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Tetrandrine Therapy of Herpes Simplex Keratitis

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We isolated the active ingredient in an ancient Chinese herbal remedy for ocular inflammation, and tested it in an animal model of herpes simplex keratitis. The active ingredient, tetrandrine (TDR), was used systemically, and was compared to systemic Acyclovir in the therapy of a model of necrotizing stromal keratitis in mice. BALB/c mice are susceptible to developing such necrotizing keratitis after corneal inoculation with HSV1, and five groups of mice were studied: group 1 untreated; group 2 systemic acyclovir-treated beginning at day 0 post infection; group three acyclovir-treated from day seven post infection; group four TDR-treated from day 0 post infection; and group five TDR-treated from day seven post infection. All mice were infected in the right cornea with herpes simplex virus Type 1. The TDR concentration was 30 mg per kilogram intraperitoneally, and the acyclovir concentration was 120 mg per kilogram body weight intraperitoneally, daily. The mice were observed for 14 days after corneal inoculation, and clinical and inflammatory reactions and ocular histopathology were analyzed. Herpes specific antibody response and the delayed-type hypersensitivity response were also studied.

Of the 22 untreated mice, 16 developed necrotizing keratitis (72.7%). TDR given from day 7 reduced the HSK incidence to 8.5% ($p>0.01$); the incidence of HSK was 45.4% in mice treated with TDR from day 0. Systemic ACV given from day 0 inhibited HSK development ($p>.01$), but ACV given from day 7 resulted in HSK incidence of 50%. The specific HSV antibody response in the serum of mice treated with TDR or ACV either from day 0 or day 7 was significantly less than that of untreated mice ($p>.01$ and $>.05$ respectively). TDR treatment also suppressed DTH responses to HSV ($p>.05$).

TDR administered after HSV inoculation of the cornea significantly modulates murine HSK development at least partly by modifying the host immune/inflammatory response to the virus.