Topical Ketoconazole Antifungal Therapy

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Veterinarians have longed for a broad spectrum antibacterial and antifungal topical to handle those dermatitis cases where either mixed microbes are involved or as a broad spectrum treatment when they are not sure. Recently, some new products containing traditional antibacterial agents have been introduced into the market that are mixed with the antifungal agent, ketoconazole in the form of shampoos and otics. This discussion will describe both.

Shampoo therapy is an integral adjunctive part of the management of skin diseases in dogs and cats. Treating the skin requires TREATING-THE-SKIN; not just giving systemic medications such as steroids, antifungals, and antibiotics. Deciding which shampoo to use and which ingredients the shampoo should contain for a certain skin problem may be confusing.

Topical shampoo therapy helps to relieve itch, decrease inflammation, remove antigens from the skin, debride dead skin cells, degrease, and kill micro-organisms on the skin. Rather than just cleansing the dirt off of the skin and haircoat, when left in contact with the skin for 15 minutes or longer, these shampoos actually have beneficial effects on the skin cells. Newer shampoos contain topical pharmaceuticals as a part of their ingredients, so topical antimicrobial therapy in shampoos is now possible. Recently, 1% ketoconazole has been added to shampoos (Mal-A-Ket, GlychlorK, and Ketaclor) for dogs and cats used in treating Malassezia dermatitis and dermatophytosis/ringworm.

Ketoconazole is an azole antifungal agent that binds to the lipids in fungal cell membranes and interferes with the synthesis of ergosterol, an integral part of the fungus or yeast cell wall. When given orally, ketoconazole also has anti-inflammatory effects and inhibits t-lymphocytes. As with all azole antifungal agents, ketoconazole works principally by inhibition of an enzyme, cytochrome P-450, which is required in the ergosterol synthesis pathway. Because of this inhibition, ketoconazole also decreases the metabolism of cyclosporine, so lower doses of cyclosporine can be used in larger dogs in combination with ketoconazole to treat atopic dermatitis. Treating larger dogs with this combination therapy, it has been observed that pruritus decreases more than with either drug alone. The oral absorption of ketoconazole is greatly enhanced in an acidic environment, so giving it with food is beneficial. Antacids or H2 inhibitors may actually interfere with absorption. Cats should not be given ketoconazole orally, as it causes anorexia and liver damage.

When topically applied in a shampoo, ketoconazole should be used on a skin surface that is degreased because of its lipid affinity. The more lipid that is on the skin, the smaller the amount of ketoconazole that will be available to bind to the yeast or fungus. With some shampoos, a good degreasing shampoo should be used prior to the ketoconazole shampoo. One product that contains acetic acid actually degreases the skin as the shampoo is working (Mal-A-Ket, 2% acetic acid, 2% chlorhexidine and 1% ketoconazole and Glycozoo with 1% Ketoconazole and 1% Glycolic acid). Many veterinary ketoconazole shampoos also contain chlorhexine gluconate 2%, an antimicrobial detergent that binds to skin proteins. There seems to be a synergy with the 1% ketoconazole / 2%chlorhexidine combination when used topically. A product containing ketoconazole should have an even distribution of the drug and it should be a clear solution rather than a suspension. Ketoconazole is not very water soluble, so
when using it in a shampoo, the less water dilution there is, the higher the concentration on the skin cells.

Using a topical ketoconazole shampoo for ringworm in cats may preclude the need for systemic antifungal drugs, like itraconazole and fluconazole which are expensive. A ketoconazole containing shampoo has a much less offensive odor than other topicals like lime sulfur, which can be used in conjunction to treat dermatophytosis. In addition, topical therapy for ringworm helps to reduce shedding of spores in the environment. Twice weekly 15-20 minute shampoos are required until a negative DTM culture is obtained.

Malassezia dermatitis results as a secondary complication from allergies, adverse food reactions, and hormonal imbalances, like hypothyroidism in dogs. Atopic dermatitis dogs usually have Malassezia yeasts between the toes and results in foot licking and salivary discoloration of the hair. Atopics may also have hyperkeratosis and seborrhea, often with a very bad odor in the axillary, antecubital, pedal and ventral neck region. Of course Malassezia otitis occurs in most of these allergic dogs, too. Shampoo therapy alone may help many of these allergy dogs get relief from Malassezia dermatitis. However, systemic treatment with steroids, cyclosporine, or oclacitinib, along with antibiotics and antifungals may be necessary in more severe cases. Allergen specific immunotherapy and food elimination diets may decrease the incidence of Malassezia dermatitis. Initial skin treatment requires a 15-20 minute whole body shampooing every other day for 2 weeks, a total of 7 treatments. As mentioned earlier, greasy dogs should have a pre-treatment degreasing bath. In foot lickers, make sure that the shampoo gets between the toes and in the foot pads.

Malassezia otitis often complicates allergic disease, hypothyroidism, and other conditions in dogs. Antifungal drugs such as nystatin, clotrimazole, miconazole, and thiabendazole have been available in otic preparations for a long time. Systemic ketoconazole does not seem to have good anti-yeast effects in the ear, most likely due to the ear canal's poor blood supply. Ketoconazole is now available in some otic formulas in combination with tris-EDTA (TrizUltra/Dechra, T8 + Keto/Ivax). However, prior to using these products, a deep ear flush should be done using a wax dissolving cerumenolytic detergent in the hospital, preferably with the dog sedated or anesthetized. Initial deep ear cleaning remains an essential part of good ear therapy. Twice daily application of the tris-EDTA/ketoconazole product is recommended until negative cytology is obtained. Treatment is used for a minimum of 2 weeks. Unless the primary cause of the ear disease and/or the Malassezia dermatitis (atopy, adverse food reactions, and/or hypothyroidism) are addressed, when topical skin or otic therapy is stopped, the yeasts often return.

Ketoconazole shampoos and ear products provide additional treatment options to the veterinarian in treating common fungal diseases. When ketoconazole is mixed with other antibacterials like chlorhexidine, acetic acid, and tris-edta, it offers a broad spectrum antifungal and antibacterial tool.