正压通气(NIPPV)是目前治疗 COPD 呼吸衰竭的一线方法，研究表明其可使部分患者避免因行有创通气所造成的损伤及相关并发症，早期应用能够阻止病情恶化，甚至逆转病情[7,8]。沙美特罗替卡松(舒利迭)是一种糖皮质激素及长效β2 受体激动剂的复合剂，已常规应用于 COPD 的治疗中，能够促使气道平滑肌、小气道实行舒张，同时改善小气道通气情况，研究证实 COPD 患者使用沙美特罗替卡松能够有效改善患者的气道

作者简介：楚文丽，女，硕士研究生，主治医师，研究方向：慢性阻塞性肺病(COPD)，肺部肿瘤的放疗，电话：15109289636，E-mail：chuwenli_197910@medarticleonline.com

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重塑[9-11]。本研究主要探讨了舒利迭联合 NIPPV 治疗 COPD 合并Ⅱ型呼吸衰竭的临床疗效,具体报道如下。

1 资料与方法

1.1 研究对象

本研究对象选自 2015 年 1 月 -2015 年 12 月我院呼吸内科收治的 COPD 合并Ⅱ型呼吸衰竭患者共 120 例。纳入标准:(1)经临床、影像及实验室检查等确诊为 COPD,符合中华医学会呼吸病学会《COPD 诊治指南(2007 年修订版)》中相关诊断标准;(2)Ⅱ型呼吸衰竭符合第 8 版《内科学》中相关诊断标准,没有无创正压通气禁忌证;(3)无糖皮质激素、支气管扩张剂等相关药物禁忌症,4 周内未使用糖皮质激素;(4) 患者知情同意本研究,可配合治疗。排除标准:(1)患有支气管哮喘、尘肺、肺部肿瘤等引起肺功能减退的疾病;(2)存在吞咽反射异常;(3)合并严重感染、自身免疫系统疾病、血液系统疾病、严重糖尿病、严重肝肾功能不全、心脑等器质性病变等。

将 120 例患者按照住院号依据随机数字表法平均分为观察组和对照组各 60 例。研究组有男性 41 例、女性 19 例,年龄 63.8± 5.9 岁,病程 9.2± 3.9 年,体重 58.6± 8.2 kg;对照组有男性 39 例、女性 21 例,年龄 64.3± 6.4 岁,病程 8.7± 4.3 年,体重 58.2± 7.6 kg。两组患者的上述基本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

所有患者均予以平喘、抗感染、镇静、解痉、减轻肺水肿、纠正水电解质和酸碱平衡紊乱、氧疗及其他对症和支持治疗。在此基础上对照组予以无创正压通气(NIPPV)治疗(生产厂家:美国伟康公司),选择 S/T 模式,设定通气参数:吸入氧浓度(FiO_2)30%-45%,SaO_2>90%,CPAP 3-5 cmH_2O,EPAP 4-5 cmH_2O,I-PAP 12-15 cmH_2O,以每次增加 2-3 cmH_2O 逐渐增加 PSV,不超过 25 cmH_2O,呼吸频率每分钟 14-18 次,不超过 25 次 /min,呼吸潮气量 >7 mL/kg,一日 4-8h,注意根据患者潮气量变化对吸气和呼气正压进行调整。在对照组的治疗基础上,观察组再予以沙美特罗替卡松气雾剂治疗(商品名:舒利迭,生产厂家:英国 Glaxo Smith Kline,注册证号 H20120015,规格:50/250 μg),雾化吸入,每次 1 吸,每日早晚各 1 次。所有患者治疗 3 周。

1.3 评价指标

在治疗前和治疗 3 周结束后,对患者的以下临床指标进行测定。

1.3.1 **动脉血气** 抽取桡动脉血检测血气,参数包括 pH、血氧分压(PaO_2)、二氧化碳分压($PaCO_2$)、血氧浓度(SaO_2)。

1.3.2 **炎性因子** 取患者清晨空腹静脉血,采用 ELISA 法测定血清中白介素 33(IL-33)、肿瘤坏死因子(TNF-α)、可溶性细胞间黏附分子 -1(sICAM-1)的水平。

