Sertaconazole 2% cream vs. miconazole 2% cream for cutaneous mycoses: a double-blind clinical trial

H. Ghaninejad, K. Gholami,* P. Hashemi, M. Hajibabai,* Z. Rahbar, M. S. Farivar, F. Mastani* and A. Rashidi

*Departments of Dermatology and *Pharmacology, Tehran University of Medical Sciences, Tehran, Iran*

doi:10.1111/j.1365-2230.2009.03579.x

Summary

The efficacy of 2% creams of miconazole nitrate and sertaconazole were compared in a double-blind clinical trial carried out on 100 patients with an established diagnosis of cutaneous dermatophytosis. Assessments were performed on days 0, 15, 29 and 43 in our dermatology clinic. Cure was defined according to clinical assessment confirmed by microscopical examination and culture. The groups were similar in age, gender, weight and clinical presentation. The reported side-effects, most commonly pruritus, occurred in 22 (40.0%) and 15 (33.3%) patients in the sertaconazole and miconazole groups, respectively ($P = 0.28$), but were not serious enough to stop the treatment. The only significant difference between the groups was in per-protocol cure rate by day 15, when patients in the sertaconazole group had a higher cure rate than the miconazole group ($P < 0.01$). In conclusion, sertaconazole was superior to miconazole in producing an early response in our patients. Given the higher price of sertaconazole and the ability of the considerably less expensive miconazole to produce equally good response after a month, the usefulness of sertaconazole as an alternative to miconazole in Iran requires further study.

The inflammatory component of dermatophytosis can be controlled by antifungal agents with anti-inflammatory activity. Of these drugs, only sertaconazole has been shown to reduce the release of cytokines from activated lymphocytes.[1] Given that the same treatment may show variation in efficacy in different populations due to differences in prevalence and distribution of dermatophytoses and their resistance to the drugs, the genetic predisposition of patients and environmental factors, we aimed to compare in a double-blind randomized clinical trial the efficacy and safety of the widely used miconazole nitrate, with those of a less commonly used antifungal, sertaconazole nitrate. To our knowledge, this is the first such trial in an Iranian population.

Correspondence: Dr Armin Rashidi, No. 12, Aramesh Alley, Mellat Park, Tehran, Iran
E-mail: rasidiarmin@yahoo.com

Conflict of interest: none declared.

Accepted for publication 23 April 2009

Report

All patients gave informed consent and the study protocol was approved by the ethics committee of our university. The study was a double-blind clinical trial carried out on 100 adults (aged > 18 years) with an established diagnosis of cutaneous dermatophytosis in Razi Dermatology Hospital between June 2007 and May 2008. Diagnosis was based on suggestive history and physical examination, confirmed by microscopical examination (using potassium hydroxide solution) and culture. Patients were randomly allocated to either the miconazole group ($n = 45$) or the sertaconazole group ($n = 55$). The 2% creams were applied to the lesions twice daily for 4 weeks. Each patient was evaluated four times in our clinic: visit 1 (confirmation of the diagnosis and inclusion in the study), visit 2 (day 15; assessment of cure), visit 3 (day 29; assessment of cure and end of

treatment) and visit 4 (day 43; culture and assessment of relapse). Cure was defined as absence of fungi on microscopy, negative culture and complete resolution of all symptoms. Any side-effects were documented at each visit.

Data were analysed using the χ^2 test for frequencies and categorical variables, and Student's *t*-test for continuous variables, and significance was set at $P < 0.05$. Analyses were carried out using SPSS software (version 15.0 for Windows; SPSS Inc., Chicago, IL, USA).

There was no significant difference between the groups in age, gender, weight or clinical presentation (Table 1). The frequency of the dermatophyte species isolated was also similar in both groups, with *Epidermophyton floccosum* and *Trichophyton mentagrophytes* comprising > 80% of all cases. Twelve patients (21.8%) in the sertaconazole group and 5 patients (11.1%) in the miconazole group were lost to follow-up. One patient in the sertaconazole group failed to complete the protocol due to the development of severe contact dermatitis ($P = 0.12$). Side-effects were reported by 22 patients in the sertaconazole group and 15 (33.3%) in the miconazole group ($P = 0.28$), but their symptoms did not require cessation of treatment. The most commonly encountered disorder was pruritus, both at initial evaluation and during the course of treatment. We only considered pruritus to be a side-effect if it was increased or of new onset. There was no relapse in any patient. Table 2 shows the cure rates in the two groups based on intention-to-treat and per-protocol analyses. The only significant difference between the groups occurred in per-protocol cure rate by day 15, when the patients in sertaconazole group had a higher cure rate than those in the miconazole group ($P < 0.01$). We found no significant relationship between cure rates and the site of involvement (hand, foot, groin or trunk).

Table 1 Characteristics of patients in the two groups.

