EFFECTS OF TOLBUTAMIDE ON VITILIGO AND PHOTOSENSTISING ACTION.

By

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In 1962, while treating a case of acne vulgaris with con-commitant vitiligo with tolbutamide (Rastinon) we observed that there was considerable improvement in the vitiligo patch. A search into the literature revealed that Inder Singh, Gaind and Ram (1961) had reported improvement with Tolbutamide in four cases of vitiligo.

Vitiligo is one of the cutaneous disorders commenly met with in Skin O. P. D. of any hospital in this country. The cause of this disease is obscure-genetic, enzymatic, auto-allergy and increased liberation of melatonin have been conjectured. Its treatment is also vague like application of stimulants/irritants, U. V. radiation and application and/or administration of Psoralen compounds to augment the effect of U. V. rays. This is all in the hope of stimulating melanocytes to produce increased pigmentation. Tolbutamides are sulphonylurea compounds and are derivatives of Sulphanilamide. They have no amino/group in the para position of Benzene ring and instead have a methyl group. With this chemical change in composition the tolbutamides have no antibacterial effect but have antihyperglycemic action

Photosensitivity to sulphanilamide has been demonstrated by Epstein (1939) Blum (1941), Fowlkes (1952) and Stratigo and Magnus (1968). Photosensitivity of the derivatives of sulphanilamide like chlore and hydrochlore-thiazide which are aromatic compounds of sulphanilamide were demonstrated by Harber et al (1959), Baer and Harber (1961) and Sams and Epstien (1967). Photosensitivity of carbutamide-sulphonyl urea derivative of sulphanilamide was reported by Burckhardt et al (1957) in their case. The photosensitivity of tolbutamide (Rastinon) was mentioned by Thambiah (1962) who hypothesized that cases of psoriasis improved due to the photosensitivity of tolbutamide and mimmick Goekerman's regime and rectify the enzymatic defects.

This paper deals with the effect of tolbutamide in the vitiligo patients and its photosensitising effect. The project was conducted in 3 stages :

Stage 1 : double blind study of tolbutamide and placebo in a group of vitiligo patients.

Stage 2 : study of photosensitivity effect of tolbutamide administered orally and the reduction in the minimum erythema dose of the U. V. rays in a group of patients with different cutaneous disorders, was determined.

Stage 3 : a group of vitiligo patients who were administered tolbutamide orally and the pigmentary effect of tolbutamide in vitiligo patients and reduction in erythema dose to U. V. R. was determined simultaneously and periodically.

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MATERIAL AND METHODS

The patients suffering from vitiligo who had not received any treatment for the malady were picked up at random from the skin and V. D. OPD of the Willingdon Hospital, New Delhi for this project.

Out of 100 patients selected for this project, a group of 50 subjects was given tablets A and another group of 50 subjects was given tablets B. Tablets A & B were alike in size shape and weight, the key to the code A & B was kept with the Pharmaceutical Co. which supplied us the tablets.

The tablet was 5 gm. each and was administered orally, one tablet twice a day after meals to the patients for 3 months. The patients were instructed not to take any other drug for any ailment without showing us the prescription. This was done to ensure that the patients did not take any photosensitising drug and other medicines which are likely to influence the pigmentation.

The size of the lesions was recorded in a proforma. The lesions which were irregular in shape were traced on a transparent paper. The patients were examined every 15th day and the size, shape of the lesions and the hyperpigmented spots appearing within the area of the lesion were recorded. The area of hyperpigmentation was thus on the proforma.

Out of 50 patients who were put on Tablet A 35 were observed for the complete period of 3 months and rest of them were lost from observation due to various causes, and out of 50 patients who were given tablets B, 40 were observed for the above period and 10 were lost due to various causes.

Table I

Showing effect of Tablet A and Tablet B on Vitiligo patients.

	Tablet A		Tablet B	
	Exposed	Unexposed	Exposed	Unexposed
No improvement	32	—	1	14
Slight improvement less than 25%	1	—	1	20
Moderate 25 to 50%	1	1	7	2
Marked above 50%	—	—	31	—
Total	34	1	40	36 (4 had no lesions on unexposed parts)

CONCLUSION

This evidently showed that tablet B was tolbutamide (Rastinon) and tablet A was a placebo, this was in agreement with the code kept with the company. It was thus concluded that the pigmentary effect of tolbutamide (Rastinon) was due to photosensi-

tivity since the repigmentation was present on the exposed areas in 40 cases. The tolbutamides activate and utilize the available U. V. rays in the nature. The lesions on the lips however were excluded while counting percentage of improvement.

Stage 2: In order to confirm the above conclusion that the tolbutamides produce their pigmentary effect due to enhanced absorption of U. V. rays availabie in the nature, a study was undertaken to estimate erytnema dose of U. V. rays before and after the tolbutamide therapy.

MATERIAL AND METHOD

48 cases attending skin & V. D. OPD of Willingdon Hospital, New Delhi regardless of sex and age, suffering from various cutaneous disorders as psoriasis acne and vitiligo were picked up at random for the project.

The minimum erythema dose (in minutes) was assessed exposing 1 sq. cm. area of the flexor surface of the forearm. The subsequent exposures were not given on the site once exposed. The patients were given 5 gm. tablets of tolbutamide (Rastinon) twice a day after meals. M. E. D. to U. V. light was asses ed every 15th day for 10 weeks.

