USE OF GRISEOFULVIN OTHER THAN ANTI-FUNGAL

By

D. N. MULAY, J. S. MEHEA, B. B. AHUJA & A. K. RAIZADA

Griseofulvin has been extensively used as an oral anti-fungal antibiotic. However during last few years, its action has been further studied on various other diseases both cutaneous and systemic. The chemical formula of griseofulvin is akin in structure to colchicin and was therefore tried in gout with moderate success (1960 & 1962). It is claimed that griseofulvin has an anti-inflammatory action and was tried in Shoulder Hand Syndrome[2] (1960). A decrease in the frequency of angina pectoris[3] (1963) within a few days of the administration of griseofulvin in all the ten cases was observed. The workers have ascertined that it was not a placebo effect.

Griseofulvin was given to one patient of syphilitic keratoderma[4] (1962) of palms and soles with certain amount of relief. It has been tried for psoriasis of nails[5] (1960) in eleven cases, out of which four showed some improvement and only one showed marked improvement. While treating a large number of cases with fungal disease, it was found that 43 patients had concomitant skin disease like icthyosis, sehorrheic dermatitis, pityriasis rosea, psoriasis, herpes simplex and herpes zoster and brittle nails[6] (1960). None of these diseases showed any improvement during the treatment with griseofulvin.

Griseofulvin was given to the patients suffering from porphyria cutanea tarda[7] (1966) and to the normal subjects as a control. Though the clinical menifestations were not aggravated, there was a significant increase in erythropoetic and hepatic porphyrins in both the patients as well as in the normal subjects. Griseofulvin was used on patients with herpes zoster with good results by two workers[8, 9] (1965).

We have tried giseofulvin in a group of patients suffering from psoriasis, vitiligo and herpes zoster. There are no references in the literature on the use of griseofulvin in psoriasis and vitiligo but because of the reports of its photosensitising action, we thought that griseofulvin might give favourable results like tolbutamide[10] (1963) in psoriasis and vitiligo.

MATERIAL AND METHODS

Our of 36 patients suffering from psoriasis 8 patients were given Griseofuivin (Grisovin) 125 mg. tablet in the dose of 2 tablets twice a day and 28 patients were given 2 tablets 3 times a day. Similarly out of 25 patients suffering from vitiligo, 16 patients were given 2 tablets of Grisovin twice a day and 9 patients were given 2 tablets 3 times a day for a period of $2\frac{1}{2}$ months. The minimum erythema dose (MED) of ultra violet rays (UVR) was determined prior to treatment and every 15th day during the period of treatment. The treatment was given for a period of $2\frac{1}{2}$ months. Administration of other photosensitising drugs was prohibited.

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RESULTS :

The percentage reduction in the MED was observed in all the cases.

Table 1.

Percentage reduction in MED of UVR

Disease	Total no of cases	Reduction less than 25%	25–49%	50–74%	75–100%
Psoriasis					
2 B. D.	8	1	4	3	Nil
2 T. D. S.	28	1	11	15	1
Total	36				
Vitiligo					
2 B. D.	16	3	6	7	Nil
2 T. D. S.	9	1	4	4	Nil
Total	25				

COMMENTS

Reduction in MED in majority of cases was about 50–75 percent. The improvement in the lesion of psoriasis was more marked on the exposed parts than on the unexposed parts.

Table 2.

Showing Percentage improvement in lesions of Psoriasis both on exposed and unexposed parts.

Sice of lesions	Total no. of cases	No impro-vemnt.	less than 25%	25–49%	50–74%	75–100%	No lesion on the unex-posed parts.
Exposed parts Dose of 2 T. D. S.	28	2	2	1	4	19	—
Grisofulvin 2 B. D.	8	Nil	Nil	1	2	5	—
Unexposed parts Dose of 2 T. D. S.	28	4	8	Nil	8	6	2
Grisofulvin 2 B. D.	8	3	1	Nil	2	1	1

In both the series of patients i. e. those who received a dose of 2 tablets thrice a day and those who received 2 tablets twice a day; the improvement in the lesions was more on the exposed parts than on the unexposed parts. Because the number of the patients who received 2 tablets twice a day (8 patients) is very small, the improvement in the lesions with this dose cannot be compared with the larger series of patients (28) with 2 tablets 3 times a day.

As far as the vitiligo is concerned, the results were as follows :

Table 3.

Percentage Improvement in the lesions of Vitiligo.

	No improvement	below 25%	25–49%	50–74%	75–100%	No lesion
Lesions on Exposed parts Dose of 2 B. D.	3	2	2	2	1	6
Grisofulvin. 2 T. D. S.	Nil	2	2	1	Nil	4
Lesion on unexposed parts Dose of 2 B. D.	5	3	2	3	Nil	3
Grisofulvin 2 T. D. S.	Nil	2	3	1	0	3

The improvement on the exposed parts is slightly higher than on the unexposed parts. The improvement with the dose of 2 tablets thrice a day (16) and 2 tablets twice a day (9) cannot also be compared because the number is unequal and the lesions on the exposed and unexposed parts were not present in all the patients.

