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Autor: Devadason, Chinnadurai
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Miscellanea

B. 663 (Geigy 30.320) in the Treatment of Leprosy

A Preliminary Report

CHINNADURAI DEVADASON
Rajah Charles Brooke Memorial Hospital [1]
Kuching, Sarawak, Malaysian Borneo

Leprologists throughout the world have been confronted with patients with severe reactions for which no definite or specific therapy is available. From analgesics to antimony preparations including anti-malarial drugs have been used with partial or no response. There are, however, a certain number of patients who do not respond to the usual anti-reaction regimes and the physician has to resort to the administration of corticosteroids. The use of steroids brings about effective and immediate improvement in the condition of the patients but carries with it the danger of long-term steroid therapy. Some patients become so dependent on corticosteroids that withdrawal or even lowering of the dose precipitates an attack of erythema nodosum leprosum (ENL).

Recent experiences in other parts of the world have indicated that a new drug, a phenazine derivative called B. 633 (Geigy 30.320)-3-(p-chloranilino)-10-(p-chlorphenyl)-2 (isopropylimino)-phenazine, is effective in the treatment of mycobacterial diseases including leprosy. This drug manufactured by GEIGY of Switzerland was acclaimed as exerting a possible anti-inflammatory effect in addition to its anti-bacterial property, on patients with chronic reaction or those prone to reactional episodes. Many authors have suggested that B. 663 helps in the management of reactions in leprosy patients and that the only known side-effect was the discolouration of the skin.

Through the generosity of J. R. GEIGY S.A. of Switzerland a supply of the drug was made available in 1967 and eight patients were included in this trial group.

The obvious choice was those A. who were suffering greatly with reactions, B. who had painful neuritic conditions and C. who were cases of untreated lepromatous leprosy. At the time of initiating the study, we were able to have 3 patients under group A, 3 under B, and 2 under C.

Groups A and B were essentially corticosteroid dependent and we wanted to examine if B. 663 would exert any anti-inflammatory effect and thus replace corticosteroids. Group C was included to study the anti-mycobacterial effect of this new drug.

When this report is being prepared, groups A and C had B. 663 for a period of six months while group B has completed four months of therapy. When treatment with B. 663 was started all other anti-leprosy drugs and anti-inflammatory drugs (Prednisolone) were stopped completely. Supportive treatment with iron, multivitamins and in two cases, blood transfusions were given. Monthly haemoglobin estimation, urinalysis and skin smear examination were carried out. In addition, the weight of the patient was recorded monthly.

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[1] Combined leprosarium for the three states of Sabah, Sarawak and Brunei.

The clinical summary and therapeutic details are as follows:

Group A

Group A, 1. Patient L. B. K. Case No. D. 794. 29-year-old male Indonesian from Sabah was admitted in July 1967 as a case of lepromatous leprosy with chronic ENL. BI [2] was 5 + on admission and the entire body surface was covered with ulcerated ENL. He responded initially to a course of Streptomycin and INAH but the reaction never totally subsided. At the time of treatment with B. 663 the ulcerations had reappeared and there was deterioration in the general condition, the patient being continuously febrile. B. 663 was given in a dose of 200 mg daily and there was dramatic improvement, clinical, bacteriological and emotional within the first two weeks. Pigmentation was marked in three months and patient had a black hue. The BI remained at 4 + but MI [3] was negative for solids in eight weeks. The ulcerations healed very quickly and the general health of the patient improved within the first two weeks. During the third month of therapy, morphologically normal *M. leprae* reappeared in the smears but cleared by the fifth month with no alteration or addition in therapy.

There was, however, a sudden episode of reaction at the end of five months and B. 663 was increased to 300 mg daily in addition to other supportive measures. While the patient was showing signs of improvement, death came suddenly possibly due to myocardial infarction.

Group A, 2. Patient J. B. K. Case No. M. 222. 28-year-old Indonesian from Sabah. He had spent three years in the hospital wards with recurrent and relapsing episodes of reactions, responding only to Prednisolone at a dose of 20–40 mg daily. Clinically he was BL/LL with an average BI of 3 +. MI was negative for solids. Three weeks after treatment with B. 663, there was marked clinical improvement in his general condition and this was maintained. At the end of six months the average BI was 1 + and MI negative for solids. A dose of 200 mg of B. 663 seemed sufficient. Patient was cheerful and happy and was able to sit up and walk after three years in bed. There was weight increase but the fall in his haemoglobin had to be corrected with blood transfusions twice. To our surprise a fresh episode of ENL appeared in May 1968 and B. 663 was increased to 300 mg daily in addition to analgesics and antipyretics. There was transient improvement but after four weeks, fresh lesions and ulcerations appeared and this warranted interference with Prednisolone. Signs of reaction subsided after two weeks and patient was maintained with 10 mg of Prednisolone daily in addition to B. 663. There was increasing pigmentation during the first four months but later the colour of the skin remained static. No other side effects.

