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支气管肺泡灌洗术用于重症支气管哮喘的疗效评价及对肺功能、炎症因子水平的影响 *

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摘要 目的:探讨支气管肺泡灌洗术用于重症支气管哮喘的疗效及对肺功能、炎症因子水平的影响。**方法:**选择我院 2015 年 3 月~2018 年 3 月收治的 150 例重症支气管哮喘患者,均接受支气管肺泡灌洗术治疗,分析其临床疗效,临床症状改善状况,治疗前后肺功能、炎症因子、血气指标的变化情况和不良反应的发生情况。**结果:**治疗后,150 例患者中,临床控制 70 例,好转 60 例,无效 20 例,总有效率为 86.67%(130/150),哮鸣音消失时间为 (5.17 ± 0.64) d,ACT 评分 (27.85 ± 3.86) 分、住院时间为 (5.73 ± 0.75) d。治疗后,患者用力肺活量(FVC)、1s 用力呼气容积(FEV1)、呼气峰流速(PEF)、血氧分压(PaO₂)、血氧饱和度(SaO₂)均显著高于治疗前($P < 0.05$),嗜酸性粒细胞(EOS)、干扰素- γ (IFN- γ)、肿瘤坏死因子- α (TNF- α)、白介素-6(IL-6)及二氧化碳分压(PaCO₂)低于治疗前($P < 0.05$)。150 例患者中,发生支气管痉挛 2 例,咽喉部疼痛 3 例,无猝死、大咯血、气胸等严重并发症发生。**结论:**支气管肺泡灌洗术用于重症支气管哮喘的疗效肯定,可有效改善患者肺功能,并减轻炎症反应。

关键词:重症支气管哮喘;支气管肺泡灌洗术;疗效;肺功能;炎症因子

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Efficacy of Bronchoalveolar Lavage in the Treatment of Severe Bronchial Asthma and Its Influences on the Lung Function and Inflammatory Factors*

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ABSTRACT Objective: To investigate the curative efficacy of bronchoalveolar lavage in the treatment of severe bronchial asthma and its influences on the lung function and inflammatory factors. **Methods:** 150 patients with severe bronchial asthma who were given bronchoalveolar lavage in our hospital from March 2015 to March 2018 were selected. The clinical efficacy, improvement of clinical symptoms, changes of pulmonary function, inflammatory factors and blood gas indexes before and after treatment, and the occurrence of safety adverse reactions were analyzed. **Results:** After treatment, among the 150 patients, 70 were clinically controlled, 60 were improved, and 20 were ineffective. The total effective rate was 86.67% (130/150), the disappearance time of wheezing sound was (5.17 ± 0.64) d, ACT score (27.85 ± 3.86) , and hospitalization time was (5.73 ± 0.75) d. After treatment, forced vital capacity (FVC), 1s forced expiratory volume (FEV1), PEF, PaO₂, SaO₂ were significantly higher than before treatment ($P < 0.05$), eosinophil (EOS), Interferon- γ (IFN- γ), tumor necrosis factor- α (TNF- α), interleukin-6(IL-6) and carbon dioxide partial pressure(PaCO₂) were significantly lower than before treatment ($P < 0.05$). Of the 150 patients, 2 had bronchospasm and 3 had throat pain, and no severe complications such as sudden death, massive hemoptysis and pneumothorax was found. **Conclusion:** Bronchoalveolar lavage is effective for the severe bronchial asthma, it can effectively improve the lung function and reduce the inflammation in patients.

Key words: Severe bronchial asthma; Bronchoalveolar lavage; Curative effect; Lung function; Inflammatory cytokines

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前言

支气管哮喘为临床常见的多发性慢性疾病,以发作性的咳嗽、胸闷、气急及喘息等为主要症状,反复发作可导致心功能衰竭、肺心病、呼吸衰竭等并发症,严重急性发作可危及患者生命安全^[1,2]。支气管哮喘目前尚无根治疗法,大部分患者经规范治

