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论著

急进高原对普萘洛尔药代动力学参数的影响

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摘要： 目的: 研究急进高原环境对普萘洛尔药代动力学参数的影响。方法: 健康清洁级雄性Wistar大鼠14只，体质量(200±20) g，按0.05 g/kg单次灌胃给予普萘洛尔制剂，于0，20，40 min和1，1.5，2，3，4，6，8，12，24 h在平原眼眶后静脉丛采血0.5 mL; 经过7 d清洗期后，急进海拔4010 m高原，再次给药并采血，采用液相质谱串联质谱(liquid chromatography mass spectrometry and tandem mass spectrometry，LC-MS/MS)测定血浆中普萘洛尔的血药浓度，药物与统计 (drug and statistics，DAS)2.0软件计算药物动力学参数，并进行二者药代动力学参数的比较。结果: 急进高原组与平原组相比药时曲线下面积(area under concentration-time curve，AUC)增大442.61%，平均驻留时间(mean retention time，MRT)延长47.45%，半衰期(half-life，t1/2)延长73.13%，峰浓度(peak plasma concentration，Cmax)增高352.97%，总清除率(clearance，CL)下降80.87%，表观分布容积(apparent volume of distribution，V)降低68.94%。这些方面的差异二者之间均有统计学意义(P<0.05)。结论: 在高原条件下，普萘洛尔的药代动力学参数发生显著变化，研究结果将为高原条件下普萘洛尔的合理用药提供参考依据。

关键词： 普萘洛尔 药代动力学 急进高原

Effect of acute exposure to high altitude on the pharmacokinetics of propranolol

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Abstract: Objective: To study the pharmacokinetics of propranolol in Wistar rats after acute exposure to high altitude.
Methods: Fourteen male Wistar rats (200±20) g were selected. After administration of propranolol tablets (0.05 g/kg, i.g.), blood samples (3 mL) were collected at 0, 20, 40 min,1, 1.5, 2, 4, 6, 8, 12 and 24 h, respectively. The pharmacokinetic parameters were determined by LC-MS/MS and DAS 2.0 software.
Results: The main pharmacokinetic area under concentration-time curve (AUC), mean retention time (MRT), half-life (t1/2) and peak plasma concentration (Cmax) of propranolol were increased by 442.61%, 47.45%, 73.13% and 352.97%, respectively, whereas Tmax and clearance (CL) were decreased by 80.87% and 68.94%, respectively.
Conclusion: This study displays significant changes in the pharmacokinetics of propranolol under high altitude, which may provide evidence for clinical rational application of propranolol at high altitude.

Keywords: propranolol pharmacokinetics acute exposure to high altitude

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