论著

用SCGE分析甲氨蝶呤对小鼠体内多个组织器官DNA损伤作用

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摘要 背景与目的:为进一步了解甲氨蝶呤(Methotrexate,MTX)的作用机制,探测其对不同组织器官作用的敏感性。 材料与方法: 用单细胞凝胶电泳技术(Single cell gel electrophoresis assay,SCGE)检测小鼠腹腔注射MTX 染毒1、3、6、12、24 h后对肝、脾、骨髓、胸腺、肾、睾丸、胃和外周血淋巴细胞的DNA损伤作用及其与MTX剂量间的关系。结果: 腹腔注射1.25~5 mg/kg MTX可诱发小鼠脾细胞、骨髓细胞、胸腺细胞和外周血淋巴细胞的DNA单链断裂; 核DNA损伤程度与用药剂量呈正相关。 结论: MTX可致小鼠体内多脏器细胞的DNA单链断裂,不同脏器细胞对MTX的易感性不同,脾、骨髓、胸腺、外周血淋巴细胞可考虑为MTX的遗传毒性靶细胞。

关键词 甲氨蝶呤; 单细胞凝胶电泳; DNA损伤; 靶器官

Detection of DNA Damage Induced by Methotrexate in Multiple Mouse Organs Using SCGE Assay

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Abstract BACKGROUND & AIM: In order to understand the mechanism of methotrexate (MTX) further and to investigate the genotoxic target organs.MATERIAL AND METHODS: DNA damage and the correlation with dosage treated with MTX were studied by using the alkaline single cell gel electrophoresis assay(SCGE). Liver, spleen, bone marrow, thymus, kidney, testicle, stomach and peripheral lymphocytes of mice were isolated at 1、3、6、12、24 h after MTX intraperitoneal injection. RESULTS: Significant increase in DNA migration and comet frequency in the spleen, thymus, bone marrow and peripheral lymphocytes were induced after intraperitoneal treatment of MTX at a dose of 1.25~5 mg/kg. The migration of nuclear DNA and comet frequency of spleen, thymus, bone marrow and peripheral lymphocytes in the doseresponse study showed a dose-dependent increase. CONCLUSION: The results indicate that DNA SSBs could be induced by MTX in some cells of mice. There are difference in sensitivity of various organs in the mice and cells of spleen, thymus, bone marrow and peripheral lymphocytes may be the important target cells of MTX.

Keywords methatrexate single cell gel electrophoresis DNA damage target organ

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