

• 感染与免疫 • 专家论坛 •

老年人群感染性疾病诊治的难点与对策

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【摘要】 老年人是感染性疾病的高危人群,由于其症状常不典型,容易迅速发展为重症,导致住院率和病死率显著增加,住院时间延长,医疗费用上升。随着全球老龄化进程的加速,老年人感染性疾病逐渐成为公共卫生系统面临的重大挑战。本文拟对老年人群感染性疾病的诊治难点与对策进行综述,以提高对该疾病的认识。

【关键词】 老年人;感染;诊断;治疗

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【Abstract】 The elderly are a high-risk group for infectious diseases. Due to the often atypical symptoms, these diseases can rapidly progress to severe forms, resulting in significantly increased hospitalization rates and mortality, prolonged hospital stays, and higher medical costs. As global population aging accelerates, infectious diseases among the elderly have emerged as a significant challenge to public health systems worldwide. This article aims to review the research progress on the challenges and corresponding strategies in the management of infectious diseases among the elderly population, in order to enhance awareness of these conditions.

【Key words】 The aged; Infection; Diagnosis; Treatment

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随着全球人口老龄化的加剧,老年人感染性疾病被广泛关注。WHO 将年龄在 65 岁及以上的人群定义为老年人^[1]。据统计,截至 2050 年,全球 65 岁及以上人口比例由 2022 年的 10% 升至 16%,而截至 2023 年,中国 65 岁及以上人口比例已达到 15.4%,这一局势对医疗系统提出了前所未有的挑

战^[2-3]。老年人因其生理功能退化、免疫系统衰老、合并基础疾病等诸多复杂因素,成为感染性疾病的高危人群,严重感染导致老年人的住院率和病死率显著增加^[1,4]。尽管感染性疾病的防控已使健康调整预期寿命(health adjusted life expectancy, HALE)延长,但其仍是老年人死亡的重要原因^[5]。本文围绕老年

人感染性疾病的诊治难点与对策进行阐述。

一、老年人感染性疾病的诊治难点

1. 易感性增加

老年人对于感染性疾病易感性增加是由多种因素共同作用的结果,其中最重要的是免疫衰老(immunosenescence)。随年龄增长,人体防御感染、监测和破坏肿瘤细胞或自身反应细胞的能力会逐渐下降,导致炎症、感染、恶性肿瘤和自身免疫性疾病的风险增加^[6]。免疫衰老主要表现为先天性和适应性免疫功能的双重衰退。先天性免疫方面,巨噬细胞、树突细胞等功能减弱,使人体难以识别和清除病原体;适应性免疫方面,T 细胞数量减少且功能受损,B 细胞产生抗体的能力下降,导致对感染的抵抗力显著减弱^[7]。衰老会干扰先天和适应性免疫应答,导致细胞内稳态失调,出现自噬功能紊乱、蛋白稳态变化、线粒体功能障碍、微生物群失调等,从而增强炎症细胞因子和趋化因子的分泌^[6]。免疫衰老削弱了老年人对疫苗的免疫反应,特别是流感疫苗和肺炎疫苗,流感疫苗和肺炎球菌疫苗在老年人群中的效力分别只有 30%~50%,显著低于年轻人^[8-9]。此外,老年人的慢性炎症状态(inflammaging)进一步削弱了免疫应答。慢性炎症不仅损害组织器官,还可能干扰免疫系统对感染的快速反应能力^[7,10]。

老年人感染性疾病的高发与多种基础疾病密切相关。常见的基础疾病包括糖尿病、慢性阻塞性肺疾病、心血管疾病和慢性肾病,这些疾病会削弱机体的屏障功能和免疫系统。例如,糖尿病患者的高血糖环境会促进病原体繁殖,并抑制中性粒细胞的杀菌能力;慢性阻塞性肺疾病患者的气道功能受损更容易引发细菌和病毒感染^[11-12]。

营养不良与衰弱综合征(frailty syndrome)进一步增加了老年人感染的发生率。老年住院患者中营养不良、肌少症、衰弱发生率高达 37%~84%,同时发生的重叠率高达 41.6%~49.7%^[13]。老年人的身体虚弱、运动量减少,黏膜屏障功能受损,呼吸道、泌尿道和消化道容易成为病原体入侵的通道,导致医院内感染的高发^[14-15]。营养摄入不足,进一步加剧了免疫系统的功能衰退,使他们更易受到感染^[16]。

老年人感染性疾病的高发病率与环境因素和住院治疗或长期卧床密切相关。居住在养老院或群体居住环境中的老年人,发生交叉感染的风险增加^[17]。尤其在住院治疗、长期卧床或重症监护室中,老年人由于免疫力低下和多种疾病并存,感染风险显著增加,更易受到多重耐药菌(multidrug-resistant, MDR)的威胁,而这些耐药菌通常与侵入性操作如导尿管或中心静脉置管的使用相关^[18-19]。据统计,医院和长期护理机构中分别有 6.5%(95%CI:5.4%~7.8%)和 3.9%(95%CI:2.4%~6.0%)的患者有至少一种医疗保健相关感染^[17]。

