

论著

## 三苯双脒、青蒿琥酯、蒿甲醚和吡喹酮单剂、多剂或联合用药治疗大鼠华支睾吸虫感染的实验研究

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摘要

目的 观察三苯双脒、青蒿琥酯、蒿甲醚、或吡喹酮单剂、多剂给药, 及其伍用治疗感染华支睾吸虫大鼠的疗效。方法 147只SD大鼠各感染50个华支睾吸虫囊蚴, 于感染后42~44 d分组治疗。各药物采用灌胃给药。①60只感染大鼠随机分为11组(每组4~5只), 分别为三苯双脒150 mg/kg(顿服)、75 mg/(kg·d) × 2 d、50 mg/(kg·d) × 3 d和25 mg/kg(tid) × 2 d组; 吡喹酮150 mg/kg(顿服)、75 mg/(kg·d) × 2 d和25 mg/kg(tid) × 2 d; 青蒿琥酯或蒿甲醚75 mg/kg(顿服)和37.5 mg/(kg·d) × 2 d组。②另87只感染大鼠随机分为15组(每组4~6只), 用青蒿琥酯或蒿甲醚(30 mg/kg)分别与吡喹酮(150 mg/kg)、三苯双脒(50 mg/kg和75 mg/kg)伍用组; 三苯双脒(50 mg/kg)与吡喹酮(150 mg/kg)伍用组; 三苯双脒(75 mg/kg)与吡喹酮(187.5 mg/kg)伍用组, 及各药的单用组。并设同批感染未治疗对照组。受治鼠于治疗后2周剖杀, 收集胆管和肝组织内的残留华支睾吸虫, 计算各组的平均虫数和减虫率, 用非参数统计方法(Mann-Whitney秩和检验)对相应组间的平均虫数进行分析。结果 感染华支睾吸虫的大鼠口服单剂三苯双脒或吡喹酮(150 mg/kg)的减虫率分别为57.2%和63.8%。三苯双脒各小剂量多次给药组的减虫率稍高, 达77.1%~79.4%, 而吡喹酮小剂量多次给药组的减虫率则为50.6%~54.2%。但两种药物各组间的平均虫数的差异无统计学意义。青蒿琥酯和蒿甲醚各单剂给药组与小剂量多次给药组的减虫率均较高, 分别为90.4%~98.5%和100%。三苯双脒小剂量(50或75 mg/kg)与吡喹酮(150 mg/kg 或187.5 mg/kg)伍用治疗, 减虫率为74.9%~100%, 高于其各单药组的减虫率(26.9%~79.6%)。青蒿琥酯或蒿甲醚小剂量(30 mg/kg)与吡喹酮(150 mg/kg)或三苯双脒(50或75 mg/kg)伍用治疗, 减虫率为74.9%~97.9%, 亦高于其各药组的减虫率(24.8%~79.6%)。结论 青蒿琥酯、蒿甲醚、吡喹酮和三苯双脒均为有效的抗华支睾吸虫药物, 各药物小剂量伍用具有增效作用。

关键词 三苯双脒 青蒿琥酯 蒿甲醚 吡喹酮 大鼠 华支睾吸虫 联合治疗

分类号

## Effect of Tribendimidine, Artesunate, Artemether and Praziquantel, Administered Intragastrically at Single, Multiple or Combined Doses, to Rats Infected with *Clonorchis sinensis*

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Abstract

Objective To assess the efficacy of single, multiple or combined oral doses of tribendimidine, artesunate, artemether and praziquantel against *Clonorchis sinensis* in rats. Methods A total of 147 rats, each infected with 50 *C. sinensis* metacercariae, were used in experimental chemotherapy. All the drugs used were administered intragastrically 42-44 d after infection. ① Sixty infected rats were randomly divided into 11 groups (4-5 rats per group) and the following drug dose-schedules were applied, i.e. under the same total dose tribendimidine or praziquantel was given at a single dose of 150 mg/kg, or given at smaller divided doses of 75 mg/kg (qd for 2 d), 50 mg/kg (qd for 3 d), 25 mg/kg (tid for 2 d); artesunate or artemether was given at a

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single dose of 75 mg/kg, or given a half dose of 37.5 mg/kg daily for 2 days. ②Eighty-seven infected rats were randomly divided into 15 groups (4-6 rats per group) for combined treatment with the following drug administration regimens, i.e. artesunate or artemether 30 mg/kg plus praziquantel 150 mg/kg or tribendimidine 50 mg/kg and 75 mg/kg, respectively; tribendimidine 50 mg/kg plus praziquantel 150 mg/kg; tribendimidine 75 mg/kg plus praziquantel 187.5 mg/kg. A single dose of each drug mentioned above was also involved. Untreated *C. sinensis*-infected rats served as control. Rats were killed 14 days post-treatment, worms recovered from the bile duct and the liver tissue, mean worm burden reduction calculated and mean worm burden compared between the groups using non-parametric method (Mann-Whitney test). Results Rats infected with *C. sinensis* and treated at a single 150 mg/kg dose of either tribendimidine or praziquantel resulted in a worm reduction of 57.2% and 63.8%, respectively. Whilst administration of tribendimidine at smaller but multiple doses given within 2-3 days at the same total dosage resulted in a slightly higher worm reduction (77.1%-79.4%), the opposite trend was observed for praziquantel (50.6%-54.2%). However, for both tribendimidine and praziquantel, the difference of mean worm burden lacked statistical significance between single and multiple doses. Infected rats administered either artesunate or artemether at a single dose of 75 mg/kg or a daily dose of 37.5 mg/kg for 2 days, the worm reduction was 100% and 90.4%-98.5%, respectively. Combined treatment with low doses of tribendimidine(50 mg/kg or 75 mg/kg)plus praziquantel(150 mg/kg or 187.5 mg/kg)resulted in a worm reduction of 74.9%-100%, which were higher than those of 26.9%-79.6% obtained from a single dose of each drug used. High worm reduction of 74.4%-97.9% was also observed when administering a low dose of artesunate or artemether (30 mg/kg) plus a low dose of tribendimidine (50 mg/kg or 75 mg/kg) or praziquantel (150 mg/kg). Mean worm reduction of 24.8%-79.6% were seen when drugs used at single doses. Conclusion The investigation confirmed that tribendimidine, artesunate, artemether and praziquantel are all efficacious against *C. sinensis*, and that drug combination acts synergistically.

Key words

[Tribendimidine](#) [Artesunate](#) [Artemether](#) [Praziquantel](#) [Rat](#) [Clonorchis sinensis](#)  
[Combined treatment](#)

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