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论著

三聚氰胺和三聚氰胺类似物对Wistar大鼠经口染毒8周的毒性及预后

高虹，徐艳峰，何君，贺晓玉，马耀文，秦超，高洁，秦川

中国医学科学院医学实验动物研究所 北京协和医学院比较医学中心，北京 100021

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摘要 目的 观察连续8周ig给予三聚氰胺和三聚氰胺类似物对大鼠的毒性反应及预后情况。方法选择3周龄离乳的Wistar大鼠分别ig给予三聚氰胺300 mg·kg^{-1}、三聚氰胺300 mg·kg^{-1}+腺嘌呤100 mg·kg^{-1}+氧嗪酸钾150 mg·kg^{-1}和三聚氰胺300 mg·kg^{-1}+三聚氰酸75 mg·kg^{-1}，连续8周，观察大鼠的一般体征，分别于给药2，4，6，8周及恢复期1，2，3，6，14个月时进行血液学、血生化、尿常规、尿生化、组织病理学和肾B超的检测。饲养2年后，观察各组大鼠的存活时间及自发病变的情况。结果 1 单纯连续8周给予三聚氰胺300 mg·kg^{-1}，对大鼠的生长发育和肝肾功能无明显损害，未形成结石，但引起肾小管上皮细胞变性和睾丸萎缩；停止给药1个月时，睾丸萎缩得到恢复；停止给药3个月时，肾小管上皮细胞变性得到恢复。连续观察到2年，生长发育和自发病变（纤维瘤）等情况与对照组比较无显著性差异。2 三聚氰胺300 mg·kg^{-1}+三聚氰酸75 mg·kg^{-1}或三聚氰胺300 mg·kg^{-1}+腺嘌呤100 mg·kg^{-1}可以造成大鼠贫血、营养不良和生长迟缓，肾功能严重损害并形成肾结石；使大鼠的心、睾丸、脾及膀胱等脏器发生病理改变。停止给予受试物后大鼠的肾损伤有所恢复，但未恢复到正常水平。从停止给予受试物1~13个月，上述2组的留观大鼠全部死亡，死亡原因为肾功能衰竭，与对照组相比大鼠寿命明显缩短（P<0.01）。结论 1 三聚氰胺可以造成大鼠的肾损伤，但不形成肾结石，且可以恢复，对大鼠的生存时间无明显影响。2 三聚氰胺+三聚氰酸或三聚氰胺+腺嘌呤可以造成幼年大鼠肝肾功能的严重损害并形成肾结石，且不能完全恢复，可显著增加成年大鼠的死亡率，其死因是肾功能衰竭。

关键词 三聚氰胺 肾结石 肾功能衰竭

分类号 R394.6

Toxicity and prognosis of melamine and melamine analogues in rats after oral administration for eight weeks

GAO Hong, XU Yan-feng, HE Jun, He Xiao-yu, MA Yao-wen, QIN Chao, GAO Jie, QIN Chuan

Institute of Laboratory Animal Science, Chinese Academy of Medical Sciences, Center of Comparative Medicine of Peking Union Medical College, Beijing 100021, China

Abstract

OBJECTIVE To observe the symptoms of Wistar after being ig given melamine and melamine analogues. METHODS Four hundreds rats (males and females) were ig given melamine 300 mg·kg^{-1}, and melamine 300 mg·kg^{-1}+adenine 100 mg·kg^{-1}, melamine 300 mg·kg^{-1}+cyanuric acid 75 mg·kg^{-1}. Rats in normal control group were ig given sodium carboxymethyl cellulose of 1%, once daily, for 8 weeks. The daily condition of the rats was observed. Their CBC, blood chemistry, routine urine and B scan were tested at points of 2, 4, 6, 8 weeks and during convalescence of 1, 2, 3, 6 and 14 months. Some rats in each group were kept for 2 years, during which time their survival time and spontaneous disease were observed. RESULTS 1 In melamine 300 mg·kg^{-1} group, there was no obvious harm to rat growth or to liver and kidney function. No renal stone was formed. However, renal tubules were extended and the lining epithelium cell was degenerated accompanied by testicular atrophy that was recovered three months after the end of administration, so did the reversibility of renal tubular epithelium. After 2 years, compared with control group, no significant difference was found in melamine 300 mg·kg^{-1} group or in the growth of rats and spontaneous disease. 2 In melamine 300 mg·kg^{-1}+adenine 100 mg·kg^{-1} and melamine 300 mg·kg^{-1}+cyanuric acid 75 mg·kg^{-1} groups, anemia, dystrophy, growth retardation, major injury to the kidneys, and renal stone were found. Meanwhile, pathological changes were also found in the heart, testes, spleen and urinary bladder of rats. The injury of the kidneys was slowly recovered. All the observed rats died of serious renal failure from one to three months after the end of administration. The life span of rats was significantly shorter than that in control group (P<0.01). CONCLUSION 1 Melamine can cause injury to the kidneys of rats rather than renal stone. The kidney injury could recover with time. There is also no impact on survival time and life quality of rats. 2 Melamine+adenine and melamine+cyanuric acid can cause not only serious damage to the liver and kidney function of rats but also kidney stone. Meanwhile, the death rate increases following renal failure.

Key words melamine kidney calculi kidney failure

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通讯作者 秦 川, E-mail: qinchuan@pumc.edu.cn qinchuan@pumc.edu.cn