ASPERGILLOSIS IN BIRDS: AN OVERVIEW OF TREATMENT OPTIONS AND REGIMENS

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Abstract

Aside from the therapeutic advantages associated with antimycotic drugs, predisposing factors have to be considered when treating aspergillosis in an avian patient. Predisposing influences can be affected by improving management conditions, thus decreasing the amount of fungal spores in the environment. Moreover, a veterinarian often treats a chronic disease in most cases; therefore, the treatment regimen is typically for months sometimes. The route of administration for the selected therapeutic agent is of great importance and depends on the severity of the disease condition, among other factors. Furthermore, the side effects of the individual drugs may be reduced by selecting different routes of administration. To date, in clinically ill birds, oral or parenteral administration of the drug is performed regularly to achieve a systemic effect. In principle, it would be preferable to use long-term nebulization treatment; however, careful consideration is required when determining the composition of antimycotic formulation. All currently available antimycotic agents that are in the drug market have been developed for use in human medicine. Drug dosages that are recommended for avian medicine are frequently based on the experience of individual researchers or reference values that are derived from other species. Essentially, active substances within the azoles group, as well as some allylamines and polyene antibiotics, are prescribed to avian patients with aspergillosis, with most of the patients currently being treated with azoles. Systemic administration of these compounds is effective when treating most fungal infections that involve the respiratory tract. However, treatment difficulties often occur because of the limited tolerability and the high occurrence of side effects in avian patients who are administered antimycotic drugs.

Key words: birds; aspergillosis; drugs; way of application; side effects

Respiratory disease caused by mycotic infection, especially by *Aspergillus* spp., is often diagnosed in pet birds maintained in captivity and is considered a common cause of death in avian patients. A high predisposition for these infectious agents is noted in psittacines, mynahs, waterfowl, and birds of prey kept in captivity. Apart from the anatomical peculiarities of birds, predisposing factors such as insufficient management conditions (e.g., low humidity for tropic psittacines, inadequate food, stress, and high stocking density) are associated with exposure to the fungal organism. The predisposing factors have to be considered when developing a treatment protocol for a diseased bird and are addressed by improving the management conditions through decreasing the amount of fungal spores in the environment, and by improving food quality and hygienic measures. In all cases, stress factors should be reduced or avoided. Suitable measures that can be performed, not only for prophylactic purposes but also in avian cases of clinical aspergillosis, include increasing the environmental relative humidity of tropical birds to 60%, optimization of food quality, sufficient air exchange (e.g., access to fresh air and reduction of dust concentration), and, in some instances, the addition of propionic acid in the food birds that eat corn (1 mg/kg food). Severely diseased

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patients require intensive supportive therapy that includes infusions, vitamins, assisted feeding, and antimycotic treatment.[1] Furthermore, all factors that increase immunosuppression, including long-term antibiotic treatment and the administration of steroidal antiphlogistics, should be reviewed and considered critical if indicated.

Some authors recommend the surgical removal of mycotic-encapsulated granulomas to increase treatment response of the patient.[2,3] However, the increased narcotic risk in birds with respiratory disease has to be thoroughly considered. Judging the severity of disease for selecting the right treatment cannot be achieved only through external clinical assessment but requires the use of different diagnostic tests.

Treatment success cannot be evaluated based on clinical improvement alone. Independent of the birds' species, a combination of different examinations is necessary for that purpose. A negative laboratory result alone is not significant. Hematological and blood chemistry alterations are nonspecific, but they may be used for evaluating the progression of disease.[4] Antigen and antibody evaluations via serological essays are neither sensitive nor specific for aspergillosis, and even healthy birds are constantly exposed to these fungi. However, this method may be valuable as an adjunctive assessment regarding the patient's treatment response.[5,6] The radiographic examination detects chronic alterations in the respiratory system[7,8]; however, performing repeated radiograph images does not provide much useful information. In most cases, there is no short-term radiographic evidence of significant changes, even if the treatment protocol is successful. Computed tomography may be the best method for judging treatment.

ANTIMYCOTIC THERAPY

As described earlier, treating the infectious agent using suitable antimycotic drugs is not sufficient in most clinical cases of avian aspergillosis. A successful therapy must include the detection and elimination of predisposing factors. Furthermore, when developing a treatment plan, one has to consider that the veterinarian, in most cases, has diagnosed a chronic disease, and therefore, the treatment regimen is prolonged—sometimes for months.

All commercially available antimycotic agents have been developed for use in human medicine. Drug dosages recommended for avian patients are often based only on the experience of individual researchers or on reference values that are derived from other species.

APPLICATION

The route of administration of the chosen therapeutic agent is of great importance and depends on the severity of the disease among other factors. Moreover, the side effects of the individual drugs may be reduced by selecting different routes of administration, thus increasing local drug concentrations while reducing systemic drug exposure. Amphotericin B, a water-soluble drug, has been administered to humans using aerosol, nasal spray, solutions, injections, tablets, drops, and ointment formulations. As azole compounds are highly water-insoluble derivatives, there are fewer alternative preparations. To date, in clinically ill birds, oral or parenteral administration of the antimycotic drug has to be performed regularly to achieve a systemic effect. In principle, it is preferable to use nebulization for long-term treatment because of low patient stress and fewer side effects. However, for inhaled administrations, special caution is required when determining the formulation's composition.

Nebulization

In principle, aerosol therapy has many advantages. As stated earlier, nebulization is achieved with only minor patient stress, and higher therapeutic drug levels in the lung may be attained without systemic side effects.[9] Currently, there is no antimycotic drug in the market that has been developed specifically for *per inhalationem* administration in birds. Currently, there are ongoing efforts to get antimycotic compounds approved for nebulization in the human market, as none exists.

In different avian studies that used various antimycotic drugs (i.e., drugs not developed for the nebulization route) *per inhalationem*, it was not possible to achieve therapeutic lung concentrations for a specific period. Terbinafine,[10] amphotericin B,[11] enilconazole,[12] and clotrimazole [13] have been used, diluted with physiological sodium solution