A PILOT STUDY OF TAPAZOLE

A. R. Davison, M.R.C.S. England, L.R.C.P. London

Westfort Institution
Pretoria, South Africa

Tapazole (methimazole, Lilly) is indicated in the therapy of hyperthyroidism. Arturo O'Byrne ([2]) has reported on its use in leprosy, in patients not suffering from hyperthyroidism. A pilot study with this drug, carried out in the Westfort Institution between October 3, 1960, and December 4, 1961, is reported here.

PROCEDURE

Sixty lepromatous cases were selected and divided into three groups of 20 each. In the allocation to the groups, they were made practically identical. The following factors were considered: sex and age, weight, extent of lesions, bacterial index, and previous treatment.

Group A was the control group and received diaminodiphenyl sulfone (DDS) alone. The dosage was 100 mgm. daily. Seventeen cases completed the course.

Group B received DDS (100 mgm. daily) and Tapazole. Seventeen cases completed the course.

Group C received Tapazole alone. All 20 cases completed the course.

The dosage of Tapazole was 10 mgm. twice daily for the first three weeks, then 20 mgm. twice daily thereafter. No treatments were given on Sundays. During the months of July and August 1961, the treatment was interrupted because the available stock of the drug was exhausted. The actual time the patients were under treatment was therefore approximately one year. The male patients received the drug on 296 days, receiving a total of 11,480 mgm.; the females received the drug on 311 days, with a total of 12,080 mgm.

The patients were inspected clinically once each month, when skin smears from 4 sites were taken. White-cell counts and hemoglobin estimations were also done monthly. A close watch was kept for signs of myxedema, but this was detected (or suspected) in only one case.

Protein-bound iodine (PBI) and cholesterol estimations were done on 21 occasions on 15 patients. The PBI determination was done twice on each specimen submitted, and the examination was made on more than one occasion for several of the cases.

RESULTS

Protein-bound iodine and cholesterol.—The results of these determinations are shown in Table 1. It will be noted that the cases of the DDS group showed normal readings, but some extremely low readings were found in cases of the two Tapazole groups. The patients selected for the PBI examinations were random selections except for one patient whose speech was slow and another in whom myxedema was suspected. The patient with slow speech (No. 13990) gave a PBI reading of 4.5 mcg%, and cholesterol 185 mg%. The myxedema patient (No. 14033) at first gave a very low PBI reading, but 15 days later the figure was normal. The patient with low readings appeared to be doing as well

TABLE 1.—*Estimates of protein-bound iodine and of cholesterol in 15 selected cases.*

Case	Sex	Date	PBI	Cholesterol
Group A:				
14014	M	10/18/61	3.9 meg%	235 mg%
14052	M	11/11/61	5.4 meg%	130 mg%
14053	M	11/27/61	5.1 meg%	220 mg%
Group B:				
14033	M	3/9/61	0.4 meg%	220 mg%
14033	M	3/24/61	5.7 meg%	295 mg%
14033	M	9/7/61	3.7 meg%	235 mg%
14029	M	11/27/61	0.7 meg%	265 mg%
13990	M	4/22/61	4.5 meg%	185 mg%
13927	M	6/19/61	0.2 meg%	160 mg%
13927	M	9/7/61	3.4 meg%	212 mg%
13958	M	4/22/61	2.7 meg%	380 mg%
13958	M	6/14/61	0.8 meg%	260 mg%
Group C:				
14251	M	7/22/61	3.4 meg%	305 mg%
14159	M	5/17/61	1.6 meg%	170 mg%
14159	M	6/14/61	1.3 meg%	155 mg%
14067	M	6/19/61	0.5 meg%	245 mg%
13943	M	6/24/61	1.8 meg%	285 mg%
13923	M	4/17/61	0.6 meg%	345 mg%
13923	M	6/14/61	1.7 meg%	180 mg%
14150	M	10/13/61	4.3 meg%	185 mg%
14172	M	7/14/61	1.2 meg%	225 mg%

clinically as those with normal readings, so the result of the treatment was not affected. The low readings were not reflected in the final analysis.

