ANTIFUNGAL ACTIVITY OF SN 105-843 GEL IN VIVO

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Abstract

The present work deals with the antifungal activity of SN 105-843 (Naftifine) against dermatophytes in vivo. Fifty cases suffering from various types of dermatomycoses were studied from November 1979 to September l980. The patients were supplied with 1% gel preparation of SN 105-843 for local application on the lesion for a period of 2-8 weeks. The results indicate that the drug has very significant antifungal effect on all types of dermatomycoses Out of fifty cases studied, thirty-two (64%) were cured, fifteen (30%) improved and in the remaining 3 cases (6%) the therapy had to be discontinued due to significant side-effect in the form of burning. SN 105-843 seems to be an effective antifungal agent (JPMA 31:123, 1981).

Introduction

SN 105-843 (Naftifine) is a naphthyl alkyla-mine derivative, a class of compounds that has never been used in chemotherapy. This has been synthesized by Sandoz Ltd., Switzerland. Chemically it is (E)-N-methyl-N (1-Naphthyl methyl)-3 -Phenyl-2-propen-l -amine-hydrochloride, and has the following structural formula:-

Material and Methods

Fifty patients suffering from various types of dermatomycoses were included in the study. These patients attended the Department of Dermatology, Jinnah Postgraduate Medical Centre, Karachi, for clinical diagnosis. The diagnosis-was confirmed at Microbiology Department of Karachi University, by microsopic demonstration of the fungus in clinical material followed by isolation and identification of the aetiological agent.

The geographical position and climatic condition of Karachi (Haroon, 1979) coupled with poor standards of hygiene (Uppal, 1974) are conducive to the high prevalence of dermatomy- coses. The objectives of the stuay were to clarify and establish the antimycotic effect, treatment period, frequency of recurrence and systemic and local side effects of SN 105-843. The patients were supplied with 1% gel prepa ation of SN 105-843 for local application twice daily to the affected area for a period of 2-8 weeks. The patients were asked to report every two weeks in order to observe the therapeutic effect of the drugs. The clinical material was obtained from the patients every two weeks and observed micro-scopically for the presence of fungus. The treatment was continued for eight weeks, but was stopped earlier if the patient was cured. All those patients with no clinical symptoms and negative culture and microscopy were considered as cured. Those showing some reduction in clinical symptoms, but still with positive culture were considered as improved.

Phases of Study

The study of SN 105-843 in vivo was divided into two phases. The first phase included the clinical diagnosis of the patients suffering from various types of dermatomycoses and observation of the chemotherapeutic effect of SN 105-843 by local application in form of 1% gel. The second phase comprised of microscopic demonstration of aetiological agent in clinical material, its isolation and identification.

Clinical Studies

The criteria for the inclusion of the patients in the study were: clinical and microscopic evidence of dermatophytosis; absence of treatment with griseofulvin or any other antimycotic drug systemically or orally within the previous 4 weeks; freedom from bacterial super-infection of fungal lesions.

Following laboratory investigations were performed on each patient before and after the treatment: Haemoglobin, white cell count, platelet count, erythrocyte sedimentation rate, serum bilirubin, SGOT, SGPT, alkaline phosphatase, blood glucose and serum creatinine.

Complete record of clinical and mycological diagnosis, laboratory investigations and side-effects was maintained on specific forms prepared for this purpose. Patients were supplied with 1% gel preparation of SN 105-843 for local application twice daily to the affected area for a period of 2-8 weeks, and were asked to report for follow-up every two weeks.

The therapeutic effect of the drug was determined by observing the clinical symptoms and microscopic examinations of the clinical material for fungus every two weeks. If a patient become symptom free with neeative microscopy and culture at any stage of his visit, the treatment was discontinued and the patient was rated as cured. The treatment period was never extended beyond eight weeks. Patients with some reduction in clinical symptoms but still with positive culture were considered as improved. All cured cases were reviewed clinically, microscopically and culturally two weeks after the end of treatment. In none of the cases recurrence was noted.

Mycological Studies

The clinical material comprised of scrapings from skin and hair. These were obtained after cleaning the lesion with 70% alcohol. The clinical material was collected in sterile petri plates for microscopic observations and culture.

