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综述

核苷类似物线粒体毒性机制及临床表现

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摘要 核苷类似物是目前临床上治疗艾滋病、疱疹、慢性肝炎等病毒性疾病的首选药物, 其抗病毒疗效确切, 临床应用的安全性较好。但随着核苷类似物的长期使用, 近年来关于其不良反应的报道也逐渐增多, 例如肝毒性、中毒性肾损伤、肌病、乳酸酸中毒、周围神经病等。大量研究资料表明, 此类不良反应主要来源于药物对线粒体功能的损伤, 其机制主要包括线粒体DNA聚合酶γ活性受抑制、线粒体DNA突变、氧化应激、遗传易感性和单核苷酸多态性等。本文将以核苷类似物诱发线粒体功能损伤的机制为出发点, 详细阐述此类药物临床应用中引起的不良反应。

关键词 核苷类似物 线粒体毒性 DNA聚合酶γ 肾毒性 肝毒性

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Mitochondrial toxicity mechanism of nucleoside analogues and its clinical manifestations

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Abstract

Nucleoside analogues are the drugs of first choice for clinical treatment of AIDS, herpes, chronic hepatitis and other viral diseases. They are effective in antiviral therapy and quite safe in clinical applications. However, with long-term use of nucleoside analogues, reports about adverse reactions have increased in recent years, such as liver toxicity,renal toxicity,myopathy,lactic acidosis, peripheral neuropathy. A large number of studies showed that such adverse reactions are due to drug-induced toxicity dysfunction, and the mechanisms include inhibition of the activity of mitochondrial DNA polymerase gamma, mitochondrial DNA mutations, oxidative stress, genetic predisposition, single-nucleotide polymorphism. This article is concerned with the mechanism of mitochondrial toxicity caused by nucleoside analogues and side effects resulting from these drugs during clinical application.

Key words nucleoside analogue mitochondrial toxicity DNA poly-γ nephrotoxicity hepatotoxicity

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