疗后可控制哮喘症状,但仍有部分重症支气管哮喘患者经系统治疗后的病情无法有效控制或者反复加重^[3,4]。重症支气管哮喘患者支气管有大量粘稠分泌物,导致患者呼吸功能明显受阻,及时有效的解除气道阻塞已成为此类疾病的重要治疗手段^[5,6]。支气管肺泡灌洗术具有创伤性小、操作方便、可视性等优势,可减轻患者气道堵塞,减少气道分泌物,缓解哮喘发作,其疗效已

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得到临床广泛证实^[7,8]。

研究表明支气管哮喘是多种细胞炎症因子相互作用所致,气道炎症的启动又依赖于细胞因子网络调控^[9,10]。干扰素- γ (IFN- γ)作为一种可溶性细胞因子,能够促进感染导致炎症性应答。肿瘤坏死因子- α (TNF- α)及白介素-6 (IL-6)作为临床常见的炎症因子,机体发生炎症反应后可促进其表达,引起级联炎症反应,导致病情加剧。因此,本研究主要分析了支气管肺泡灌洗术用于重症支气管哮喘的疗效及对患者肺功能、炎症因子水平的影响,结果如下。

1 资料与方法

1.1 一般资料

选择我院 2015 年 3 月~2018 年 3 月收治的 150 例重症支气管哮喘患者,入选标准:凝血功能和血小板正常;无纤维支气管镜禁忌证;肝肾等功能正常;非妊娠或者哺乳阶段。排除标准:严重冠心病心绞痛、心功能不全、大咯血窒息、心肌梗死;严重高血压、急性脑血管病变;呼吸衰竭;严重呼吸道感染、肺结核、真菌感染等传染性病变。150 例患者中男 81 例,女 69 例;年龄 24~72 岁,平均 (55.92 ± 9.61) 岁;支气管哮喘病史 5~38 年,平均病程 (18.43 ± 4.29) 年;哮喘控制测试 (ACT) 评分 (17.41 ± 2.58) 分。

1.2 诊断标准

(1)符合支气管哮喘相关诊断标准^[11](符合①至④项或者⑤至⑥项):①胸闷、气急、喘息、咳嗽反复发作,多与接触冷空气、变应原、上呼吸道感染、化学性或者物理性刺激、运动相关;②肺部可闻及弥散或者局部的哮鸣音,且主要为呼气相并延长;③临床表现可自行减轻或者于用药后减轻;④排除其他因素造成的胸闷、气急、喘息、咳嗽等临床表现;⑤若临床表现不显著者,至少需具备 1 项下列试验阳性:支气管的舒张试验为阳性、支气管的运动试验或者激发试验为阳性、最大呼气流量 (PEF) 的昼夜波动率或者日内变异率在 20%以上。(2)哮喘重度发作后经营养支持、维持酸碱及水电介质平衡、抗感染、解痉平喘、氧疗等规范治疗 7~14 d 后症状反复加重或者无法缓解,出现呼吸困难、端坐呼吸,查体可见意识障碍加重,严重者可出现心律失常、昏迷,双肺闻及大量痰鸣音或者干啰音。

1.3 治疗方法

所有患者术前禁饮食 3~4 h,常规检测心电图、动脉血气、出凝血时间及血常规等,并进行充分的抢救准备工作。鼻导管吸氧 2 L/min,吸入 2 喷沙丁胺醇。术前给予 2%利多卡因进行咽部及鼻粘膜的局部麻醉,于单侧相对宽大的鼻腔入镜,对

准声门于气管喷入 2 mL 利多卡因,去除环甲膜穿刺注药。支气管进入声门后在气管、支气管注入 1~2 mL 利多卡因麻醉,以减轻支气管痉挛和咳嗽。术中采用心电监护仪密切监测患者血压、血氧饱和度 (SaO₂) 及心率,参照 SaO₂ 调节吸氧浓度,维持 SaO₂ ≥ 90%。常规查看支气管及气管,充分吸入痰栓和分泌物,选择 1~2 个痰栓较多叶段实施肺泡灌洗术,每次注入 10~20 mL 37℃ 盐水,总量 < 100 mL,保持回收量 > 40%,将回收液进行培养和药敏试验。操作期间动作应迅速、轻柔,最大程度的缩短操作时间,总操作时间保持在 10~15 min。注意术后不良反应及并发症,记录临床症状改善状况。

