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论著

左旋盐酸去甲基苯环壬酯对大鼠和小鼠震颤与行为的影响

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摘要

目的 评价抗胆碱药左旋盐酸去甲基苯环壬酯(R-DM8021)的帕金森病(PD)治疗作用。**方法** ① 使用脑单侧立体定向注射6-羟基多巴胺(6-OHDA)损毁大鼠中脑黑质-多巴胺神经元的方法建立PD动物模型。观察大鼠单次ig给予R-DM8021 0.2，0.5，1.0和2.0 mg·kg^{-1}旋转行为；观察大鼠连续ig给予R-DM8021 0.2，0.5和2.0 mg·kg^{-1} 21 d对大鼠旋转行为；观察大鼠连续ig给予R-DM8021 0.2，0.5和2.0 mg·kg^{-1} 7 d后自发活动情况。② 昆明小鼠ig给予R- DM8021 0.25～40 mg·kg^{-1}，30 min后ip给予氢溴酸槟榔碱35 mg·kg^{-1}，观察肌肉震颤持续时间。③ C57BL/6小鼠ip给予MPTP 30 mg·kg^{-1} 7 d建立MPTP帕金森病模型，ig给予R- DM8021 5，10和20 mg·kg^{-1}后观察小鼠自发活动情况。**结果** ① 与6-OHDA损毁模型对照组相比，单次ig给予R-DM8021 0.2，0.5，1.0和2.0 mg·kg^{-1}分别使APO诱导的旋转次数增加(17.3±4.5)%、(29.8±9.3)%、(30.2±13.9)%和(31.7±5.5)%；苯海索3.0，5.0和10.0 mg·kg^{-1}组分别增加(18.8±4.8)%、(22.2±17.3)%和(36.9±10.0)%。连续给药21 d，大鼠APO诱导的旋转次数显著增加(P<0.01)，并维持在稳定的水平。与等剂量的苯海索相比，R-DM8021对APO诱导旋转的作用更强。建模成功后，大鼠10 min内自发活动路程较正常组显著降低(P<0.01)，连续给予R-DM8021和苯海索7 d可明显提高大鼠自发活动路程，R-DM8021对大鼠自发活动的改善效果显著优于等剂量的苯海索(P<0.01)。② ip给予槟榔碱35 mg·kg^{-1}，小鼠出现明显肌肉震颤，持续时间为(8.9±1.0)min，R-DM8021和苯海索均可剂量依赖性地降低小鼠肌肉震颤持续时间，两药对槟榔碱致小鼠肌肉震颤持续时间抑制作用的ED_{50}分别为(6.87±1.33)mg·kg^{-1}和(41.14±9.31)mg·kg^{-1}，两者相比具有显著性差异(P<0.01)。③ ip连续给予MPTP 7 d，小鼠3 min内自发活动路程较正常组显著降低，连续ig给予R-DM8021和苯海索3 d可明显提高小鼠自发活动路程，R-DM8021对小鼠自发活动的改善效果显著优于等剂量的苯海索(P<0.01)。**结论** R-DM8021对3种模型PD均有治疗作用且效果均优于苯海索。

关键词 盐酸去甲苯环壬酯 抗胆碱药 苯海索 帕金森病

分类号 R964，R971.5

Effect of *l*-demethyl phencynonate hydrochloride on tremor and behavior of rats and mice

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Abstract

OBJCETIVE To evaluate the therapeutic effect of anticholinergic agents *l*-demethyl phencynonate hydrochloride (R-DM8021) and trihexyphenidyl on Parkinson′s disease (PD) model animals. **METHODS** ① The cerebral unilateral stereotactic directionally injection of 6- Hydroxydopamine (6-OHDA) was given to substantia nigra- striatum neurons of rats. The rotation test evoked by apomorphine (APO) and locomotor activity were observed in the rat model after single and chronic treatment(21 d) with R-DM8021 0.2-2.0 mg·kg^{-1} and trihexyphenidyl. ② R-DM8021 0.25-40 mg·kg^{-1} was ig given to mice and arecoline hydrobromide 35 mg·kg^{-1} was ip given 30 min later before the duration of tremor was recorded. ③ C57BL16 mice PD model was established after mice were ip given 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) consecutively for 7 d and locomotor activity was observed after administration of R-DM8021 5-20 mg·kg^{-1}. **RESULTS** ① Compared with the model control group, single administration of R-DM8021 0.2, 0.5 and 2.0 mg·kg^{-1} increased rotation times evoked by APO by (17.3±4.5)%, (29.7±9.3)%, (30.2±13.7)% and (31.7±5.5)%, and for trihexyphenidyl 3.0, 5.0 and 10.0 mg·kg^{-1} by (18.8±4.8)%,

(22.1±17.3)% and (36.9±9.9)% by trihexyphenidyl 3.0, 5.0 and 10.0 mg·kg^{-1}. The rotation times kept increasing during R-DM8021 treatment for 21 d. ② Mice exhibited apparent tremor after arecoline hydrobromide administration. The duration was decreased significantly in R-DM8021 and trihexyphenidyl groups. ED_{50} of inhibition on duration time of R- DM8021 and trihexyphenidyl was (6.87±1.33)mg·kg^{-1} and (41.14±9.31)mg·kg^{-1}, respectively. ③ Compared with normal control group, locomotor activity in MPTP model group significantly decreased. After treatment with R-DM8021 5.0, 10.0 and 20.0 and trihexyphenidyl 20.0 mg·kg^{-1} for 3 d, the locomotor activity of mice showed obvious improvement. **CONCLUSION** R-DM8021 shows better therapeutic effect on 3 PD models than trihexyphenidyl.

Key words demethyl phencynonate hydrochloride anticholinergic agents trihexyphenidyl Parkinson′s disease

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