1.3.3 **肺功能** 使用肺功能仪检测(生产厂家:德国 Jaeger 公司),参数包括用力肺活量(FVC)、呼气高峰流量(PEFR)、第 1s 用力呼气容积占预计值的百分比(FEV1%)、第 1s 用力呼气容积占用力肺活量的百分比(FEV1/FVC)。

1.3.4 CAPS **评分** 采用慢性阻塞性肺疾病和支气管哮喘生理评分(CAPS),各项生理参数和实验室检查结果均选取入院后第一个 24 h 内的最差值,总分 100 分,分数越高表示患者预后越差。

1.4 统计学分析

使用 SPSS 19.0 软件,计量资料以($\bar{x}$± s)表示,采用独立样本 t 检验,以 P<0.05 为差异具有统计学意义。

2 结果

2.1 两组治疗前后动脉血气分析结果比较

治疗前,两组患者的 pH、PaO_2、$PaCO_2$、SaO_2 相比较差异均无统计学意义(P>0.05)。治疗后,两组患者的 pH、PaO_2、SaO_2 均较治疗前明显升高,$PaCO_2$ 明显降低,且观察组以上指标的变化较对照组更加明显(P<0.05)。

表 1 两组治疗前后动脉血气参数比较($\bar{x}$± s)

Table 1 Comparison of the arterial blood gas parameters between two groups ($\bar{x}$± s)

Groups	pH		PaO_2 (mm Hg)		$PaCO_2$ (mm Hg)		SaO_2 (%)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group(n1=60)	7.27± 0.13	7.38± 0.08[①]	54.28± 6.81	80.34± 7.21[①]	85.12± 7.24	53.43± 6.42[①]	81.53± 5.24	92.33± 4.76[①]
Control group (n2=60)	7.26± 0.09	7.30± 0.16[①②]	53.16± 7.24	71.63± 8.03[①②]	84.54± 6.53	64.37± 5.98[①②]	82.14± 6.36	85.29± 5.32[①②]

Note: Compared with before treatment in the same group, [①] P<0.05; compared with the observation group, [②] P<0.05.

2.2 两组治疗前后血清炎性因子水平的比较

治疗前, 两组患者的血清 IL-33、TNF-α、sICAM-1 水平相比较差异均无统计学意义(P>0.05)。治疗后,两组患者的上述指标均较治疗前明显降低,且观察组以上指标的变化较对照组更为明显(P＜0.05)。

2.3 两组治疗前后肺功能指标的比较

治疗前,两组患者的 FVC、PEFR、FEV1%、FEV1/FVC 比较差异均无统计学意义(P>0.05)。治疗后,两组患者的上述指标均较治疗前明显升高,且观察组以上指标的变化较对照组更为明显(P＜0.05)。

2.4 两组治疗前后 CAPS 评分的比较

治疗前,观察组与对照组的 CAPS 评分分别为 29.13± 7.62 分、28.89± 8.03 分,两组相比较差异无统计学意义(P>0.05)。治疗后,两组患者的 CAPS 评分均较治疗前明显下降,且观察组(20.42± 6.85 分)明显低于对照组(24.35± 7.41 分)(P＜0.05)。

表 2 两组治疗前后血清炎性因子水平的比较($\bar{x}\pm s$)

Table 2 Comparison of the serum inflammatory factors levels betweentwo groups before and after treatmen($\bar{x}\pm s$)

GroupS	IL-33 (ng/mL)		TNF-α (ng/L)		sICAM-1 (ng/mL)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group (n_1=60)	15.34± 1.03	6.42± 0.65[a]	127.45± 25.83	87.34± 18.28[a]	184.26± 18.54	97.43± 10.13[a]
Control group (n_2=60)	15.41± 0.84	10.30± 0.98[a b]	126.84± 27.24	103.63± 20.32[a b]	182.31± 20.63	129.24± 13.28[a b]

Note: Compared with before treatment in the same group, [a] P<0.05; compared with the observation group, [b] P<0.05.