2. 症状不典型或延迟出现

老年人感染后的症状常常不典型或者延迟出现,对疾病的早诊早治带来了一定挑战,可能导致患者病死率增加。主要表现在:(1)发热反应不明显:老年人感染后可能没有显著的体温升高,部分患者甚至表现为体温过低。这是由于老年人下丘脑体温调节功能的退化以及免疫系统反应不足所致。发热不明显可能掩盖感染的严重程度,增加漏诊和误诊的风险^[20-21]。(2)症状模糊:感染常表现为乏力、食欲下降、精神状态改变(如意识模糊或谵妄)等非特异性症状,而这些症状可能与其他非感染性疾病(如药物副作用或神经退行性疾病)混淆^[22]。(3)感染部位症状不典型:特定感染部位的症状可能不明显。例如,肺炎的患者可能没有咳嗽、咳痰等典型呼吸道症状,而主要表现为呼吸急促或心力衰竭,甚至被原有的慢性阻塞性肺病、冠状动脉粥样硬化性心脏病等基础疾病掩盖病情;尿路感染患者可能没有尿频、尿急等症状,而表现为意识模糊或功能减退^[23-24]。

3. 高病死率

感染性疾病是老年人死亡的主要原因之一。老年人社区获得性肺炎是常见的老年人感染性疾病,其住院病死率高达 22%~30%,在脓毒症或急性呼吸窘迫综合征等并发症出现时,病死率进一步增加^[25]。在流感流行季节,老年人因流感相关肺炎和心肺并发症的病死率显著增加,在 80 岁及以上人群中,流感相关住院病死率可以达到 8%~10%^[26]。全球数据显示,老年人呼吸道合胞病毒(respiratory syncytial

virus, RSV) 相关急性呼吸感染的住院患者病死率为 14%, 特别是在合并心肺疾病的患者中比例更高^[27]。老年人血流感染的 30 d 病死率显著高于年轻患者, 在 80 岁以上的患者中, 病死率可达到 33.2%, 其中耐甲氧西林金黄色葡萄球菌 (methicillin resistant *Staphylococcus aureus*, MRSA) 感染和肠球菌感染是死亡风险增加的重要原因^[28]。尿路感染在老年患者中常合并脓毒症, 住院病死率为 15%~20%, 基础疾病 (如糖尿病和肾功能不全) 显著增加了死亡风险^[29]。

由于老年人对感染性疾病易感性增加, 症状不典型或延迟出现, 导致老年人感染性疾病发病率和病死率居高不下, 给临床诊治带来了巨大的挑战^[30]。

二、老年人感染性疾病诊治及预防策略

1. 早期识别

医务人员应警惕老年患者的急性功能退化、精神状态改变等非特异性表现, 并考虑感染的可能性, 进行全面的病史采集、体格检查与人体植入物评估。血液学检查 (如 C 反应蛋白和降钙素原)、尿液检测 (如尿常规和尿沉渣) 和影像学 (如 X 光和 CT) 在老年人感染的诊断中具有重要意义, 尤其是在症状不典型的情况下^[31]。根据临床症状及一般检查结果进行针对性检测, 例如呼吸道常见病原体核酸检测, 尿抗原检测, 呼吸道分泌物、尿液、血液微生物培养等^[32]。

2. 抗生素合理使用

老年患者的抗生素治疗受以下因素的影响: 年龄相关的药物 (代谢) 动力学 (pharmacokinetics) 改变、基础疾病以及暴露于或感染多重耐药微生物的风险^[33]。有研究显示, 尿路感染老年患者中, 在 60 d 随访期间, 延迟使用抗生素和不使用抗生素组的血流感染发生率高于立即使用抗生素组 (2.2% *vs* 0.2%; $P=0.001$), 全因死亡风险也高于立即使用抗生素组 [校正危险比分别为 1.16 (95%CI: 1.06~1.27) 和 2.18 (95%CI: 2.04~2.33)], 建议在老年人群中尽早开始使用推荐的一线抗生素治疗尿路感染^[34]。近期住院、接受透析治疗、近期使用抗生素或有留置装置, 感染耐药微生物的风险增加。对于重病的老年人, 怀疑脓毒症、重症肺炎或其他危及生命的感染, 初始宜用更广谱的抗生素治疗。在获得培养结果后, 应

缩小抗生素治疗方案的覆盖范围, 以降低引起抗生素耐药和艰难梭菌感染的风险^[35]。

3. 噬菌体在感染性疾病中的应用

噬菌体 (bacteriophage) 是专门感染和裂解细菌的病毒。它已成为代替抗菌药物或辅助治疗多重耐药菌感染的重要研究, 在老年人感染性疾病的治疗中具有潜在的价值^[36-37]。噬菌体能够识别特定的细菌受体, 选择性地攻击病原体而不破坏正常菌群, 同时通过在感染部位自我复制提高疗效^[38]。噬菌体被逐渐用于解决多重耐药菌引起的感染, 如耐药金黄色葡萄球菌、铜绿假单胞菌、肺炎克雷伯菌等引起的感染^[39-41]。然而, 噬菌体的靶向性使其需要个性化设计, 同时细菌可能通过基因突变对噬菌体产生耐受性。宿主免疫反应和噬菌体的质量控制问题也是目前应用的主要挑战^[42]。