1.4 观察指标

1.4.1 临床疗效 治疗 48 h 后,评价临床疗效^[12]:症状和哮鸣音消失,动脉血气无二氧化碳潴留及低氧血症,或者恢复至本次急性发作前基础状态为临床控制;症状由重度转为轻度或者中度为好转;症状未见改善或者转为危重度、死亡为无效。临床控制率及好转率为总有效率。

1.4.2 肺功能 于治疗前及治疗后 48 h 采用肺功能仪测定用力肺活量 (FVC)、1s 用力呼气容积 (FEV₁)、呼气峰流速 (PEF)。

1.4.3 血液指标 于治疗前及治疗后 48h 采集患者空腹外周静脉血,常规处理后保存待检。采用全自动分析仪测定外周血嗜酸性粒细胞 (EOS) 水平,采用酶联免疫法检测血清干扰素- γ (IFN- γ)、肿瘤坏死因子- α (TNF- α) 及白介素-6 (IL-6) 水平。

1.4.4 血气指标 于治疗前及治疗 48h 后采用全自动血气分析仪测定患者血氧分压 (PaO₂)、二氧化碳分压 (PaCO₂) 及 SaO₂ 浓度。

1.5 统计学分析

数据处理选用 SPSS18.0 软件包,计量资料用 $(\bar{x} \pm s)$ 表示,治疗前后比较选用配对 t 检验,以 $P < 0.05$ 表示差异有统计学意义。

2 结果

2.1 患者临床疗效分析

150 例患者中,临床控制 70 例,好转 60 例,无效 20 例,总有效率为 86.67% (130/150)。

2.2 患者临床症状改善情况分析

150 例患者哮鸣音消失时间为 (5.17 ± 0.64) d、ACT 评分 (27.85 ± 3.86) 分、住院时间为 (5.73 ± 0.75) d。

2.3 患者治疗前后肺功能比较

治疗后,患者 FVC、FEV₁ 及 PEF 均显著高于治疗前,组间比较有统计学差异 ($P < 0.05$),见表 1。

表 1 两组患者治疗前后肺功能的比较 $(\bar{x} \pm s)$

Table 1 Comparison of the lung function before and after treatment $(\bar{x} \pm s)$

Time	n	FVC(%)	FEV ₁ (%)	PEF(L/s)
Before treatment	150	61.08 ± 7.61	54.02 ± 6.95	0.84 ± 0.14
After treatment	150	79.11 ± 9.43 [#]	77.43 ± 10.63 [#]	1.42 ± 0.21 [#]

Note: Compared with before treatment [#] $P < 0.05$.

2.4 患者治疗前后 EOS、血清 IFN- γ 、TNF- α 及 IL-6 水平的比较

治疗后,患者 EOS 计数、血清 IFN- γ 、TNF- α 及 IL-6 水平

均低于治疗前,差异有统计学意义 ($P < 0.05$),见表 2。

表 2 患者治疗前后 EOS 及血清炎症因子水平比较($\bar{x} \pm s$)

Table 2 Comparison of the EOS and serum inflammatory factor level before and after treatment between two groups($\bar{x} \pm s$)

Time	n	EOS($\times 10^6$)	IFN- γ (ng/L)	TNF- α (ng/L)	IL-6(μ g/L)
Before treatment	150	467.31 $\pm$ 68.42	862.10 $\pm$ 105.77	209.71 $\pm$ 29.86	128.05 $\pm$ 14.02
After treatment	150	251.02 $\pm$ 35.01 [#]	531.02 $\pm$ 68.50 [#]	117.29 $\pm$ 13.82 [#]	81.26 $\pm$ 10.85 [#]

Note: Compared with before treatment [#] $P < 0.05$.

2.5 患者治疗前后动脉血气指标的比较

较治疗前显著下降,差异有统计学意义($P < 0.05$),见表 3。

治疗后,患者 PaO₂、SaO₂ 均较治疗前显著上升,PaCO₂ 均

表 3 患者治疗前后动脉血气指标的比较($\bar{x} \pm s$)

Table 3 Comparison of the arterial blood gas index before and after treatment($\bar{x} \pm s$)

Time	n	PaO ₂ (mmHg)	PaCO ₂ (mmHg)	SaO ₂ (%)
Before treatment	150	59.04 $\pm$ 6.59	50.14 $\pm$ 6.03	63.90 $\pm$ 7.95
After treatment	150	89.42 $\pm$ 11.41 [#]	38.75 $\pm$ 4.77 [#]	93.11 $\pm$ 12.09 [#]

Note: Compared with before treatment [#] $P < 0.05$.

