

Refractory feline sporotrichosis treated with itraconazole combined with potassium iodide

Feline sporotrichosis is caused by pathogenic fungi in the genus *Sporothrix*. In Brazil, the most prevalent agent and primary pathogen of feline sporotrichosis is *Sporothrix brasiliensis* (Rodrigues *et al.* 2013). The disease usually ranges from a single skin lesion that can progress to multiple skin lesions and fatal systemic involvement. Nodules and ulcers are the most common skin lesions, and respiratory signs and nasal mucosa involvement occur frequently (Gremião *et al.* 2015).

Currently, there are a limited number of oral antifungal agents for the treatment of cats with sporotrichosis, especially for cases refractory to itraconazole (ITZ), which is the drug of choice. Potassium iodide (KI) is an important option in the treatment of cats from the endemic area of Rio de Janeiro. In addition, KI is less expensive than ITZ (Reis *et al.* 2012). The effectiveness of both drugs as monotherapy had already been documented but cases of therapeutic failure are common (Gremião *et al.* 2015). In this context, ITZ combined with KI has been successfully used in treating naïve cats (Reis *et al.* 2016), as well as in a preliminary study conducted by our group, which included cats refractory to ITZ (Rocha *et al.* 2013).

The study we report here evaluated the effectiveness and safety of the KI combined with ITZ in an observational study of cats from Rio de Janeiro with sporotrichosis refractory to ITZ. Cats included were those with lack of clinical response for at least 8 weeks of ITZ therapy 100 mg once daily (Itraconazol; Prati-Donaduzzi), and presented with persistent skin or mucosal lesions. A regimen of 100 mg ITZ and 5 mg/kg KI (formulated drug) was administered once daily with food by the owners.

If there was no clinical response observed over 4 weeks, the KI dose was increased to 10 mg/kg once daily, and the ITZ was maintained at the same dose. The cats were observed monthly for clinical examination and laboratory tests. A follow-up was carried out 3 months after the clinical cure. The procedures were approved by the Animal Ethics Committee (LW-40/12).

Of the 38 cats included, 35 (92.1%) had lesions in the nasal region (bridge of the nose, nasal planum and/or nasal mucosa lesions) (Fig 1a). Respiratory signs (nasal discharge, sneezing and dyspnoea) were observed in 27 cats (71%). As observed by Gremião *et al.* (2015), a higher frequency of lesions refractory to antifungal therapy occurs on the nasal region.

Seven cats (18.4%) needed an increase of KI dose. Twenty-four cats were cured (63.2%) (Fig 1b) within a median treatment time of 20 weeks (16 to 32 weeks). Therapeutic failure occurred in five cases (13.1%), and death in three cases (7.9%). Death in one cat was not associated with sporotrichosis but the other two showed worsening clinical signs. Six cats (15.8%) were lost during follow-up. Three months after clinical cure, recurrence was observed in two cats.

The median time until clinical cure in this study was longer than that observed in naïve cats treated with the same protocol (Reis *et al.* 2016). In addition, the overall cure rate (62%) was lower than that in naïve cats (96%) with sporotrichosis treated with ITZ and KI.

Of the 38 cats included in the study, three (8%) showed adverse clinical signs only, eight (21%) presented only elevation in transaminase levels and 12 cats (32%) presented both clinical adverse events and elevation in transaminases levels. The

a



b



FIG 1. (a) Cat with sporotrichosis: lack of clinical response following 11 weeks of itraconazole therapy. Tumour-like lesion with erythematous and irregular surface on the nasal and periocular regions, unilateral ocular seropurulent secretion, polyp-like mass in the nostrils and respiratory signs (nasal discharge, sneezing and dyspnoea). (b) Clinical cure achieved after 31 weeks of itraconazole and potassium iodide therapy; a scar remains on the nasal region.

most frequent adverse clinical events were hyporexia and weight loss, observed in six cases (40%). Of the animals that presented an elevation in transaminase levels, 16 cats (80%) presented only a mild elevation in alanine aminotransferase (ALT) levels (<415 U/L), three (15%) showed a moderate increase in ALT (498, 544 and 636 U/L), and one had severe increase (927 U/L). Cats that required increased KI dose had a higher frequency of clinical or laboratory adverse effects.

Due to the adverse effects, seven cats (18%) had the therapy temporarily suspended for 7 days. Increased ALT and gastrointestinal adverse effects are considered dependent on dose of ITZ and have been reported in cats with sporotrichosis under KI therapy (Pereira *et al.* 2010, Gremião *et al.* 2015). The adverse clinical effects observed here were higher and the increase of the ALT levels was more severe than those reported using ITZ and KI (2.5 to 5.4 mg/kg) in naïve cats with sporotrichosis (Reis *et al.* 2016). This fact may be explained by a higher KI dose used here.

Potassium iodide combined with ITZ represents an effective option in the treatment of cats with sporotrichosis refractory to ITZ, especially in those cases presenting nasal mucosal lesions and respiratory signs.

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**R. F. D. B. da Rocha, T. M. P. Schubach, S. A. Pereira,
É. G. dos Reis, B. W. Carvalho and I. D. F. Gremião**

Laboratory of Clinical Research on Dermatозoonosis in Domestic Animals, Evandro Chagas National Institute of Infectious Diseases/Oswaldo Cruz Foundation (Fiocruz), 21045-900 Rio de Janeiro, Brazil

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