4. 并发症管理

老年患者感染后的并发症风险较高。例如, 肺炎患者可能会发展为急性呼吸窘迫综合征, 加重充血性心力衰竭、急性冠状动脉综合征和心律失常; 尿路感染可能会引发肾功能衰竭; 脓症患者可能会出现器官功能衰竭^[43-44]。因此, 临床医生不仅要着眼于感染的病原和抗菌药物治疗, 还要密切监测并发症的发生, 并采取积极的治疗措施。早期识别并发症并及时干预, 对于老年患者的恢复至关重要。

5. 营养干预

研究发现, 及时的营养治疗可以显著改善患者临床结局。EFFORT 研究中, 营养治疗组采用个体化营养支持以达到蛋白质和热卡目标, 营养治疗组患者 30 d 的全因死亡风险较低 [7% *vs* 10%, 校正比值为 0.65 (95%CI: 0.47~0.91), $P=0.011$]。研究表明, 适量的蛋白质摄入可以改善老年人身体的免疫功能并帮助恢复健康^[45]。推荐有营养不良风险的老年急性或慢性疾病患者每日蛋白摄入量为 1.2~1.5 g/kg^[46]。足够的维生素 D 有助于提高钙的吸收, 减少骨折的风险^[46]。补充微量元素 (如锌、硒和铁) 和维生素 (如维生素 A、C、D、E、B2、B6、B12 和叶酸) 有助于改善免疫功能, 从而增强对感染的抵抗力和促进感染后更快的恢复。另外, 仅靠饮食补充营养可能是不够的, 需

要根据特定的年龄相关需求来补充微量营养素^[47-48]。维生素、矿物质、蛋白质等口服营养补充剂(oral nutritional supplementation, ONS)能改善老年住院患者、有衰弱风险社区老人以及养老院居民的 Fried 表型和活动能力,对于老年人的总体健康有显著的提升作用^[49]。此外,ONS 有可能以较低的成本改善营养不良老年住院患者的健康和生存^[49]。

6. 疫苗接种

疫苗接种是预防老年人感染性疾病的有效策略。流感疫苗能显著降低流感相关的住院率和死亡率,建议 60 岁以上老人每年接种流感疫苗^[50]。肺炎球菌疫苗有助于预防由肺炎链球菌引起的肺炎、败血症和脑膜炎^[51-52]。带状疱疹疫苗可降低 50 岁及以上人群带状疱疹的发生率及其后遗症^[53]。RSV 是老年人群中引起严重呼吸道感染的主要病原之一,欧洲药品管理局(European Medicines Agency, EMA)和美国食品药品监督管理局(Food and Drug Administration, FDA)已建议批准 AS01E-佐剂 RSVPreF3 OA 疫苗上市,这是第一种保护>60 岁人群免受 RSV 感染的疫苗^[54]。研究显示,针对 RSV 相关住院治疗的疫苗有效性为 80%(95%CI:71%~85%),针对 RSV 相关危重症的疫苗有效性为 81%(95%CI:52%~92%)^[55]。

7. 免疫调节

除了加强疫苗免疫保护,增强宿主免疫应答的免疫治疗成为新的方向。免疫检查点抑制剂(immune checkpoint inhibitors, ICIs),如程序性细胞死亡蛋白 1/程序性死亡配体 1,已在多种感染相关疾病(如结核、慢性病毒感染)中显示出潜在的治疗前景^[56]。近年来研究表明,尽管免疫衰老可能影响 ICIs 的疗效,但老年人群仍能从此类疗法中获益^[57]。靶向 IL-6 受体的单克隆抗体被应用于老年人重症新型冠状病毒感染等感染性疾病,但长期使用可能增加感染风险^[58]。胸腺肽能够促进 T 细胞成熟、提高细胞免疫力,在慢性病毒感染(如乙型肝炎、丙型肝炎)及败血症治疗中显示出一定疗效^[59]。静脉注射免疫球蛋白被广泛用于治疗老年人败血症、细菌感染及某些病毒感染,并起到免疫调节和抗炎作用^[60]。此

外,肠道微生物群与免疫系统密切相关,针对老年人微生物群失调的干预措施(如益生菌、粪菌移植)可能改善免疫功能^[61]。

三、结语

综上所述,老年人感染性疾病症状不典型,容易发展为重症,早期识别非常关键。医务人员应提高对老年人非特异性症状的关注,加强早期筛查、精准诊断,合理使用抗生素,强化老年人疫苗接种、营养干预和免疫治疗,预防并发症的发生。

利益冲突 所有作者均声明不存在利益冲突

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