Characteristics	Miconazole (*n* = 40)	Sertaconazole (*n* = 42)	*P*
Age, years, mean ± SD	36.1 ± 15.1	34.3 ± 12.7	0.07
Males, *n* (%)	25 (62.5)	32 (76.2)	0.18
Weight, kg, mean ± SD	70.6 ± 12.3	70.7 ± 12.3	0.97
Clinical presentation, *n* (%)*			
Tinea cruris	17 (42.5)	24 (57.1)	0.40
Tinea pedis	16 (40.0)	10 (23.8)	0.40
Tinea corporis	11 (27.5)	10 (23.8)	0.40
Tinea manuum	1 (2.5)	2 (4.8)	0.40

*Some patients had simultaneous involvement of > 1 part of the body.

Table 2 Intention-to-treat and per-protocol analyses of cure.

	Miconazole	Sertaconazole	*P*
Started treatment, *n*	45	55	–
Completed treatment, *n* (%)	40 (88.9)	42 (76.4)	–
Intention-to-treat cure rate, %			
Day 15	20.00	23.60	0.66
Day 29	66.70	69.10	0.80
Day 43	88.90	76.40	0.09
Per-protocol cure rate, %			
Day 15	2.20	13.00	< 0.01
Day 29	73.20	82.60	0.36
Day 43	100.00	100.00	1.0

In contrast to miconazole, which is an inexpensive antifungal drug widely used in Iran, sertaconazole is a relatively expensive drug and thus is less commonly used. Based on our results, sertaconazole is superior to miconazole nitrate in its early therapeutic effect. However, using sertaconazole was associated in our series with a significantly higher loss to follow-up ($P < 0.05$); we do not know the reason for this. Patients who received sertaconazole experienced mild side-effects more commonly than those who received miconazole nitrate. The high rate of loss to follow-up in the sertaconazole miconazole group may be due to the occurrence of side-effects that were not as easily tolerated by the patients. The other possible reason for not returning to follow-up is a superior response to treatment and/or patients judging themselves as cured.

Sertaconazole nitrate is a broad-spectrum antifungal with both fungicidal and fungistatic effects.[2] Clinical trials with sertaconazole nitrate cream 2% show its efficacy in treatment of superficial cutaneous fungal infections.[3–6] In particular, it has been shown to be superior to other topical azoles in clinical studies of tinea pedis.[7,8] *In vitro* studies have shown the potency of sertaconazole to be equal to that of miconazole for *Microsporum gypseum*, *T. mentagrophytes* and *Microsporum canis.* Against *Trichophyton rubrum*, however, sertaconazole had a more potent effect than miconazole.[9] To our knowledge, the only clinical study to compare the efficacy of sertaconazole with that of miconazole is that of Alomar *et al.*[7] They found a significant superiority of sertaconazole in both early (day 14) and eventual cure rates. Our data in early response supports the results obtained by Alomar *et al.* One reason why we could not show a significant difference in cure rates at the end of treatment may be due to our comparatively small sample size and the resulting low power. We also had only a small number of cases with *T. rubrum* infection, and most of our patients were infected with one of two dermatophyte species (*E. floccosum* or

T. mentagrophytes), which may further limit the extent to which our results can be generalized.

In conclusion, sertaconazole was superior to miconazole in producing an early response in our patients. However, given the higher price of sertaconazole and the ability of the less expensive miconazole to produce equally good response after a month, the usefulness of sertaconazole as an alternative to miconazole in Iran requires further studies.

References

1 Liebel F, Lyte P, Garay M *et al.* Anti-inflammatory and anti-itch activity of sertaconazole nitrate. *Arch Dermatol Res* 2006; **298**: 191–9.

2 Pfaller MA, Sutton DA. Review of in vitro activity of sertaconazole nitrate in the treatment of superficial fungal infections. *Diagn Microbiol Infect Dis* 2006; **56**: 147–52.

3 Carrillo-Munoz AJ, Tur-Tur C. Comparative study of antifungal activity of sertaconazole, terbinafine, and bifonazole against clinical isolates of Candida spp. Cryptococcus neoformans and dermatophytes. *Chemotherapy* 1997; **43**: 387–92.

4 Carrillo-Munoz AJ, Fernandez-Torres B, Cardenes DC, Guarro J. In vitro activity of sertaconazole against dermatophyte isolates with reduced fluconazole susceptibility. *Chemotherapy* 2003; **49**: 248–51.

5 Carrillo-Munoz AJ, Guglietta A, Palacín C *et al.* In vitro antifungal activity of sertaconazole compared with nine other drugs against 250 clinical isolates of dermatophytes and Scopulariopsis brevicaulis. *Chemotherapy* 2004; **50**: 308–13.

6 Pedragosa R, González B, Martín M *et al.* Therapeutic efficacy and safety of the new antimycotic sertaconazole in the treatment of cutaneous dermatophytosis. *Arzneimittelforschung* 1992; **42**: 760–3.

7 Alomar C, Bassas S, Casas M *et al.* Multi-centre double-blind trial on the efficacy and safety of sertaconazole 2% cream in comparison with miconazole 2% cream on patients suffering from cutaneous mycoses. *Arzneimittelforschung* 1992; **42**: 767–73.

8 Savin R, Jorizzo J. The safety and efficacy of sertaconazole nitrate cream 2% for tinea pedis. *Cutis* 2006; **78**: 268–74.

9 Palacin C, Sacristan A, Ortiz JA. In vitro activity of sertaconazole. *Arzneimittelforschung* 1992; **42**: 699–705.

