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Controlled Long-Term Therapy of Leprosy with B663 (Lamprene, Clofazimine) Compared with DDS[1]

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In the working conference on B663 under the auspices of Geigy in London in 1968 (3), some investigators were of the opinion that the drug was comparable to DDS in effectiveness in the treatment of leprosy. However, this claim did not have the support of controlled studies, so no valid comparison was possible until such findings were available. The results of a controlled 48-week trial of B663 were published by us in 1971 (4), which served to indicate tentatively how effective B663 is in comparison to DDS. That study was continued for four years to enable us to report observations also on a long-term trial of the drugs, and to arrive at more reliable conclusions.

MATERIALS AND METHODS

The materials and methods of this study were described in our preliminary report (4), and need not be repeated here. Suffice it to say that periodic clinical examinations made by the principal investigator were now done every three months, instead of every month as previously, and the examinations for solid bacilli in the skin smears were discontinued as they were not found to be of value in our cases who had very low MI determinations to begin with.

RESULTS

Clinical improvement. Of the 43 patients originally qualified for this study, only 16 completed four years of treatment; nine patients under B663 and seven patients under DDS. Table 1 shows that all of the 16 patients treated with the two drugs were improved clinically in four years, a finding which suggests that B663 and DDS are about equally effective as antileprosy agents. However, it may be noted that under B663, one case was slightly improved, seven moderately and one markedly; while of the seven cases under DDS three were improved moderately and four markedly, so that there seems to be a slightly better clinical improvement of the group under DDS than that under B663, although again this advantage is not significant. These results, therefore, confirm our earlier finding after 48-week therapy, that the difference in the rates of clinical improvement in the two therapy groups was not significant.

Bacteriologic improvement. The average preliminary Bacterial Index (BI) of the nine patients in the B663 group (Table 2) was 4.8, and after four years of therapy this average dropped to 1.4, a reduction 3.6. Of the seven patients in the DDS group, the preliminary BI was 4.6, and after four years it became 1.8, a reduction of 2.8. While the reduction was greater by 0.8 under B663 than under DDS, the difference, as in our earlier report, is small.

TABLE 1. *Clinical improvement after four years of therapy.*

Therapy groups	Clinical improvement			Number of cases	Percent improved
	Marked	Moderate	Slight		
B663	1	7	1	9	100
DDS	4	3	0	7	100
Total	5	10	1	16	100

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Erythema nodosum leprosum. As a rule, *erythema nodosum leprosum* (ENL) occurs mostly in the first two years of therapy, and gradually decreases in incidence and severity in subsequent years as the basic leprosy infection progressively improves clinically and

TABLE 2. *Bacterial Index (BI) reduction after four years of therapy.*

Therapy groups	Number of cases	Bacterial Indices (BI)		
		Initial	After 4 years	Reduction
B663	9	4.8	1.4	3.6
DDS	7	4.6	1.8	2.8
Total	16	4.7	1.6	3.2

bacteriologically. Table 3 shows the findings respecting ENL in this study.

There were 6 of 16 cases, or 37.5%, under B663 and 11 of 16 cases (68.8%), or almost twice as many, under DDS who developed ENL in the first year of therapy. No new case under B663, but two under DDS developed this reaction in the second year, and none thereafter under either drug. However, some of those who had ENL in the first year continued to have it for some time, so that in the fourth year there were three under B663 and two under DDS who still had occasional reactional lesions.

It can also be seen in Table 3 that there were no severe cases of ENL in the B663 group during the entire four years of observation, while under DDS there were five in the first year, four in the second year and two in the third year of therapy. It is, therefore, evident that ENL reaction was not only more frequent but also more severe under DDS than under B663.

Skin pigmentation. Pigmentation of the skin occurred in patients treated with B663 but not with DDS. It appeared as early as the first week of therapy in some patients, but in general it developed after two to four weeks and reached maximum intensity in six to twelve months. While in some cases pigmentation developed all over the body, in others it was limited only to the leprotic lesions, such as thick infiltrations, plaques and nodules.

As a rule, cases with slight to moderate pigmentation in the first year did not become more intensely pigmented in subsequent years, although they continued taking B663 in the same dose. There was one, for example, who was only slightly pigmented throughout the four years of therapy, and one who was slightly pigmented for one and a half years but subsequently the pigmentation disappeared although he did not stop treatment.

Resistance to treatment. There has been no occasion for us to observe a case whom we considered to have developed resistance either to B663 or to DDS in this study. All our cases have shown satisfactory clinical and bacteriologic improvement. One who was only slightly improved in four years of B663 therapy had a prolonged and moderately severe ENL reaction which continued up to the fourth year when the reaction became mild. Our results do not support the early

TABLE 3. *Incidence and severity of ENL under B663 and DDS therapy.*

Therapy and year of observation	*Erythema nodosum leprosum*				
	Severity			Incidence	
	Severe	Moderate	Mild	Total number of cases	Percent of ENL cases
B663					
First year		1	5	16	37.5
Second year		4	2	16	37.5
Third year		2	2	10	40.0
Fourth year			3	9	33.3
DDS					
First year	5	4	2	16	68.8
Second year	4	5	3	15	80.0
Third year	2	1	3	9	77.7
Fourth year			2	7	28.6

finding of Browne *et al* ([1,2]) that, given alone, B663 appeared to cause a form of drug resistance in *M. leprae*.

Drug toxicity. No toxic reactions worth reporting were observed with either drug, except for the skin pigmentation seen with B663. There was no occasion in which treatment had to be suspended because of untoward reactions.

SUMMARY

The results of our controlled clinical trial with B663 in the treatment of lepromatous leprosy for four years confirm our earlier findings and the observations of other workers who based their opinions on uncontrolled clinical trials, that B663 is comparable in efficacy and safety to DDS in producing clinical improvement and in reducing the BI of the skin smears. It has also the advantage of having less frequent and less severe cases of ENL among patients treated with it than those treated with DDS.

RESUMEN

Los resultados de nuestra experiencia controlada para el tratamiento de la lepra lepromatosa con B663 durante cuatro años, confirman nuestros hallazgos preliminares y las observaciones de otros investigadores que basaron su opinión en experiencias clínicas no controladas, de que el B663 es comparable en eficiencia y seguridad al DDS para producir mejoría clínica y para reducir el IB en los extendidos de piel. También tiene la ventaja de producir casos menos frecuentes y memos graves de ENL entre los pacientes que se tratan con esta droga que en los pacientes que se tratan con DDS.

RÉSUMÉ

Les résultats de l'essai clinique contrôlé avec témoins, de traitement de la lèpre lépromateuse par le B663, mené sur une période de quatre ans, ont confirmé les observations antérieures, de même que les résultats d'autres chercheurs qui ont basé leur opinion sur des essais cliniques non-contrôlés, à savoir que le B663 est comparable en efficacité et en tolérance à la DDS, produisant une amélioration clinique et réduisant l'indice bacillaire dans les prélèvements cutanés. Ce produit a également l'avantage d'entraîner une incidence plus faible, ainsi qu'une moindre gravité de l'érythème noueux lépreux, parmi les malades traités, par comparaison avec les sujets recevant de la DDS.

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