·老年人呼吸系统疾病专栏·

老年下呼吸道感染病原学特点及对策

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【摘 要】 老年人群是下呼吸道感染的主要人群,发病率和死亡率都较高。随着年龄的增长,基础疾病增多,口腔、上呼吸道的定植菌增加,吞咽功能障碍发生率增高,导致吸入性肺炎发生率增高,从而导致老年人群下呼吸道感染致病菌的病原谱分布与总体人群相比出现差异,革兰阴性肠杆菌科细菌、铜绿假单胞菌、金黄色葡萄球菌和厌氧菌的比例增加。本文在介绍老年人群特点的基础上着重探讨下呼吸道感染病原学及细菌耐药特点,并引用相关指南提供最佳的抗菌药物治疗选择方案,为临床医师提供指导。

【关键词】 老年人;下呼吸道感染;致病原;治疗
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Etiologic characteristics and therapeutic strategies of lower respiratory infections in the elderly

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【Abstract】 Older patients are the main population suffering from lower respiratory infections, which is of high incidence and mortality. Because of the increasing age, presence of one or more co-morbidities, colonization of bacteria in the oral cavity and upper respiratory tract, and high incidence of dysphagia, all these factors increase the occurrence of aspiration pneumonia. Thus, the distribution of causative agents for lower respiratory infection in the older people is different from general population. The percentages of Gram-negative *Enterobacteriaceae*, *Pseudomonas aeruginosa*, *Staphylococcus aureus* and anaerobic bacteria become larger. Based on the characteristics of the elderly population, this paper focused on the features of pathogens and bacterial resistance in lower respiratory tract infection, and provided the best antibiotic treatment options according to the relative guidelines so as to provide references to the clinicians.

【Key words】 aged; lower respiratory infection; pathogen; therapy
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呼吸道感染是常见的感染性疾病,有较高的发病率和死亡率[1,2]。老年人群是呼吸道感染的主要人群,并随着年龄增长感染率增高。西班牙学者Bosch等[3]研究显示,≥75岁人群社区获得性肺炎(community acquired pneumonia, CAP)的发病率是<60岁人群的6倍;Vila-Corcoles等[4]的研究显示:65~74岁人群CAP的发病率为10/1000人年,75~84岁人群增长到16.9/1000人年,≥85岁人群的发病率高达29.4/1000人年。高龄本身也是呼吸道感染患者初始治疗失败及死亡率增加的独立高风险因素之一[5]。德国学者Kothe等[5]的研究结果显示,≥65岁CAP患者30 d的死亡率为10.3%,显著高于<65岁的患者,多因素分析显示年龄是CAP死亡的独立危险因素。需要住院的老年肺炎患者的病死率甚至可高达30%~57%[6]。因此,了解老年人群的特征、呼吸道感染病原学特点和治疗策略,才能使他们得到更好的治疗。

1 老年人群的特征

1.1 基础疾病多

随着年龄的增长,老年患者常常伴有越来越多的基础疾病。某些基础疾病本身就可以增加肺炎的发生率和死亡率。西班牙学者Vila-Corcoles等[4]的研究显示:≥65岁人群CAP的总发病率为

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14.0/1000人年,合并心脏疾病的患者CAP发病率增长到25.5/1000人年,合并肾脏疾病的增长到27.2/1000人年,吸烟人群为29.2/1000人年,合并慢性肺部疾病的人群高达46.5/1000人年。日本的研究显示[7],因CAP去世的患者,超过98%是≥60岁的老年人。与年轻患者相比,老年患者临床上常常伴有其他基础疾病,如心脏病、慢性阻塞性肺疾病、脑血管疾病等。德国学者Kothe等[5]关于CAP的研究也显示,慢性心脏疾病、脑血管疾病、慢性肝病、慢性肾病、糖尿病等都是CAP死亡率增加的危险因素。

1.2 吸入性肺炎风险增加

随着年龄的增长,老年患者吞咽功能障碍发生率增加,误吸的风险增高,吸入性肺炎发生率增加[8]。合并神经系统疾病(比如痴呆、中风)的患者更容易发生误吸,误吸率可达22%~65%[9]。西班牙学者Cabre等[10]研究了134例≥70岁的老年肺炎患者,结果显示55%存在吞咽功能障碍,从而容易导致吸入性肺炎的发生。Kikuchi等[11]的研究也显示,患肺炎的老年患者隐性误吸的发生率为71%,而未患肺炎的老年人仅有10%。

1.3 定植菌增加

老年患者因为基础疾病相对较多、反复住院、反复应用抗感染药物、营养不良、牙周疾病、口腔卫生状态差、唾液清除下降等,导致口腔、上呼吸道的定植菌增加,从而导致下呼吸道感染发生率增加[12,13]。一项日本的研究显示[14],64.5%的老年人口腔的牙菌斑上定植了下呼吸道致病菌,成为下呼吸道感染致病原的储存库。

