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老年重症肺炎患者病原菌分布及支气管镜肺泡灌洗术的治疗效果与安全性

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Abstract: **Objective** To investigate the distribution characteristic of pathogenic bacteria in elderly patients with severe pneumonia and the therapeutic effect and safety of bronchoscopy alveolar lavage. **Methods** A total of 120 elderly patients with severe pneumonia admitted to the Daxing Teaching Hospital of Capital Medical University from January 2016 to January 2020 were selected as the research objects and they were randomly divided into control group ($n = 60$) and observation group ($n = 60$). All patients were given conventional therapy; based on conventional therapy, the patients in the observation group were treated with bronchoscopy alveolar lavage. The bronchoalveolar lavage fluid was cultured, and the pathogen distribution characteristics were analyzed. Before and after treatment, 4 mL of fasting peripheral venous blood were taken from the patients in the two groups, and the levels of interleukin-6 (IL-6) and tumor necrosis factor- α (TNF- α) in serum were detected by enzyme-linked immunosorbent assay, the level of high-sensitivity C-reactive protein (hs-CRP) in serum was detected by hypersensitive latex enhanced immunoturbidimetry. The clinical efficacy and the incidence of adverse reactions during treatment were compared between the two groups. **Results** A total of 238 pathogenic bacteria were isolated from the patients in the observation group, including 147 strains (61.76%) of gram-negative bacilli, mainly *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Escherichia coli* and *Enterobacter cloacae*; 54 strains (22.69%) of gram-positive bacilli, mainly *Staphylococcus epidermidis*, *Staphylococcus hemolyticus*, and *Staphylococcus aureus*; 37 strains (15.55%) of fungi, mainly *Candida albicans*, *Candida parapsilosis* and *Aspergillus fumigatus*. There was no significant difference in the levels of serum IL-6, TNF- α and hs-CRP of patients in the two groups before treatment ($P > 0.05$). The levels of serum IL-6, TNF- α and hs-CRP of patients after treatment were significantly

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lower than those before treatment in the two groups ($P < 0.05$). After treatment, the levels of serum IL-6, TNF- α and hs-CRP of patients in the observation group were significantly lower than those in the control group ($P < 0.05$). The effective rates of patients in the control group and the observation group were 81.67% (49/60) and 93.11% (55/60), respectively; the effective rate of patients in the observation group was significantly higher than that in the control group ($\chi^2 = 5.175, P < 0.05$). The total incidence of adverse reactions of patients in the control group and the observation group were 6.67% (4/60) and 3.33% (2/60), respectively; there was no significant difference in the total incidence of adverse reactions of patients between the two groups ($P > 0.05$). **Conclusion** Bronchoscopy alveolar lavage can be used for the treatment of severe pneumonia in the elderly. Analysis of the distribution of pathogens in the alveolar lavage fluid before antibiotics is helpful to guide doctors to medication. Bronchoscopy alveolar lavage can reduce the inflammatory response of patients, it is safety and its curative effect is remarkable.

Key words: severe pneumonia; bronchoscopy alveolar lavage; pathogenic bacteria

重症肺炎是常见的危急重症,常由多种细菌感染引起^[1]。老年群体由于身体机能下降,免疫功能减退,容易在重症肺炎的基础上并发其他脏器功能障碍,从而使其治疗更为困难,且预后不佳,严重影响患者正常的工作和生活^[2]。因此,对老年重症肺炎应尽早进行积极治疗。重症肺炎治疗的关键在于及时清除气道分泌物,减轻感染,临床常使用抗生素进行治疗,但该疗法治疗时病灶内药物常无法达到预期浓度,导致治疗效果不理想^[3]。支气管镜肺泡灌洗术可清除气道内分泌物,使患者的呼吸通畅,是治疗重症肺炎的常用手段^[4]。重症肺炎患者的细菌耐药性也是临床广泛关注的问题,明确病原菌分布并进行药物敏感性分析有利于对疾病进行精确治疗,从而减少耐药性^[5]。基于此,本研究分析了老年重症肺炎患者支气管肺泡灌洗液病原菌分布特征并观察了支气管镜肺泡灌洗术治疗老年重症肺炎的效果和安全性,现报道如下。

