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论著

雷公藤甲素急性中毒对大鼠心肌的损伤

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摘要 目的 观察雷公藤甲素（TP）急性中毒的心肌毒性。方法 用急性毒性实验统计学软件AOT425StatPgm上下增减剂量法检测po给予TP的半数致死量（LD_{50}）。将60只大鼠分为正常对照组，TP 0.6，1.2和2.4 mg·kg^{-1}组，除正常对照组外，大鼠一次性ig给予TP。观察其外观体征和行为活动，测定心电图；Aeroset全自动生化分析仪检测血清肌酸激酶（CK）和乳酸脱氢酶（LDH）活性；HE染色观察心肌组织病理改变；用图像分析技术测定心肌损伤面积百分比；透射电镜观察心肌超微结构的变化；免疫组化SP法测定心肌细胞肌钙蛋白(CTn T)的表达。结果 雄性SD大鼠po TP的LD_{50}值为1.19 mg·kg^{-1}。大鼠ig给予TP 0.6，1.2和2.4 mg·kg^{-1}后15～20 h，TP 1.2和2.4 mg·kg^{-1}组心率与对照组比较明显减慢（P<0.01），并可见S-T段压低、T波高尖、Q波增宽和脱失等心电图改变。大鼠ig给予TP 0.6，1.2和2.4 mg·kg^{-1}后20 h，血清CK和LDH活性较正常对照组485±70和(712±105)U·L^{-1}明显升高，CK活性分别为661±60，917±101和（1220±157）U·L^{-1}，LDH活性分别为1013±155，1362±208和（2013±224）U·L^{-1}。HE染色结果表明，心肌损伤面积随TP剂量增加而增大（r=0.8，P<0.01），心肌组织病理改变主要为心肌细胞肿胀、空泡变性、溶解坏死和收缩带坏死，电镜观察可见线粒体肿胀、嵴减少、空泡形成和心肌纤维断裂，免疫组化观察可见心肌细胞CTn T缺失。结论 TP急性中毒可导致心肌急性损伤，并呈剂量相关性；其作用机制可能与线粒体损伤和细胞膜破坏有关。

关键词 雷公藤甲素 急性毒性 心脏毒性

分类号 R285.1, R99

Injury of myocadium of rats by acute triptolide poisoning

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Abstract

OBJECTIVE To investigate the cardiotoxicity by triptolide (TP) and its toxicological mechanism. **METHODS** TP LD_{50} with po was counted with Up and Down Procedure by AOT425StatPgm, the statistic software of acute toxicity testing. In the experiment, sixty male rats were randomized into 4 groups: control group, TP 0.6, 1.2 and 2.4 mg·kg^{-1} groups. Rats were ig given TP, except control group. After being lavaged, rats′ appearance and behavior were observed, and the ECG was detected. The activities of creatine kinase (CK) and lactate dehydrogenase (LDH) were detected by Aeroset automatic biochemistry analyzer; the myocardial changes of rats were observed with HE staining. Image analytical technique was used to measure the rate in myocardial damage area and visual field area. The change in myocardium ultramicrostructure was observed by electron microscope. The expression of cardiac troponin T (CTn T) in myocardium was detected by immunohistochemistry with SP method. **RESULTS** LD_{50} of TP on SD male rats was 1.19 mg·kg^{-1}. After being lavaged TP with the dose of 0.6，1.2 and 2.4 mg·kg^{-1} for 15-20 h, the heart rate (HR) of TP 1.2 mg·kg^{-1} group and TP 2.4 mg·kg^{-1} group slowed down significantly compared with the control group and ECG changed, such as ST depression, T wave heighten, Q wave widen or loss. After being lavaged, TP with the dose of 0.6, 1.2 and 2.4 mg·kg^{-1} for 20 h, the activities of CK and LDH raise significantly compared with control group 485±70 and (712±105)U·L^{-1}. The activities of CK were 661±60, 917±101 and (1220±157)U·L^{-1}, and the activities of LDH were 1013±155, 1362±208 and (2013±224)U·L^{-1}, separately. The result of HE staining showed that the area of myocardial damage was expanded when the dosage of TP increased (P<0.01). Main pathological changes were myocardium swelling, denaturation, cytolysis and contraction band necrosis. Ultrastructural changes were mitochondrial swelling, crista breakage and myofibrilla cytolysis. Depletion of CTn T in myocardium was observed by immunohistochemistry. **CONCLUSION** TP acute poisoning can make acute myocardial damages. The level of myocardial damages increasing with the dose of TP added. The toxicological mechanism of TP may be correlated with the destruction of mitochondria and cell membrane.

Key words triptolide acute toxicity cardiotoxicity

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