OPTIMIZATION OF TETRANDRINE TREATMENT IN RAT HEPATIC FIBROSIS MODEL

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Abstract: Objective To optimize the therapeutic dosage of tetrandrine (Tet) in rat hepatic fibrosis model. Methods 50 Wistar rats were divided into 5 groups at random including normal control, model control, Tet-treated model groups of 10mg·kg-1 ·d-1, 5mg·kg-1 ·d-1 and 2.5mg·kg-1 ·d-1 (n =10 in each group). All rats, except for the normal controls, were injected with axenic porcine serum (0. 5ml each time, twice a week) intraperitoneally for 8 weeks to establish hepatic fibrosis. After the 8th week, rats of Tet-treated model groups were given by gavage once a day with different doses of Tet for another 8 weeks. Then the liver function, serum levels of hyaluronic acid (HA), laminin (LM), and procollagen type II (PC II) were tested. Collagen type I and III, pathological changes in liver tissue were also assessed. Results Most indices of liver function including alanine minotransferase (ALT), aspartate aminotransferase (AST), albumin (ALB), albumin/globulin ratio (A/G) and alkaline phosphatase (ALP) improved significantly in Tet-treated groups with the exception of γ-glutamyl transpeptidase (γ-GT) and total bilirubin (TBIL). Secondly, markedly lowered levels of HA, LM and collagen type I, II were also detected by radioimmunology and immunohistochemistry in the 5 mg·kg-1 ·d-1 Tet-treated model group. Moreover, pathological findings confirmed the statistically significant improvement in hepatofibrotic degree resulted from the treatment of 5mg·kg-1 ·d-1 rather than other doses of Tet. Conclusion For experimental Wistar rats, Tet exhibited an anti-hepatofibrotic action in doses within the range of 2.5mg·kg-1 ·d-1 to 10mg·kg-1 ·d-1, and 5mg·kg-1 ·d-1 may be the optimum one among all doses.

Keywords: tetrandrine;hepatic fibrosis;liver function;extracellular matrix;pathology

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