Lesion index.— The lesion index is obtained by grading the extent of the infiltrations, the nodules and the plaques as 1+, 2+, or 3+. The sum of the lesions is the "lesion index." This index was calculated at the beginning and the end of the project.

Bacterial index.—Bacterial index is obtained by grading the degree of positivity of four skin smears from 0 to 4+ (1) and adding the totals.

Improvement.—The combined findings at the end of the period of experimental treatment were recorded as marked improvement, slight improvement, stationary (no change), or worse.

Table 2 shows the clinical and bacterial indices before and after treatment, in relation to the degrees of improvement, if any. It will be noted that the changes in bacteriology were slight, so that, in practice,

the final assessment depends largely upon the external appearances. The degrees of improvement were practically identical in all groups.

TABLE 2.—*Total lesion and bacterial indices, before and after the experimental treatment periods, in relation to the degree of clinical improvement.*

Improvement		Total lesion index		Total bacillus index	
Degree	Cases	Before	After	Before	After
Group A (17 cases)					
Marked	5	34	14	71	50
Slight	8	54	39	119	119
None	4	12	11	53	39
Group B (17) cases					
Marked	6	52	28	85	75
Slight	8	50	30	114	94
None	3	20	21	46	40
Group C (20) cases					
Marked	6	53	24	93	92
Slight	10	59	40	146	140
None	3	18	18	42	38
Worse	1	6	7	14	13

DISCUSSION OF THE GROUPS

Group A.—Reactional episodes of the erythema nodosum leprosum (ENL) type were marked in this group. Eleven patients developed it. The total degree of severity was rated at 19. Painful acute edema of the hands and feet developed in 6 cases.

Group B.—ENL was slightly less severe in this group. Ten patients developed it, and the severity rate was 13. Dermatitis developed in 2 cases. Slow speech developed in another case, and myxedema was suspected in still another.

Group C.—The experience of ENL in this group was similar to that in Group B. Nine patients developed it, and the severity rate was 12. Four patients developed transient dermatitis. One developed acute edema of the hand. One patient suffering from diabetes had inadvertently been included in this group, without detriment to him. One patient developed a leucopenia of 3,300 and was off treatment for a month. She ended up, however, among the "markedly improved" patients.

The white cell counts, the hemoglobin estimations, and the weights showed no abnormalities, so they are not discussed.

Bacteriology.—In the treatment of leprosy, the bacteriologic response is considered to be the only true yard-stick of the efficacy of

