Treatment of cutaneous sporotrichosis with one daily dose of potassium iodide

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Abstract

Background

Recommended treatment for cutaneous sporotrichosis consists of a saturated solution of potassium iodide (SSKI) administered in three daily doses (tid). Because compliance with this regimen has been a problem in our previous experience, we evaluated the use of one daily (qd) full dose of SSKI.

Methods

patients with culture-confirmed cutaneous sporotrichosis were entered in a randomized, nonblinded study to compare the safety and efficacy of qd *vs.* tid dosage of SSKI.

Results

Fifty-seven patients were enrolled to receive either qd (29) or tid (28) SSKI. Three (1 in the qd and 2 in the tid group) were not compliant with the assigned regimen. Side effects were common but mild in both treatment groups (61% in the qd and 42% in the tid group, *P* = 0.17); treatment had to be discontinued because of side effects in 3 cases (2 in the qd and 1 the tid group). Overall 26 (89.6%) and 25 (89.2%) of the individuals initially assigned to the qd and tid dosing schedule, respectively, were cured by the treatment. No relapse was detected after 45 days of follow-up.

Conclusion

These findings suggest that a single daily full dose of SSKI appears to be appropriate therapy for cutaneous sporotrichosis; further studies with larger numbers of patients are required.

INTRODUCTION

Sporothrix schenckii is a dimorphic fungus common in the tropics where it can be found in soils and plants. When accidentally inoculated into the subcutaneous tissue of humans it causes sporotrichosis, characterized by the development of a nodule and an ulcer with further spread of the fungus through the lymphatics. Sporotrichosis can be cutaneous or extracutaneous. Cutaneous sporotrichosis presents as a single ulcerative lesion (fixed cutaneous), a rosary of lesions along lymphatic vessels (lymphocutaneous) or multiple skin lesions from different inoculations (multiple cutaneous). Extracutaneous sporotrichosis can present as osteoarticular, pulmonary, ocular or central nervous system disease.[1, 2] Currently recommended treatment for cutaneous sporotrichosis includes a saturated solution of potassium iodide (SSKI, 1 g/ml) in a dosage of 5 to 10 drops three times a day in milk or juice and

increased 3 to 5 drops/day until a total of 40 to 50 drops three times a day is reached or signs of toxicity occur. Pediatric dosing is started at 1 to 2 drops per year of age and increased to a maximum of 30 to 40 drops three times a day. The treatment is continued until the lesions heal.[1-4]

Abancay, Peru, is an area endemic for sporotrichosis.[5, 6] Previous experience in our group, as well as others, has shown that the recommended treatment with SSKI is effective when followed properly. However, as many as 29 to 62% of individuals abandon treatment with consequent therapeutic failure.[6, 7] The reasons for abandoning treatment are complex and multifactorial, but two of the reasons mainly cited by our patients are the presence of side effects and the inability to follow multiple daily dosing schedules.

In an effort to simplify the treatment of sporotrichosis we evaluated, in a randomized nonblinded study, the effect of once daily full dose SSKI compared with the standard three times daily dosage. The outcome variables were the appearance of side effects and the healing of the primary lesion at the end of treatment and 2 to 3 months later. This work was presented in a preliminary form elsewhere.[8]

PATIENTS AND METHODS

Patients at the Santa Teresa Health Center in Abancay, Peru, with culture-confirmed diagnosis of cutaneous sporotrichosis were included in the present study. Pregnant women were excluded. The guidelines of Universidad Peruana Cayetano Heredia for the use of human subjects were followed; informed consent was obtained from each volunteer participating in this study or from a legal guardian.

After a thorough clinical examination, patients were assigned randomly to receive the daily total dosage of SSKI either as a single dose (qd) or divided in three doses (tid). For simplicity the starting daily dose of SSKI was standardized to 3 drops (1 drop = 50 mg of KI) and increased by 3 drops every day until clinical response or signs of toxicity appeared. The patients were instructed to ingest the medicine dispersed in milk and after a meal. The treatment was supervised daily until full dosage was reached, and then once a week at the health center. Patients who missed appointments were visited at home the next day to ensure compliance with therapy. Compliance was monitored by interview and visual inspection of the dispensing bottle to verify a proportional decrease in the level of remaining fluid.

Follow-up evaluation included a weekly questionnaire on the presence of side effects and examination of the lesions. Cure was decleared when the primary lesion showed complete reepithelization and there was no evidence of satellite lesions. At that point the treatment with SSKI was stopped and the patients were followed clinically by office or home visits for the next 45 days to detect relapses.

Statistical analysis was performed with the Epi-Info® package. Continuous variables were compared by Student's *t* test and categorical variables by chi square analysis. $P < 0.05$ was considered significant for a two-tailed analysis.

RESULTS

Fifty-seven patients were enrolled in the study, 29 were randomized to receive SSKI qd and 28 to receive SSKI tid. Before start of therapy the groups were comparable in terms of age, gender, time of illness and disease type (Table 1).