1 资料与方法

1.1 一般资料 选择首都医科大学大兴教学医院2016年1月至2020年1月收治的老年重症肺炎患者120例为研究对象,并随机分为对照组($n = 60$)和观察组($n = 60$)。病例纳入标准:(1)符合《中国成人社区获得性肺炎诊断和治疗指南》^[6]中有关重症肺炎诊断标准;(2)入院时间 < 48 h;(3)首次就诊者;(4)依从性良好,配合治疗者。排除标准:(1)合并有心源性肺水肿、恶性肿瘤、其他脏器重大疾病者;(2)有支气管镜肺泡灌洗术禁忌证者。对照组:男28例,女32例;年龄62~88(68.56 ± 7.31)岁,体质质量指数13~32(23.76 ± 3.78) $\text{kg} \cdot \text{m}^{-2}$ 。观察组:男29例,女31例;年龄62~89(69.31 ± 7.72)岁,体质质量指数15~38(22.55 ± 5.38) $\text{kg} \cdot \text{m}^{-2}$ 。2组患者一般资料比较差异无统计学意义($P > 0.05$),具有可比性。本研究获医院伦理委员会审核批准,且患者及家属知情同意。

1.2 治疗方法 2组患者均给予抗感染、营养支持、维持患者体内水电解质平衡、机械通气、气管插

管等常规治疗,在此基础上,观察组患者给予支气管镜肺泡灌洗术治疗。支气管镜肺泡灌洗术主要步骤:治疗前向患者介绍支气管镜肺泡灌洗术的操作及注意事项,治疗时使用心电监护仪监测患者的生命体征,注射 $20 \text{ g} \cdot \text{L}^{-1}$ 利多卡因(泰兴市济川药业集团有限公司,国药准字H20059049)5 mL局部麻醉患者咽喉、鼻腔,患者取仰卧位,经鼻腔置入电子支气管镜,清除大气道内的分泌物,有较大块异物时以钳夹取出,各气道清理完成后继续进入支气管镜,待其到达病灶后,注入 37°C 的生理盐水与盐酸氨溴索(上海勃林格殷格翰药业有限公司,国药准字H20031314)混合液100 mL进行灌洗,反复冲洗,直至灌洗液清晰,收集灌洗液置于无菌集痰瓶中,2 h内送检,结束治疗后撤出支气管镜。

1.3 观察指标 (1)支气管肺泡灌洗液中病原菌分布。取观察组患者支气管肺泡灌洗液,在 4°C 下 $600 \text{ r} \cdot \text{min}^{-1}$ 离心5 min,弃上清,将所取标本均质化,接种于血琼脂、麦康凯、巧克力培养皿中,置于 35°C 、含体积分数5% CO_2 培养箱中孵育18~24 h,观察细菌生长情况,挑选培养皿中的可疑菌种进行纯培养后,应用WALKAWAY-96SI全自动分析仪(德国西门子)对菌种进行分离鉴定。(2)血清白细胞介素-6(interleukin-6, IL-6)、肿瘤坏死因子- α (tumor necrosis factor- α , TNF- α)、超敏C反应蛋白(high sensitivity C-reactive protein, hs-CRP)水平。分别于治疗前后抽取2组患者空腹外周静脉血4 mL, $3\,200 \text{ r} \cdot \text{min}^{-1}$ 离心8 min,取上清液,采用酶联免疫吸附法检测血清中IL-6、TNF- α 水平(试剂盒购自上海碧云天生物科技有限公司),超敏乳胶增强免疫比浊法检测血清中hs-CRP水平(试剂盒购自南京基蛋生物科技股份有限公司)。(3)临床疗效。参照文献^[7]中的标准判断2组患者的治疗效果。显效:胸部X片、血气分析及临床表现均正常;有效:胸部X片显示阴影好转,血气分析基本正常,肺部可听到湿啰音;无效:病情无好转。总有效率=(显效例数+有效例数)/总例数 $\times 100\%$ 。(4)不良反应。记录2组患者治疗期间不良反应发生情况。

1.4 统计学处理 应用 SPSS 23.0 软件进行统计学分析。符合正态分布的计量资料以均数 ± 标准差 ($\bar{x} \pm s$) 表示,组间比较采用独立样本 t 检验,组内比较采用最小显著性差异法- t 检验;计数资料以例数和百分率表示,组间比较采用 χ^2 检验,当 $1 \leq$ 理论频数 < 5 时,采用 Fisher 确切概率法; $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 支气管肺泡灌洗液中病原菌分布特征 观察组 60 例患者的支气管肺泡灌洗液中共分离出病原菌 238 株,其中革兰阴性杆菌 147 株 (61.76%),革兰阳性杆菌 54 株 (22.69%),真菌 37 株 (15.55%)。革兰阴性杆菌中主要为肺炎克雷伯菌 (29.25%, 43/147)、铜绿假单胞菌 (25.85%, 38/147)、大肠埃希菌 (23.81%, 35/147) 和阴沟肠杆菌 (8.16%, 12/147),革兰阳性杆菌中主要为表皮葡萄球菌 (35.19%, 19/54)、溶血葡萄球菌 (31.48%, 17/54) 和金黄色葡萄球菌 (20.37%, 11/54),真菌中主要为白色念珠菌 (56.76%, 21/37)、近平滑念珠菌 (23.32%, 9/37) 和烟曲霉菌 (10.81%, 4/37)。

