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论著

环维黄杨星D对大鼠的肾脏毒性

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摘要 目的 观察环维黄杨星D(CVB-D)对大鼠的肾脏毒性及其可逆性。方法 120只大鼠随机分为正常对照组, CVB-D 2.5, 5和10 mg·kg^{-1}组，每组30只。CVB-D组大鼠分别ip给予CVB-D 2个月，并于给药后第1和第2个月末每组各取10只大鼠的眼眶血分离血清，检测尿素氮(BUN)、肌酐（SCr）、Tamm Horsfall 蛋白(THP)、β_2微球蛋白(β_2-MG)；收集24 h尿液检测N-乙酰-β-氨基葡萄糖苷酶(NAG)、微量白蛋白(mAlb)、免疫球蛋白G(IgG)、视黄醇结合蛋白(RBP)、β_2微球蛋白（β_2-MG）和转铁蛋白（TRF）；并做肾脏组织病理学检测。作为恢复期观察，停药4周后每组另10只大鼠做同样检查。结果 与正常对照组相比，ip给予大鼠CVB-D 1个月后，大鼠血清中的β2-MG明显升高（P<0.01），CVB-D 5和10 mg·kg^{-1}组的THP含量明显降低(P<0.01)，CVB-D 10 mg·kg^{-1}组大鼠血清中BUN含量升高(P<0.01)；同时，CVB-D 10 mg·kg^{-1}组大鼠尿液中NAG, TRF, β_2-MG和IgG含量显著升高，CVB-D 5和10 mg·kg^{-1}组尿液mAlb含量及RBP含量均显著升高（P<0.05，P<0.01）。持续给药2个月后，CVB-D 5和10 mg·kg^{-1}组大鼠血清中β_2-MG含量显著升高（P<0.05），CVB-D 5 mg·kg^{-1}组BUN含量明显升高（P<0.05），CVB-D 10 mg·kg^{-1}组THP含量显著降低（P<0.05）；同时，CVB-D 10 mg·kg^{-1}组大鼠尿液中NAG和IgG含量明显升高（P<0.05，P<0.01），CVB-D 5和10 mg·kg^{-1}组β_2-MG和TRF含量明显升高（P<0.01）；病理组织切片显示CVB-D 2.5 mg·kg^{-1}组部分动物肾小球及肾小管出现坏死的现象，CVB-D 5和10 mg·kg^{-1}组部分动物出现组织自溶现象。在恢复期，血清及尿液中仍有部分指标显著高于正常对照组，病理组织切片显示CVB-D组仍有部分肾单位出现肾间质内少量炎细胞浸润或不同程度淤血的现象。结论 长期应用CVB-D可能引起大鼠肾毒性，且病变在停药后不能彻底恢复。

关键词 黄杨属 肾 毒性作用

分类号 R285.1

Nephrotoxicity of cyclovirobuxine D in rats

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Abstract

OBJECTIVE To observe the effect of cyclovirobuxine D (CVB-D) on nephrotoxicity in rats and the reversibility of nephrotoxicity. **METHODS** One hundred and twenty rats were randomly divided into normal control group, CVB-D 2.5, 5 and 10 mg·kg^{-1} groups. Rats in CVB-D groups were ip given CVB-D for 2 months. At the end of first and second month, blood urea nitrogen (BUN), creatinine（SCr）, Tamm Horsfall protein (THP) and β_2-microglobulin (β_2-MG) were detected and N-acetyl-β-D-glucosaminidase (NAG), microalbumin(mAlb), immunoglobulin G (IgG), retinol binding protein (RBP), β_2-microglobulin（β_2-MG） and transferrin（TRF） in urine were tested while the pathological changes in renal tissue were observed by electron microscope. After the third month, all the indicators for the remaining 10 rats in each group were recorded during the recovery phase. **RESULTS** Compared with normal control group, after rats were ip given CVB-D for 1 month β_2-MG in serum in CVB-D group was significantly increased, but THP levels were sharply reduced in CVB-D 5 and 10 mg·kg^{-1} groups. BUN level increased in CVB-D 10 mg·kg^{-1} group. NAG, TRF, β_2-MG and IgG levels increased in CVB-D 10 mg·kg^{-1} group, and mAlb and RBP levels in urine increased in CVB-D 5 and 10 mg·kg^{-1} groups. After rats were given CVB-D for 2 months, compared with normal control group, β_2-MG levels in serum in CVB-D 5 and 10 mg·kg^{-1} groups were significantly increased (P<0.05). The BUN level was significantly higher in CVB-D 5 mg·kg^{-1} and THP was significantly lower in CVB-D 10 mg·kg^{-1} group (P<0.05). The contents of NAG and IgG in urine rats in CVB-D 10 mg·kg^{-1}

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remarkably increased ($P<0.05$, $P<0.01$), also β_2-MG and TRF raised significantly($P<0.01$). Histopathology showed glomerular and tubular necrosis was observed in CVB-D 2.5 mg·kg^{-1} group and tissue autolysis in CVB-D 5 mg·kg^{-1} group. In the recovery phase, some serum and urine indicators were higher than those in normal control group. Also, histopathology showed some units within a small amount of renal interstitial infiltration of inflammatory cells or varying degrees of congestion. **CONCLUSION** CVB-D for long-term use may cause nephrotoxicity, which can not be completely recovered after the drug is suspended.

Key words buxus kidney toxic actions

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