Microscopic Observations

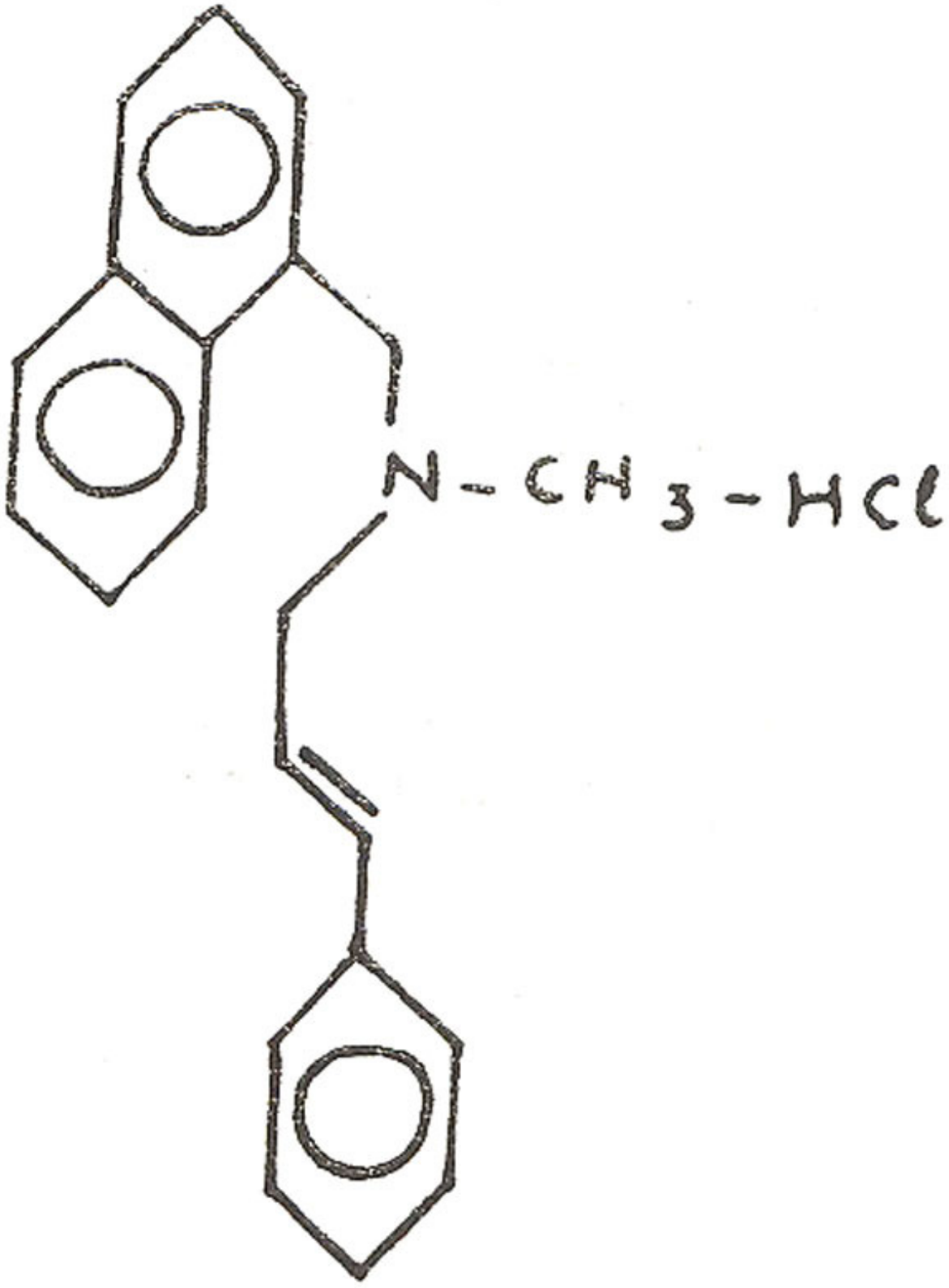
Both types of clinical materials were treated with 10% KOH Solution and observed under the microscope. The morphology of the fungus was recorded.

Culture

Skin scrapings and hair obtained from the patients were inoculated on mycobiotic agar (Difco Supplimentary Literature, 1962) and incubated at 32°C for one to three weeks. Clinical material showing no growth on mycobiotic agar after four weeks was discarded. Pure cultures of the aetiological agents were isolated and identified on the basis of colonical characteristics on mycobiotic agar (Difco), microscopic morphology and physiological characteristics. Nutritional media (Trichophyton agar No. 1-7 Difco) were also employed for identification of Trichophyton species. All those cases whose clinical material was negative for fungus microscopically and had negative culture were dropped from the study.