Five patients (2 in the qd and 3 in the tid regimen) missed appointments; when visited at home, 3 of them (1 in the qd group and 2 in the tid group) were found to be noncompliant with the assigned treatment and were excluded from follow-up.

Among those followed up side effects were commonly reported (Table 2), occurring in 17 (61%) of the 28 subjects receiving SSKI qd and in 11 (42%) of the 26 on the dosing schedule ($P = 0.17$). In 3 patients the side effects warranted discontinuation of the therapy (1 case of severe urticarial rash in each treatment group and 1 case of erythema nodosum leprosum in the qd group).

The 51 patients who completed therapy (26 and 25 in the qd and tid groups, respectively) showed complete resolution of the primary lesion with no relapse detected after 45 days of follow-up. The maximum dose tolerated, the number of days to reach the maximum dose and the total number of days of therapy required for healing were similar for the 2 treatment groups (Table 3). Overall 26 (89.6%) and 25 (89.2%) of the individuals initially enrolled in the qd and tid dosing schedule, respectively, had a favorable outcome with the assigned treatment.

DISCUSSION

The killing effect of potassium iodide on the yeast form of *S. shenckii*[9] renders this drug effective for treatment of sporotrichosis. Complete healing of lesions is achieved in almost all patients.[1-3] Its low cost makes SSKI especially useful in underdeveloped countries. However, the main drawback to the utilization of the drug is noncompliance which can be as high as 64% in rural areas like Abancay.[6] One of the reasons for stopping the therapy is the complexity of adhering to a three times a day schedule by a population that spends all day working in the field, that has only one main meal a day and whose conception of time is different from Western standards. We believe from our previous experience[7] that a once daily schedule of treatment would be more suitable for them.

In the present evaluation of once daily SSKI therapy, we found that the occurrence of side effects was somewhat increased compared with the standard tid dosing. However, in most cases they were mild and did not preclude the continuation of therapy. More importantly, the final outcome was similar for both groups with almost 90% of patients being cured after the completion of therapy. Also, the time and total dose required to achieve healing of the lesion were similar among both groups. These findings suggest that a single daily full dose of SSKI might be a safe and effective treatment of cutaneous sporotrichosis, but a larger number of patients need to be studied.

Compliance to the once daily dosing schedule was not evaluated here. Because we aimed to compare the side effects and clinical response of the two regimens, we were rigorous in the follow-up of the population under study. We are planning next to assess the impact of the once daily regimen on a busy rural outpatient setting in assuring completeness of treatment and cure of the patients. We will also evaluate whether the administration of the daily dose at bedtime might decrease the number of reported side effects.

Azole compounds (e.g. itraconazole) are being evaluated for their safety and efficacy in the treatment of sporotrichosis, with the advantage of one daily dosing.[10-12] However, because of the cost involved we believe that SSKI will remain the drug of choice in underdeveloped countries.

Factor	SSKI qd (N = 29)	SSKI tid (N = 28)	P
Age (yr)			
Mean	7.2	7.8	0.67
Range	2–16	3–18	
Gender, male	14 (48)*	16 (57)	0.59
Time of illness (mo)	13.0 ± 2.0	13.3 ± 1.7	0.59
Disease type			
Fixed cutaneous	14 (48)	16 (57)	
Lymphocutaneous	15 (52)	11 (39)	0.25
Multiple cutaneous	0 (0)	1 (4)	

* Continuous variables expressed as median ± SD; categorical variables expressed as number (percent).

Reported Side Effect*	SSKI qd (N = 28)	SSKI tid (N = 26)	P
Nausea	4 (14)†	3 (12)	0.76
Headache	2 (7)	1 (4)	0.59
Abdominal pain	4 (14)	3 (12)	0.76
Metallic taste	1 (4)	2 (8)	0.50
Diarrhea	1 (4)	0 (0)	0.33
Rhinorrhea	3 (11)	1 (4)	0.33
Severe urticaria	1 (4)	1 (4)	0.95
Erythema nodosum leprosum	1 (4)	0 (0)	0.33
Any side effect	17 (61)	11 (42)	0.17

* Some patients reported more than one side effect.
† Numbers in parentheses, percent.

Factor	SSKI qd (N = 26)	SSKI tid (N = 25)	P
Complete healing	26 (100)*	25 (100)	1.00
Time to reach maximal dose (days)	11 ± 3.2	10 ± 4.7	0.54
Maximal daily dose (mg/kg)	160 ± 9	160 ± 2	0.59
Duration of treatment (days)	33.8 ± 7.7	32.2 ± 6.7	0.55

* Continuous variables expressed as median ± SD; categorical variables expressed as number (percent).

160 mg/kg x 70 kg = 11.2 gm
KI = 8.6 gm I- !!

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