The minimum erythema dose was 3–4 minutes in the majority (37 patients out of 48 patients) and the range was 2–16 minutes. 8 subject 8 had the M.E D. above 4 minutes and in one it was 16 minutes. 3 patients had M. E. D. less than 3 minutes.

Subjects were put on Rastinon and the M. E. D. was estimated after every 15th day. The reduction in the time was seen in almost all the cases as tabulated below. 5 subject could not be observed (2 discontinued after 15th day and 3 after $1\frac{1}{2}$ month) and they were not taken into account for final assessment.

Table 2

Showing percentage reduction in MED (in minutes) to U. V. rays with PL-7 Siemen's machine after Rastinon therapy.

Percentage reduction in Erythema dose	No. of patients
40 – 49	1
50 – 59	10
60 – 69	16
70 – 79	12
80 – 90	4
	43

CONCLUSION

The reduction was above 50 percent in 42 cases out of 43 cases. So it was concluded that the tolbutamides have the photosensitising property.

Stage 3. In order to correlate the above findings that the tolbutamides reduce the erythema dose and improve the vitiligo simultaneously.

MATERIAL AND METHOD

23 cases of vitiligo attending skin & V. D. OPD of Willingdon Hospital, New Delhi were picked up at random for this study.

The lesions were recorded and measured as explained in the material and methods of Ist stage.

The initial minimum erythema dose in minutes was determined in the manner as explained in Stage II.

The patients were given tolbutamide one tablet of 5 gm. B. D. after food and asked to report on every 15th day for assessment of M.E.D. and for observation of the conditions of the lesions.

OBSERVATIONS

The M.E.D. prior to therapy was two minutes to 18 minutes and the percentage reduction is shown in Table 3.

TABLE 3.

Showing percentage reduction In the minimum erythema dose after Rastinon therapy.

Reduction in percentage	No. of patients
Slight (less than 25)	2
Moderate (upto 50)	8
Marked (above 50)	13
Total..	23

The patients having the lesions on exposed parts were 20 out of 23. The patients having lesions on the unexposed parts were 12 out of 23. 8 patients had lesion on both exposed and unexposed parts.

The results were as follows:

Table 4

Percentage improvement in the pigmentation

	Lesions on Exposed parts	Lesions on Unexposed parts
	20	12
No improvement	4	6
Improvement less than 25%	3	2
Moderate upto 50%	11	3
Marked above 50%	2	1

ERYTHEMA DOSE IN MINUTES

S.No. of Patients	Prior to Treatment.	After 2½ months treatment with tolbutamide	Reduction in Erythema Time in 2½ months	Percentage of Reduction in Erythema dose	Percentage of improvement in exposed parts.	Percentage of improvement in unexposed parts.
1.	18	16	2	11.1	50	No lesion
2.	16	14	2	12.5	10	5
3.	15	10	5	33.3	No improvement.	No improvement.
4.	14	9	5	35.7	80	No lesion
5.	12	7	6	46.1	50	No improvement.
6.	13	8	5	38 4	No lesion	80
7.	11	6	5	45.5	25	No lesions
8.	10	5	5	50	25	No lesions
9.	10	6	4	40	50	5
10.	8	4	4	50	No lesion	50
11.	8	4	4	50	25	No lesions
12.	8	4	4	50	100	No improvement.
13.	7	3	4	57.1	25	No lesions
14.	7	3	4	57.1	5	No lesions
15.	7	4	3	42.8	No lesion	25 improvement.
16.	6	3	3	50	25	No lesions
17.	5	3	3	50	No improvement.	No improvement.
18.	5	2	3	60	No improvement.	No improvement.
19.	5	2	3	60	25	50
20.	5	3	2	40	No improvement.	No improvement.
21.	5	2	3	60	25	No lesion
22.	7	3	4	57.1	15	No lesion
23.	2	1	1	50	50	No lesion

CONCLUSION

The results show that there was more pigmentation on the lesions present on the exposed than on the unexposed parts. The M. E. D. of U. V. R. was reduced above 50 percent in majority of the cases (13 out of 23).

COMMENTS

It is clear from our double blind study that the tolbutamides have the pigmentary effects and confirm the findings of Inder Singh, Gaind and Ram. This effect was more marked on the exposed surface than the unexposed ones. This we thought was due to availability of U. V. rays in the nature.

The pigmentary effect of tolbutamide is due to photosensitivity. This property of photosensitivity has been mentioned by Burckhardt et al (1957) and Thambiah (1962). We have been able to demonstrate that there is marked reduction in erythema dose after the administration of tolbutamides.

We could not correlate the percentage improvement with the percentage reduction in the minimum erythema dose of U. V. R. Only 4 patients (i. e. case no. 5,9,12 & 23) could show this correlation. This is probably due to uncontrolled exposure to natural sun rays by the patients.

SUMMARY

1. The effectiveness of tolbutamides in vitiligo and its photosensitising capacity was investigated.

2. The project was divided into 3 stages. In the 1st stage the double blind study indicated the improvment in the lesion on exposed parts with tolbutamide (Rastinon) therapy and no improvement was obscured in those on placebo. In the 2nd stage the reduction in M.E.D. was demonstrated in 43 subjects. In the 3rd stage the pigmentation and simultaneous reduction in the M.E.D. was correlated.

2. The improvement in pigmentation observed in the exposed areas was marked as compared to the lesions on the covered (unexposed) areas.

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