2.2 2 组患者治疗前后血清炎症因子水平比较 结果见表 1。治疗前 2 组患者血清中 IL-6、TNF- α 、hs-CRP 水平比较差异无统计学意义 ($P > 0.05$)。2 组患者治疗后血清中 IL-6、TNF- α 、hs-CRP 水平均低于治疗前,差异有统计学意义 ($P < 0.05$)。治疗后,观察组患者血清中 IL-6、TNF- α 、hs-CRP 水平显著低于对照组,差异有统计学意义 ($P < 0.05$)。

表 1 2 组患者治疗前后血清炎症因子水平比较
Tab.1 Comparison of serum inflammatory factor levels of patients between the two groups before and after treatment
($\bar{x} \pm s$)

组别	n	IL-6/($\mu\text{g} \cdot \text{L}^{-1}$)	TNF- α /($\text{ng} \cdot \text{L}^{-1}$)	hs-CRP/($\text{mg} \cdot \text{L}^{-1}$)
对照组	60			
治疗前		83.25 \pm 8.48	147.59 \pm 11.47	15.92 \pm 1.48
治疗后		59.74 \pm 19.51 ^a	105.11 \pm 8.36 ^a	6.51 \pm 0.72 ^a
观察组	60			
治疗前		82.88 \pm 8.93	147.60 \pm 11.49	15.26 \pm 1.63
治疗后		47.82 \pm 4.38 ^{ab}	82.19 \pm 7.31 ^{ab}	4.59 \pm 0.41 ^{ab}

注:与治疗前比较^a $P < 0.05$;与对照组比较^b $P < 0.05$ 。

2.3 2 组患者临床疗效比较 治疗后,对照组患者中显效 11 例,有效 38 例,无效 11 例,有效率为 81.67% (49/60);观察组患者中显效 20 例,有效 35 例,无效 5 例,有效率为 93.11% (55/60)。观察组患者治疗有效率显著高于对照组,差异有统计学意义 ($\chi^2 = 5.175, P < 0.05$)。

2.4 治疗期间 2 组患者不良反应发生情况 对照组患者中发生轻度腹泻 1 例,低氧血症 2 例,支气管痉挛喘息 1 例,总不良反应发生率为 6.67% (4/

60);观察组患者中发生轻度腹泻 1 例,低氧血症 1 例,总不良反应发生率为 3.33% (2/60);2 组患者总不良反应发生率比较差异无统计学意义 ($P > 0.05$)。

3 讨论

重症肺炎是呼吸科常见的危重症之一,患者主要表现为严重低氧血症或急性呼吸衰竭,或者出现低血压、休克等循环衰竭表现和其他器官功能障碍,甚至会发生死亡^[8]。老年人群大多存在基础疾病,如糖尿病、慢性阻塞性肺疾病、慢性肝病等可能会增加肺炎严重程度的慢性疾病,且老年重症肺炎患者全身和气道局部的防御和免疫力下降,病情容易恶化,因此,老年重症肺炎治愈率较低,病死率较高^[9]。对老年重症肺炎患者,需尽早实施药物治疗以尽快缓解症状,促进患者恢复。

抗感染治疗是肺炎治疗的最主要环节,全身使用抗生素为治疗肺炎的首要方法,但是对老年重症肺炎患者而言,部分患者的疗效受多种因素的限制,如老年重症肺炎患者机体内存在血-支气管屏障,使得局部病灶内药物浓度不足,且患者气道炎症分泌物可能阻塞气道,从而造成疗效不佳^[10]。随着支气管镜在临床的普及使用,支气管镜肺泡灌洗术在治疗老年重症肺炎的作用中逐渐得到临床医师的认可^[11]。该疗法是在纤维支气管镜检查基础上发展起来的一项新技术,是利用支气管镜将液体直接灌注肺段或肺亚段的病变部位,稀释较为黏稠的炎症分泌物,清除气道和肺泡滞留物质,缓解气管阻塞,灌洗液还可以刺激呼吸道,促进药物分散到各级支气管,有助于提高疗效^[12]。此外,在实施支气管镜肺泡灌洗术时使用的盐酸氨溴索是临床常用的呼吸道祛痰剂,作为一种表面活性物质激活剂和黏液溶解剂,不仅可以溶解黏痰和润滑呼吸道,促进痰液排出,还能促进表面活性物质的合成与分泌,有效保护肺脏,且具有良好抗炎效果。