Results

Out of fifty cases, twenty were suffering from tinea corporis, sixteen from tinea capitis, eight from tinea cruris, one from tinea pedis, one from tinea manuum, and four from candidiasis.



Different species of dermatophytes isolated from the fifty cases included Trichophyton rub runt, Trichophyton violaceum, Trichophyton men-tagrophytes and Candida albicans. Details of these results are set out in Table I.

Table I: Dermatophytes Isolated from Patients

Dermatomycoses	*Trichophyton rubrum*	*Trichophyton mentagrophytes*	*Trichophyton violaceum*	*Candida albicans*	*Total*
Tinea corporis	14	2	4	Nil	20
Tinea capitis	1	Nil	15	Nil	16
Tinea cruris	8	Nil	Nil	Nil	8
Tinea pedis	1	Nil	Nil	Nil	1
Tinea manuum	1	Nil	Nil	Nil	1
Candidiasis	Nil	Nil	Nil	4	4
Total	25	2	19	4	50

Out of fifty cases treated with SN 105-843, thirty two (64%) were cured, fifteen (30%) improved. The types of dermatomycoses and their response to SN 105-843 are illustrated in Table II.

Table II: Vivo Effect of SN 105-843 on Patients Suffering from Various Types Dermatomycoses.

Dermatomycoses	*Cured*	*%*	*Improved*	*%*	*Side-effects*	*%*
Tinea corporis	19	95%	1	5%	Nil	
Tinea capitis	2	12.5%	11	68.75%	3	17.85%
Tinea cruris	7	87.5%	1	12.50%	Nil	
Tinea pedis	1	100%	Nil		Nil	
Tinea manuum	1	100%	Nil		Nil	
Candidiasis	2	50%	2	50%	Nil	
Total	32	64%	15	30%	3	6%

The duration of treatment of cured cases and their percentages are shown in Table III.

Table III: Duration of Treatment of Cured Cases

Treatment period	*Number of cured patients*	*% of cured patients*
2 weeks	1	06%
4 weeks	15	47%
6 weeks	12	38%
8 weeks	3	09%

Only 3 cases (6%) showed significant side effects in the form of intense burning which required interruption of therapy. Mild side-effects included burning, irritation, redness and dryness and these were observed in twenty-sevtn cases. These symptoms were tolerable, shortlived and reported only on direct questioning and did not require interruption in therapy. No subjective or objective changes of general condition were observed with the drug.

In the clinical symptoms the most dramatic changes were observed in exudation: drop from 30 to 0 cases in the first 2 weeks pruritus: drop from 49 to 26 cases within 2 weeks and to 9 cases upto week 8. erythema: drop from 36 to 20 cases within 2 weeks and to 3 cases upto week 8.

The remaining symptoms of desquamation, incrustation, vesiculation and pustulation were less frequently noted but also showed marked improvement.

The haematological studies of the patients before and after the treatment were compared, and no deviation from the prior values were recorded in any of the cases.

Discussion

Encouraging therapeutic results with SN 105-843 were obtained on patients suffering from various types of dermatomycoses. The drug" was found to be very effective on infections involving glabrous skin. Out of twenty cases of tinea corporis nineteen (95%) were cured, and out of eight cases of tinea cruris, seven (87.5%) were cured. Although both the cases of tinea pedis and tinea manuuni were cured by the drug, but their number is too small to be significant. Out of four cases of candidiasis two were cured and two improved. Again the number of cases are too few to derive any conclusive results. Out of sixteen cases of tinea capitis only two were cured (12.5%), eleven improved (68.75%) and three showed side effects (18.75%). The lower percentage of cured cases in tinea capitis is due to the fact that dermatophyte infections of the scalp usually needs a longer period of treatment. It is interesting to note that all the four cases of tinea corporis caused by Trichophyton violaceum were cured, while only two out of fifteen cases of tinea capitis caused by the same fungus were cured. This is because of low penetration of the drug on the scalp and endothrix infection of the hair coupled with sporolation of the

fungus. The local application of SN 105-843 on scalp infections in these cases, for eight weeks did not respond well due to inadequate period of treatment. There is every possibility that if the duration of treatment is prolonged the drug may give very effective and pronounced results.
Recurrence of the disease was not seen upto two weeks in any of the cured cases.
In conclusion, SN 105-843 1% Gel seems to be an effective and safe antifungal agent.

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