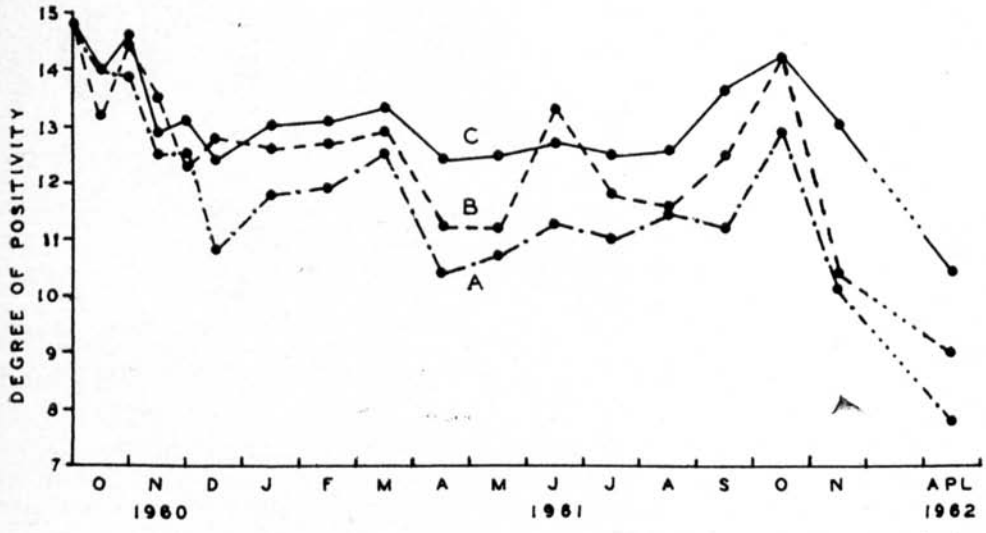

FIG. 1.—Bacillus indices of the three treatment groups on monthly examinations during the experimental treatment period, and (added) in April 1962. The black bar indicates the period (June 26 to August 28, 1961) when the administration of Tapazole was discontinued for lack of supply.

the medicament employed. To observe changes, smears were examined twice a month for the first three months, after that only once a month.

The somewhat extraordinary fluctuations in the monthly results, despite the fact that the same doctor made all of the examinations, are shown in Fig. 1. That graph shows that all the groups entered the project with a high degree of positivity, i.e., 14.8. The Tapazole group emerged at the end of the experimental period with a bacterial index of 13.0. The DDS group and the DDS-plus-Tapazole group emerged with indices of 10.1 and 10.4, respectively. From this it appears that, while Tapazole may not be inert in leprosy, it is not as efficacious as DDS.

SUMMARY

1. Three groups of 20 lepromatous patients each were treated by DDS, by DDS plus Tapazole, and by Tapazole alone.

2. Each group showed some clinical improvement.

3. The effect of Tapazole on the bacilli was not as marked as that of DDS. Adding Tapazole to DDS did not improve the efficacy of either drug.

It is concluded that DDS is superior to Tapazole for the treatment of lepromatous leprosy.

RESUMEN

1. Tres grupos, compuesto cada uno de 20 enfermos lepromatosos, fueron tratados con DDS, con DDS más Tapazol y con Tapazol solo.

2. Cada grupo reveló alguna mejoría clínica.

3. El efecto de Tapazol sobre los bacilos no fué tan destacado como el de DDS. La adición de Tapazol a DDS no realzó la eficacia de una u otra droga.

Se deduce que la DDC es superior al Tapazol para el tratamiento de la lepra lepromatosa.

RESUMÉ

1. Trois groupes, comprenant chacun 20 malades lépromateux, ont été traités par la DDS, par la DDS avec Tapazole, et par le Tapazole seul.

2. Dans chacun de ces groupes, une amélioration clinique a été notée.

3. L'effet du Tapazole sur le bacilles n'a pas été aussi marqué qu'avec la DDS. L'addition du Tapazole à la DDS n'a pas accru l'efficacité de l'un ou l'autre de ces médicaments.

On en conclut que la DDS est supérieure au Tapazole pour le traitement de la lépromateuse.

Acknowledgments.—Thanks are extended to Dr. P. L. Kurtz, of the Lily Research Laboratories, for the supplies of Tapazole used, and to the Department of Pathology, University of Pretoria, for making the determinations of protein-bound iodine. The Secretary for Health, Republic of South Africa, is thanked for permission to publish this report.

REFERENCES

1. Doull, J. A. Clinical evaluation studies in lepromatous leprosy. First series: Diasone (diamidin), 4,4′-diaminodiphenyl sulfone, dihydrostreptomycin. Internat. J. Leprosy **22** (1954) 377-402.

2. O'Byrne, A. Antithyroid substances in the treatment of leprosy. Internat. J. Leprosy **28** (1960) 401-407.

Addendum.—After the project period ended and the administration of Tapazole was discontinued, all of the groups were continued on the regular DDS therapy. Smears examined in April 1962 showed considerable reduction of the bacillus indices of all groups. These were—as is indicated in Fig. 1—Group A, 7.8; Group B, 9.0; and Group C, 10.4. The level of the Tapazole group at that time was still somewhat higher than that of the DDS group in November 1961.