DISCUSSION

Grisofulvin in both the diseases i. e psoriasis and vitiligo showed appreciable improvement. Though the etiology of both the diseases is not completely understood and the pathogenesis is different, it is known that the ultra violet has beneficial effect on both. Grisovin, it seems, acts due to its photosensitising activity. It is thought that grisofulvin affects the porphyrin metabolism and the uroporphyrins are detected in the urine. The photosensitivity is probably supposed to be due to the increase in uroporphyrin. But we could not detect the presence of uroporphyrins in the samples of our patients. The reduction in the M. E. D. in our series was less marked than in Tolbutamide. The dosage that we have given and the time limit of $2\frac{1}{2}$ months is probably not enough to give remarkable results. We have presented this pilot study and this needs further evaluation with larger number of patients and a long duration trial before its effect in psoriasis and vitiligo is properly assessed.

Lastly, we have tried grisovin in 19 patients suffering from herpes zoster. The patients came to us from 2nd to 8th day after the appearance of lesions though the majority of the cases attended the hospital within 2-4 days after the appearance of the lesions. These patients were given grisovin tablets 125 mg. 2 tablets thrice a day The patients were observed on alternate days and an assessment was done regarding the reduction in pain, appearance of new lesions, increase or decrease in the severity of already present lesions, disappearance of vesicles and erythema, complete healing and post herpetic neuralgia. The patients were not given any other local or systemic treatment such as lotio calamina, analgesics or injections of vitamin B_1 & B_{12}. Out of these 19 cases, 18 were male and 1 female. The age groups were below 25 year 6, 25-50 years 7, and above 50 years 6. None of the patients gave

history of contact with a case of chicken pox. During the same time, 11 patients were treated with novalgin as required for pain, lotion calamine, Injection B_1 100 mg. and Inj. B_{12} 100 ugs. daily for 10 days. The age group of the patient was upto 25 years 2 patients, 25–50 years 5 patients, above 50 years 4 patients. The patients presented pain, burning, erythema, vesiculation varying from mild to severe in both the groups. The results of the 19 patients on grisovin are as follows.

Table 4.

Presenting signs and symptoms of patients on grisofulvin.

	Mild	Moderate	Severe
Pain	3	8	8
Burning	6	8	5
Erythema	Nil	9	10
Vesiculation	1	2	16
Onset-Sudden-all cases			
Sex Male	Female		
18	1		

1 patient discontinued treatment from 3rd day and was lost for observation after that. None of the patients got new lesions after the start of the treatment. The observation on the 3rd, 5th and 7th day regarding pain, burning, vesiculation and ervthema is given below:

Table 5.

Improvement in subjective symptoms–total 19 patients.

Days	Pain	Burning	Erythema	Vesiculation
3	50%	50%	50%	25%
5	90%	90%	100%	100% No new vesicles
7	100%	100%	100%	100% No new vesicles

All the symptoms and signs regressed very rapidly and by 7th day the recovery complete and uneventful. No case reported for post herpetic neuralgia. The control group of patients has the following symptoms.

Table VI.

Presenting symptoms–control group

	Mild	Moderate	Severe
Pain	2	3	6
Burning	3	2	6
Erythema	1	3	7
Vesiculation	1	2	8

The improvement in the control group was as follows :

Table VII.

Improvement in control group.

Days	Pain	Burning	Vesiculation	Erythema
3	No improvement	No	No	No
5	2 cases improvement	No	No	No
7	2 cases reduced 25%	1 case	4 cases	5 cases
10	1 cases reduced	1 case	5 cases	3 cases
15	4 cases	2 case	2 cases	3 cases
Balance	2 cases	7 cases	Nil	Nil

In the control group the improvement was much slower, new lesions continued to appear after the institution of treatment upto the 5th day, the severity of pain reduced from 25–50% on 5th to 10th day in 5 cases only and upto 15th day in 4 cases and the balance of 2 cases persisted with post herpetic neuralgia. The vesiculation and erythema took longer period to disappear.

DISCUSSION

The mode of action of grisovin in herpes zoster is not fully understood but probably it acts as an antiinflammatory agent. The effect of grisovin was remarkable and dramatic in all the patients we have treated. A further trial of this drug on a larger series of patients is warranted and its exact mode of action needs to be determined.

CONCLUSION

A group of patients of psoriasis and vitiligo were treated with different dosage of griseofulvin administered for $2\frac{1}{2}$ months. The M.E.D. of U.V.R. was determined pre and post treatment. Grisofulvin showed moderate decrease in the M.E.D. in all the cases. The improvement in both the diseases was also moderate.

The control study in patients suffering from herpes zoster showed remarkable improvement in shorter period with the administration of grisovin. Further studies on a larger series to determine the exact mode of action of grisovin is suggested.

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