

Activity and Safety of Inhaled Itraconazole Nanosuspension in a Model Pulmonary *Aspergillus fumigatus* Infection in Inoculated Young Quails.

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Abstract

Pulmonary aspergillosis is frequently reported in parrots, falcons, and other birds held in captivity. Inhalation is the main route of infection for *Aspergillus fumigatus*, resulting in both acute and chronic disease conditions. Itraconazole (ITRA) is an antifungal commonly used in birds, but its administration requires repeated oral dosing, and the safety margin is narrow. To investigate the efficacy of inhaled ITRA, six groups of ten young quails (*Coturnix japonica*) were inoculated intratracheally with 5×10^6 spores (3 groups) or 5×10^7 spores (3 groups). Animals were exposed to nebulized ITRA nanosuspension as 10 % suspension or 4 % suspension, once daily for 30 min, starting 2 h after inoculation for 6 days. Control groups were exposed to nebulized saline for the same period of time. Survival and clinical scores were evaluated, and animals were subjected to gross pathology. In control animals, aspergillosis resulted in systemic disease without pulmonary or air sac granulomas. Animals died from multiple organ failure. Inhalation of 10 %

ITRA nanosuspension blocked lethality and prevented disease-related symptoms in the quails exposed to the low dose of spores, while the disease course in quails inoculated with the high-spore dose was retarded. Inhalation of 4 % ITRA nanosuspension was less effective. Both inhalations were well tolerated, and gross pathology did not reveal signs of local toxicity. The data indicate that inhaled administration of 10 % ITRA nanosuspension is capable of alleviating an acute *A. fumigatus* infection in quails. A lower ITRA concentration may be only active in chronic pulmonary aspergillosis.

Involved units

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