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论著

抗HIV治疗失败后HIV 1耐药基因的变异

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摘要：

目的研究抗人免疫缺陷病毒（HIV)治疗失败后，HIV 1遗传基因变异情况，并分析其耐药性。方法选取抗HIV治疗失败的57例患者(其中采用D4T/3TC/NVP治疗方案者45例，3TC/AZT/NVP方案者7例，3TC/TDF/克立芝方案者5例），从其血浆中提取病毒RNA，运用逆转录-聚合酶链反应（RT PCR）和套式PCR扩增HIV 1 pol区基因片段,并对扩增的目的片段进行测序,将测序结果提交Web站点（http://HIVdb.stanford.edu），分析耐药变异情况。结果3种治疗方案治疗失败者均出现耐药。57例患者，7例发生针对蛋白酶抑制剂的位点变异，其中1例（1.75%）M46IM蛋白酶抑制剂的位点变异，导致了抗ATV/r、FPV/r、IDV/r、LPV/r的潜在低度耐药和抗NFV的高度耐药；32例（56.14%）患者体内HIV 1发生了逆转录酶基因变异，且均对不同逆转录酶抑制剂产生了耐受性，其中14例（43.75%，14/32）患者对斯坦福数据库中的11种药物全都耐药，且11例（78.57%）治疗方案为D4T/3TC/NVP。TDF、克立芝等二线药物的治疗方案突变位点少于一线药物D4T、3TC、NVP、AZT。结论耐药变异是导致抗HIV治疗失败的主要原因。在开展抗病毒治疗过程中，应适时进行耐药性检测，以获得较好疗效。

关键词： 艾滋病 人免疫缺陷病毒 获得性免疫缺陷综合征 抗病毒治疗 抗药性 微生物 耐药基因

Drug resistance variation in HIV 1 after the failure of highly active antiretroviral therapy

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Abstract:

ObjectiveTo study genetic variation and drug resistance of HIV 1 after the failure of highly active antiretroviral therapy(HAART) in HIV 1/AIDS patients.MethodsFifty seven patients with HAART failure, including 45 with D4T/3TC/NVP regime, 7 with 3TC/AZT/NVP, and 5 with 3TC/TDF/ LPV/r, were enrolled in the study, viral RNA was extracted from plasma, partial HIV 1pol gene was amplified by reverse transcription polymerase chain reaction(RT PCR)and nested PCR,and the amplified fragment was sequenced,the phylogenesis of sequences were analyzed by landing the websites http://HIV 1db.stanford.edu., and drug resistance variation was analyzed.ResultsPatients with the failure of 3 types of therapeutic regimes all developed drug resistance. Among 57 patients, drug resistant variation in protease inhibitors(PIs) was identified in 7 patients, 1 of whom （1.75%）produced variation in M46IM which resulted in low level resistance to ATV/r,FPV/r,IDV/r,LPV/r and high level resistance to NFV; Drug resistant variation in reverse transcriptase inhibitors (RTs) was identified in 32 patients（56.14%）,and 14 （43.75%,14/32）of whom had resistance to 11 kinds of inhibitors(//HIV 1db.stanford.edu), 11 (78.57%,11/14) cases were with the regime of D4T/3TC/NVP. Mutation site in patients with second line drugs(TDF,LPV/r)were less than first line drugs(D4T,3TC,NVP,AZT). ConclusionDrug resistance variation is the major cause of failure of HIV 1 therapy, drug resistance should be monitored during the course of anti HIV therapy.

Keywords: acquired immunodeficiency syndrome human immunodeficiency virus; anti

virus theray drug resistance,microbial; drug resistance gene

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