表 3 两组治疗前后肺功能指标的比较($\bar{x}\pm s$)

Table 3 Comparison of the pulmonary function between two groups before and after treatment($\bar{x}\pm s$)

Groups	FVC (L)		PEFR (L/s)		FEV_1% (%)		FEV_1/FVC (%)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group(n_1=60)	1.68± 0.61	2.16± 0.68[a]	2.35± 0.98	3.17± 1.02[a]	44.85± 10.76	67.83± 12.29[a]	34.85± 8.68	64.87± 9.42[a]
Control group (n_2=60)	1.66± 0.75	2.01± 0.56[a b]	2.33± 0.86	2.68± 1.09[a b]	44.90± 11.12	54.13± 11.54[a b]	34.79± 8.74	45.34± 10.14[a b]

Note: Compared with before treatment in the same group, [a] P<0.05; compared with the observation group, [b] P<0.05.

3 讨论

在 COPD 的进行性发展过程中,粒细胞、巨噬细胞、$CD8^+$T 细胞等均会参与到慢性炎症反应过程中,且会释放多种炎症介质、黏附因子和蛋白酶等[12-14]。炎症可引起肺部纤毛功能失调,从而使气流受限,导致气体交换异常[15]。当 COPD 急性加重时,由于小气道阻力升高,过度充气,呼吸肌疲劳,气体交换障碍加重,进而出现多种呼吸形态的改变,极易发展为呼吸衰竭[16,17]。COPD 合并呼吸衰竭的治疗主要在于增加肺通气,缓解呼吸困难,改善血气指标,减轻呼吸道炎症反应,解除支气管痉挛[18]。

NIPPV 的原理是建立气管外口与肺泡之间的压力差,从而改善肺氧合,维持通气,减轻呼吸耗氧,维持血流动力学的稳定[19]。对于 COPD 可能通过两种机制发挥作用,一是使患者处于长期慢性疲劳的呼吸肌得到休息,减轻负荷,二是可以改善夜间睡眠失调及呼吸情况[20,21]。NIPPV 已在 COPD 合并呼吸衰竭的治疗中取得了良好效果[22,23]。舒利迭是一种复合制剂,沙美特罗扩张支气管、抑制炎性细胞的聚集和活化,丙酸氟替卡松抑制炎性细胞活化及炎性因子生成,并提高 β2 受体的敏感性。二者协同作用能够激活气道平滑肌上 β2 肾上腺素能受体,充分舒张气道平滑肌[24]。舒利迭对于 COPD 患者可有效缓解临床症状,改善病情,也有助于长期治疗[25]。研究表明舒利迭联合 NIPPV 可以改善 COPD 合并呼吸衰竭患者的血气和肺功能指标,效果显著,转归良好[26,27]。

IL-33 是一类由辅助性 T 细胞 2 主导分泌的促炎因子,可作用于嗜酸性粒细胞,并参与到体液免疫与细胞免疫机制中[28,29]。sICAM-1 也是近年来得到诸多研究的一种细胞黏附因子,可提示机体的免疫异常状态,在 COPD 炎症的急性加重及慢性迁延过程中发挥了重要作用[30,31]。TNF-α 被广泛认为是重要炎症启动因子之一,可以很好地反映机械通气治疗期间机体的炎症反应情况[32]。本研究结果显示与治疗前相比,两组患者治疗后的血清 IL-33、TNF-α、sICAM-1 水平均较治疗前明显降低,且观察组以上指标变化更为明显,说明联合治疗对于炎症反应的控制效果更佳。在患者的肺功能和动脉血气方面,治疗后与治疗前相比,两组患者的 pH、PaO_2、SaO_2 均明显升高,$PaCO_2$ 明显降低,FVC、PEFR、FEV1%、FEV1/FVC 均明显升高,且观察组以上指标变化更为明显,说明联合治疗可有效缓解患者肺功能下降,纠正高碳酸血症和低氧血症。另外,CAPS 评分在 COPD 急性加重期的病情评估方面表现出了良好的应用价值,专门监测患者的各项临床生理指标,从而量化地评价病情危重程度,有效预估患者预后[33]。本研究中,两组患者治疗后的 CAPS 评分均明显下降,且观察组明显低于对照组,说明联合治疗的患者预后更佳。

综上所述,舒利迭联合 NIPPV 能够较单用 NIPPV 更有效降低 COPD 合并Ⅱ型呼吸衰竭患者炎性因子水平,改善血气和肺功能,患者预后较好。

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