2 老年下呼吸道感染病原学特点

2.1 病原谱

老年下呼吸道感染患者中,革兰阴性肠杆菌科细菌、铜绿假单胞菌和金黄色葡萄球菌、厌氧菌的比例增加[15,16]。西班牙塔拉戈纳连续3年多的老年CAP流行病学调查结果显示,在142名检测到致病源的患者中,虽然肺炎链球菌仍然是最常见的致病菌(占49.3%),但铜绿假单胞菌已成为第二位的致病菌,占15.5%[4]。我国全国性CAP致病源流行病学调查显示[17,18]:肺炎支原体为我国成人CAP的首要致病源(占20.7%),其次为肺炎链球菌(10.3%)、流感嗜血杆菌(9.2%)、肺炎衣原体(6.6%)、肺炎克雷伯杆菌(6.1%)、嗜肺军团菌(5.1%)、金黄色葡萄球菌(3.8%)、大肠埃希菌(1.6%)等;但是在>50岁的患者中,肺炎克雷伯杆菌的感染率显著高于≤50岁的患者(8.5% *vs* 3.0%, $P<0.05$);合并心肺基础疾病的患者中有12.4%(21/170)存在肺炎克雷伯杆菌或铜绿假单胞菌感染,而无上述疾病的患者,这2种菌的感染率仅为5.0%(22/440, $P<0.05$)。我国2008年8月至2010年12月13家教学医院的医院获得性肺炎(hospital acquired pneumonia,HAP)多中心调查研究结果显示[19],前四位的致病菌为鲍曼不动杆菌(30.0%)、铜绿假单胞菌(22.0%)、金黄色葡萄球菌(13.4%)及肺炎克雷伯菌(9.7%),虽然入选的是≥18岁的HAP患者,但68.5%的患者年龄≥65岁,基本上可以代表老年人群的致病菌谱。孙安民等[16]回顾了2010年至2013年老年下呼吸道感染患者痰标本中培养获得的1626株病原菌,以肺炎克雷伯菌、鲍曼不动杆菌、金黄色葡萄球菌为主,分别占40.7%、24.8%、16.0%。而这些细菌也常常是导致治疗失败的致病菌。El-Solh等[20]分析了治疗失败的老年肺炎患者的病原菌,结果显示甲氧西林耐药的金黄色葡萄球菌占33%,革兰阴性杆菌占24%,铜绿假单胞菌占14%。老年人误吸风险高,这部分患者容易合并厌氧菌的感染[21],如消化链球菌属及拟杆菌属[22]。

2.2 致病菌耐药比例增高

因为老年患者基础疾病多,反复住院,应用抗菌药物比例高,常常导致感染耐药菌增加。孙安民等[16]对1626株老年下呼吸道感染致病菌的分析显示:肺炎克雷伯菌产超广谱β-内酰胺酶(extended spectrum β-lactamase, ESBL)的比例高达43.5%(288/662);鲍曼不动杆菌对大多数抗菌药物的耐药率>50.0%;甲氧西林耐药的金黄色葡萄球菌(methicillin-resistant *Staphylococcus aureus*,MRSA)的检出率为54.6%(142/260)。我国2008年至2010年HAP多中心调查研究结果显示[19],鲍曼不动杆菌和铜绿假单胞菌对碳青霉烯的敏感度甚至<40%,MRSA已占到金黄色葡萄球菌的87.8%。

3 老年下呼吸道感染治疗策略

3.1 抗菌药物的选择

治疗老年下呼吸道感染患者时,首先要根据患者有无基础疾病、可能感染的病原谱、病情轻重进行抗感染药物选择,同时还要兼顾老年人的肝肾功能进行必要的增减。病情严重程度评估是治疗过程中的关键,对初始治疗方案的确定及患者的预后会产生重要影响;初始治疗失败发生率随肺炎病情严重程度增加而显著上升。常用CURB-65评分对CAP患者病情危重程度进行评估[23],共有5条评分标

准:意识障碍、血尿素氮 >7 mmol/L、呼吸频率≥30次/min、低血压(收缩压 <90 mmHg 或舒张压≤60 mmHg)、年龄≥65岁,存在1项即得1分。0~1分:原则上门诊治疗即可;2分:建议住院或在严格随访下的院外治疗;3~5分:应住院治疗。区分不同治疗类型人群,按照2016年中国成人社区获得性肺炎诊断和治疗指南分别选择抗感染药物(表1)[21]。对于HAP同样需要覆盖常见致病菌,并根据患者病情严重程度进行药物选择[2](表2)。

3.2 抗感染药物选择时的注意事项

疑有吸入风险时优先选择氨苄西林/舒巴坦、阿莫西林/克拉维酸、碳青霉烯类、莫西沙星等有抗厌氧菌活性的药物,或者联合应用甲硝唑、克林霉素等治疗[22,24];对于有产超广谱β-内酰胺酶菌感染高风险(有产ESBL菌定植或感染史、曾使用三代头孢菌素、有反复或长期住院史、留置植入物以及肾脏替代治疗等[25,26])的患者,经验性治疗可选择头霉素类[27]、哌拉西林/他唑巴坦、头孢哌酮/舒巴坦或厄