对老年重症肺炎患者而言,病原学检测与敏感药物的选择是治疗成功与否的关键,病原学培养作为病原学诊断的金标准受到广大临床及基础医学研究者的关注,临床常用痰培养检测,然而经口留取痰液容易受口腔定植菌影响,且检测结果阳性率低。采用支气管肺泡灌洗液培养细菌,使得病原学检测结果阳性率提升,对老年重症肺炎患者的病原菌分布及用药指导具有重要意义^[13]。本研究结果发现,观察组 60 例患者的支气管肺泡灌洗液中共分离出病原菌 238 株,其中革兰阴性杆菌 147 株 (61.76%),以肺炎克雷伯菌、铜绿假单胞菌、大肠埃希菌、阴沟肠杆菌为主,其中大肠埃希菌感染者灌

洗液较稀薄,未闻及特殊臭味,而阴沟肠杆菌感染者气道黏膜坏死较明显,常堵塞气道,在抗感染治疗同时需反复清理气道;革兰阳性杆菌 54 株(22.69%),以表皮葡萄球菌、溶血葡萄球菌、金黄色葡萄球菌为主,其中葡萄球菌感染者气道黏膜糜烂,分泌物多,呈黄色脓肿,壅塞气道,临床症状多表现为高热、剧烈咳嗽、胸痛,并常伴有胸腔积液,气管镜检查后常用发热,灌洗液呈脓性,镜下治疗需注意,以免发生气胸;真菌 37 株(15.55%),以白色念珠菌、近平滑念珠菌及烟曲霉菌为主。细菌耐药性的变迁是当前抗感染治疗失败的主要原因之一。有研究表明,革兰阳性菌对青霉素、红霉素、头孢他啶、头孢西丁等药物耐药率已超过 50%,革兰阴性菌中对头孢呋辛钠、阿莫西林克拉维酸钾及氨苄西林耐药率占前 3 位,故对于病原菌尚不明确的重症肺炎患者应避免应用上述 3 种药物^[14]。总之,细菌耐药现象较严重,需引起高度重视,在正确评估病情严重程度的同时进行病原菌检测,有助于提高选择抗菌药物时的针对性。通过明确患者的病原学诊断给予目标治疗可更有效地控制感染。

各种炎症因子参与了重症肺炎的发生发展,IL-6、TNF- α 和 hs-CRP 均是反映机体炎症状态的因子,其水平的异常升高可造成肺泡上皮细胞通透性增加及细胞功能损伤,造成肺水肿及微血栓的形成^[15]。本研究结果发现,治疗后 2 组患者血清中炎症因子 IL-6、TNF- α 及 hs-CRP 水平均低于治疗前,且观察组患者上述炎症因子水平低于对照组;这提示支气管镜肺泡灌洗术可减轻重症肺炎患者的炎症反应及肺组织损伤,抑制病程进展。纤维支气管镜肺泡灌洗毛刷可直达病灶部位,采用生理盐水反复冲洗,可彻底清除肺泡深部痰液,从而促使炎症分泌物排出体外,缓解气道堵塞。本研究结果还显示,观察组患者治疗有效率显著高于对照组,且 2 组患者不良反应发生率比较差异无统计学意义;这提示支气管镜肺泡灌洗术治疗老年重症肺炎疗效肯定,且未增加不良反应,安全性较高。杨晓纲等^[16]研究发现,纤维支气管镜肺泡灌洗术可改善重症肺炎患者的呼吸功能及炎症反应状态,疗效肯定。雷莉莉等^[17]研究发现,对支气管镜肺泡灌洗液主要病原菌及耐药性进行分析,有助于提高支气管镜肺泡灌洗术的治疗效果。以上研究与本研究结果类似,肯定了分析支气管镜肺泡灌洗液病原菌分布特征的必要性及支气管镜肺泡灌洗术治疗老年重症肺炎患者的疗效。

综上所述,支气管镜肺泡灌洗术可用于治疗老年重症肺炎,使用抗生素前分析肺泡灌洗液病原菌分布,有助于指导医生用药;该方法可减轻患者的炎症反应,安全性较高,疗效显著,值得在临床推广使用。

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