2.6 患者不良反应的发生情况分析

150 例患者发生支气管痉挛 2 例、咽喉部疼痛 3 例,无猝死、大咯血、气胸等严重并发症发生。

3 讨论

支气管哮喘为气道慢性变态反应性疾病,具有周期性、长期性及反复性等特点,重症支气管哮喘急性发作时可引起猝死,临床资料显示^[12]支气管哮喘已成为仅次于癌症的第二大致残及致死疾病。西医治疗支气管哮喘虽可快速控制病情,但疗效维持时间较短,且有一定的副作用^[13,14]。机械通气虽可治疗危重哮喘,但难以消除小气道广泛出现的肺不张及黏液栓,严重影响通气效果,甚至可能使患者发生窒息,导致致死性哮喘^[15,16]。既往研究显示^[17,18]痰栓所致的支气管阻塞是支气管哮喘对内科治疗无反应的重要诱因之一,因此辅助清除气道痰栓疗法可能是重症支气管哮喘患者的重要治疗手段。

支气管肺泡灌洗术借助纤维支气管镜,可在直视状态下查看病灶形态学改变以及有无出血、堵塞及变形等病理学变化,且可结合电视、电脑等影像保存图像,以便反复观察分析^[19,20]。支气管肺泡灌洗术能够直达小气道部位,有效清除患者气道内的粘稠性分泌物,缓解气道梗阻,维持支气管畅通,从而明显减轻患者症状^[21,22]。本研究结果显示支气管肺泡灌洗术对重症支气管哮喘的疗效较好,考虑原因为支气管肺泡灌洗术可直接到达病灶部位,局部药物浓度较高,且可清除局部分泌物及痰栓,从而发挥良好的治疗作用。

重症支气管哮喘患者多伴程度不一的可逆性气道受阻,导致患者肺功能下降,肺功能能够客观反映患者大气道通气及阻力情况,是评估支气管哮喘病情程度的可靠量化指标,可帮助患者制定治疗方案^[23]。本研究结果显示患者治疗后肺功能指标均上升,提示其能有效改善患者的肺功能,有利于机体恢复。

EOS 聚集是重症支气管哮喘的主要标志,可导致气道炎症和气道高反应性,相关研究报道 EOS 和哮喘严重程度有良好关系^[24,25]。近年来,随着临床对支气管哮喘病理生理和发病机制研究的不断深入,有学者认为哮喘^[26]的发病有多种炎症因子参与,IFN- γ 为巨噬细胞激活因子,可破坏病原体,参与哮喘发病。TNF- α 能够导致气道高反应性,具有促进细胞分化、细胞生长

及促进急性期蛋白合成的作用^[27]。IL-6 能够刺激 T 淋巴细胞激活及增殖,诱导 EOS 及免疫球蛋白 E 增殖分化至呼吸道^[28]。本研究结果显示患者治疗前 EOS、IFN- γ 、TNF- α 及 IL-6 水平均较高,说明重症支气管哮喘可能存在一定程度的炎症反应,治疗后以上指标均下降,提示其能有效下调机体炎症因子表达,减轻气道炎症反应,从而缓解气道高反应性。重症支气管哮喘患者由于气道粘液阻塞,可出现一定程度的血气异常,本研究结果显示患者治疗后血气指标均得到恢复,说明支气管肺泡灌洗术还可改善患者动脉血气指标,改善机体通气状态,减轻气道阻塞^[29,30]。但支气管肺泡灌洗术作为介入疗法,可能会对机体产生一定的损伤,因此其治疗的安全性越发得到临床重视。本研究显示少数患者发生支气管痉挛及咽喉部疼痛,处理得当后均得明显纠正,说明支气管肺泡灌洗术的安全性尚可^[31]。

综上所述,支气管肺泡灌洗术用于重症支气管哮喘的疗效肯定,可有效改善患者肺功能,并减轻炎症反应。

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