表1 老年社区获得性肺炎患者初始经验性抗感染药物的选择

Table 1 Recommended initial empiric antibiotic therapy for community-acquired pneumonia in old patients

Group	Empiric antibiotic therapy	Comment
Outpatient treatment	Penicillins/lactamase inhibitors; second or third generation cephalosporin (oral); respiratory fluoroquinolone; penicillins/lactamase inhibitors, second or third generation cephalosporin plus doxycycline, minocycline or macrolide	Presence of comorbidities, such as chronic heart, lung, liver, or renal disease; diabetes mellitus; alcoholism; immunosuppressing conditions or use of immunosuppressing drugs; use of antimicrobials within the previous 3 months are the risks for drug-resistant *Streptococcus pneumoniae* infections, not recommended using doxycycline, minocycline or macrolide alone
Inpatient, non-ICU treatment	Penicillins/lactamase inhibitors; third generation cephalosporin or third generation cephalosporin/lactamase inhibitors, cephamycin, oxacephems, carbapenems; above drugs plus macrolide; respiratory fluoroquinolone	Presence of comorbidities are the risks for Enterobacteriaceae infection; aspiration should be considered in the elderly
Inpatient, ICU treatment	Penicillins/lactamase inhibitors, third generation cephalosporin or third generation cephalosporin/lactamase inhibitors, carbapenems plus macrolide; penicillins/lactamase inhibitors, third generation cephalosporin or third generation cephalosporin/lactamase inhibitors, carbapenems plus respiratory fluoroquinolone	Evaluating risks of ESBL-producing enterobacteriaceae infections
With factors increasing the likelihood of Pseudomonas infection	Antipseudomonal β-lactam; antipseudomonal fluoroquinolone; antipseudomonal β-lactam plus antipseudomonal fluoroquinolone or aminoglycoside; antipseudomonal β-lactam plus antipseudomonal fluoroquinolone plus aminoglycoside	Risk factors for infection include respiratory tract colonization of *Pseudomonas aeruginosa* or repeated use of antibacterials or steroid because of chronic respiratory diseases

表2 老年医院获得性肺炎患者初始经验性抗感染药物的选择

Table 2 Recommended initial empiric antibiotic therapy for hospital-acquired pneumonia in old patients

Group	Empiric antibiotic therapy	Comment
Not at high risk of mortality and no factors increasing the likelihood of MRSA	Piperacillin-tazobactam; cefepime; levofloxacin; imipenem, meropenem patient has factors increasing the likelihood of gram-negative infection and has structural lung disease, two antipseudomonal agents are recommended	Not at high risk of mortality but with factors
Increasing the likelihood of MRSA	Piperacillin-tazobactam; cefepime, ceftazidime; levofloxacin, ciprofloxacin; imipenem, meropenem; aztreonam; one of the above plus vancomycin or linezolid	Factors increasing the likelihood of MRSA: intravenous antibiotic treatment during the prior 90 days, and treatment in an unit where the prevalence of MRSA among *Staphylococcus aureus* isolates is >20%, previous detection of MRSA by culture
High risk of mortality or receipt of intravenous antibiotics within prior 90 days	Piperacillin-tazobactam; cefepime, ceftazidime; levofloxacin, ciprofloxacin; imipenem, meropenem; aztreonam; amikacin, gentamicin; two of the above plus vancomycin or linezolid	Risk factors for mortality include need for ventilatory support due to pneumonia and septic shock

MRSA: methicillin-resistant *Staphylococcus aureus*

他培南等。对于重症肺炎，建议早期采用广谱强效的抗菌药物治疗，待病情稳定后根据病原学进行降阶梯治疗。因为老年人出现铜绿假单胞菌、金黄色葡萄球菌、克雷伯菌属或厌氧菌的机会增加，这些细菌容易导致肺组织坏死，抗菌药物疗程可以根据情况延长至 14 ~ 21 d[1,28]。老年人群脏器功能减退，治疗时应根据年龄和肌酐清除率等情况适当调整药物剂量，避免发生副作用。

3.3 支持对症治疗

除了抗感染治疗，对于老年患者来讲，协助祛痰、改善营养状态、将基础疾病控制稳定也是治疗成功的关键。对于有误吸危险因素的老年患者需要加强护理，若无禁忌证，应把床头抬高 35° ~ 40°，减少吸入性肺炎的发生；对严重吞咽困难和已发生误吸的老年患者，应酌情留置胃管给予鼻饲饮食[29,30]。

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·消 息·

《中华老年多器官疾病杂志》调整文末参考文献著录格式

自2017年1月起,我刊调整录用稿件的文末参考文献著录格式:(1)中文参考文献采用中英文双语著录,中文在前,英文在后;(2)参考文献如有"数字对象唯一标识符(DOI)"编码,应著录,列于末尾。

示例:

[1] Williamson JD, Supiano MA, Applegate WB, *et al*. Intensive *vs* standard blood pressure control and cardiovascular disease outcomes in adults aged ≥75 years: a randomized clinical trial[J]. JAMA, 2016, 315(24): 2673 - 2682. DOI: 10.1001/jama.2016.7050.

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