

与其相仿,为我国独有;替考拉宁血浆蛋白结合率高、消除半衰期长,应用次日起仅需每天给药 1 次。尽管抗革兰阳性菌药物不断增加,糖肽类仍被 IDSA 指南推荐为治疗多数 MRS 尤其是 HA-MRSA 感染的首选药物。糖肽类药物的不足包括:在肺、脑脊液等组织或体液中浓度较低,肾功能不全患者需要调整剂量,存在敏感性下降和耐药的隐忧。

目前认为,以往报道的万古霉素肾毒性很大程度是产品杂质所致,制作纯度提高后,常规剂量给药很少再引起肾功能损害。IDSA 根据 MRSA 治疗指南和万古霉素治疗药物监测共识^[20]推荐:万古霉素给药剂量应以实际体质量计,每次 15~20 mg/kg (单次剂量不超过 2 g),每 8~12 小时给药 1 次,重症患者可给予 1 次 25~30 mg/kg 负荷剂量。出于对肾功能损害的担忧,治疗肾功能正常的感染患者时临床给予万古霉素剂量明显不足,影响疗效;而治疗肾功能损害患者时,又未能根据内生肌酐清除率充分减量,导致剂量过大。

利奈唑胺属噁唑烷酮类,上市 10 年余,积累了较多循证医学资料。利奈唑胺与糖肽类无交叉耐药和交叉过敏,在肺和脑脊液等组织或体液中浓度高^[21-22],肾功能损害患者无需调整剂量,口服利用率接近 100%,可经静脉或口服序贯给药,与糖肽类具有很好的互补性。但该药存在骨髓抑制、视神经损害和外周神经损害等不良反应,并已有肠球菌及金葡萄菌对其耐药的报道^[23-24]。

达托霉素属环脂肽类抗生素,对 MRS 具有良好的抗菌活性,近期已在我国上市。适应证为复杂皮肤软组织感染、血液感染及心内膜炎, IDSA 指南推荐用其治疗 MRSA 所致血液感染、自身瓣膜心内膜炎、骨髓炎、化脓性关节炎和皮肤软组织感染。由于达托霉素会被肺表面活性物质灭活,所以不能用于肺部感染,应用于儿童的经验也尚在积累中。曾有在治疗过程中因细菌耐药导致失败的报道^[25]。研究结果提示,达托霉素 MIC 值升高与万古霉素应用史及万古霉素 MIC 值升高相关,提示两者存在交叉耐药^[26]。

替加环素属甘氨酸四环素类,对 MRS 具有良好的抗菌活性,用于复杂性皮肤软组织感染、复杂性腹腔感染和 CA-MRSA。我国已完成上市前临床试验。但美国食品药品监督管理局 2010 年 9 月在对 13 项临床试验进行荟萃分析后,认为替加环素组病死率高于对照药物组,因此提出警告^[27]。

夫西地酸对 MRS 具有良好的抗菌活性,但对腐

生葡萄球菌、链球菌科细菌抗菌性差。不良反应以静脉炎多见。

关于克林霉素、SMZ-TMP、多西环素以及米诺环素, IDSA 推荐以这些药物口服治疗 CA-MRSA 引起的皮肤软组织感染。但我国 CA-MRSA 感染的流行病学资料尚不充分, MRS 对这些药物的耐药率较高,应尽可能根据药物敏感试验结果选用。

磷霉素、利福平组织浓度高,对肾功能影响小,常与万古霉素联合治疗 MRS 感染。 IDSA 指南推荐以万古霉素联合利福平治疗 MRSA 血液感染、心内膜炎、肺炎、中枢神经系统感染、骨髓炎、化脓性血栓性静脉炎。

其他具抗 MRS 活性新抗菌药,如链阳性菌素奎奴普丁/达福普汀、脂糖肽类药物特拉万星、达巴万星、第五代头孢菌素 ceftoprole 和 ceftaroline 尚未在我国上市。

6 小结

MRS 的广泛传播将加重治疗困难和医疗开支,不断研发的抗革兰阳性菌药物又增加了临床的选择。充分了解各类药物特点,结合药物敏感试验结果及患者情况多元化用药,通过洗手、隔离和 MRSA 带菌者去定植措施的强化实施减少耐药菌传播,有利于更为安全有效地治疗患者,减轻抗菌药物选择压力,延缓耐药性上升趋势。

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