Group A, 3. Patient R. L. Case No. C. 572. This young Chinese lady of 28 has been a patient here since 1965. Clinically she was a case of lepromatous leprosy. During the years she has suffered greatly with reactions and had to be frequently hospitalised for careful management. She was comfortable with a maintenance dose of Prednisolone (5 mg) and this dosage had to be frequently raised in order to avoid a fresh attack of reaction. When B. 663 was started the BI was 1.5 + and MI 50% fragmented. At the end of six month period the BI is 1 with an MI of 100% fragmentation. During the therapy there was increase in weight

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[2] The bacterial index has been assessed according to Ridley's logarithmic scale from 1 to 6.

[3] The morphological index is the percentage of solid and deeply staining organisms on the smears.

and the patient appeared cheerful — though being very conscious of increasing pigmentation. A dose of 100 mg seemed adequate and the pigmentation was uniformly pinkish — thus rendering the patient more presentable than before.

She had persistent complaint of giddiness and upper abdominal discomfort, for which no cause was established and no specific treatment given. Reassurance and encouragement proved sufficient. The patient's improvement and absence of reaction culminated in her marriage in July this year.

The above three patients with a history of chronic reactions have shown varying response to treatment with B. 663. While there was undoubted improvement, a dose of 300 mg was not sufficient in the first two cases. The second patient either became refractory to B. 663 or interference with an increased dose of B. 663 was a little too late that we could not effectively prevent a fresh reaction state. Response has been consistently good in the case of the Chinese girl. The anti-inflammatory effect of B. 663 is obvious but the dose required to suppress has to be established after longer periods of trial. While the anti-bacterial dose seems to be low, the anti-inflammatory dose seems to vary with each patient. In our experience pigmentation due to B. 663 was not a major problem nor did this factor stand in the way of acceptance. The pigmentation seems to vary according to the racial origin of the patient and the dose of drug administered. The anti-inflammatory property of B. 663 needs to be evaluated further though the property is not in question. The effective period of the drug and possible resistance to B. 663 need to be studied in detail.

Group B

Group B, 1. Patient W. S. Y., female Chinese 23 years. Case No. C. 589. This young girl was treated with B. 663 200 mg daily as she had a large painful right median nerve with few ENL lesions in the arms and legs. Eight weeks of B. 663 brought great relief from nerve pain and ulcerated lesions. Patient was very cheerful and put on weight. Patient was able to do away with Prednisolone on which she was dependent for relief from pain and suffering. Pigmentation was the only side effect but not of great significance after four months of treatment with B. 663.

Group B, 2. Patient L. B. L., male, 47 years. Case No. M. 161. This Indonesian patient from Sabah had a tender fusiform swelling of the right ulnar nerve and was free from symptoms only with the administration of Prednisolone. 200 mg of B. 663 was sufficient to relieve the pain and reduce the nerve swelling without any neurological deficit. His BI and MI were always negative. Pigmentation was not pronounced as the patient was basically dark skinned. With B. 663 no further episodes of neuritis was encountered during the past four months.

Group B, 3. Patient L. K. F., a 21-year-old Chinese girl who had lepromatous leprosy, was suffering from recurrent episodes of reaction with painful ulnar nerve. Prednisolone had to be administered to relieve the pain in the nerves. She was given B. 663 100 mg daily and the symptom of pain was no more in two weeks. The nerves were no more swollen or tender and her general condition improved very much and the sad-looking patient was made cheerful and relieved of her suffering. Pigmentation conferred a deep red colour but not as intense as in other patients.

In our brief experience in the treatment of nerve swellings with B. 663, we have had very satisfactory and encouraging results. We were able to withdraw Prednisolone completely and an average dose of 100 mg of B. 663 was sufficient to prevent acute neuritic conditions. The relief from this painful condition brought great relief to the patient and helped in the improvement of the mind and the body.

Group C

Group C, 1. Patient K. B. J. Case No. M. 250. This middle-aged Javanese patient was admitted as a case of untreated lepromatous leprosy with a BI of 4+ and MI 60% fragmented and 40% solids. He was essentially a dark skinned man and a dose of 300 mg of B. 663 turned him pitch dark in eight weeks so that we decided to lower the dose to 200 mg. Solid form of bacilli cleared from skin smears in four weeks and at the end of six months his BI was 2+ with MI 100% fragmented. No side effects other than intense pigmentation.

Group C, 2. Patient Y. N. P. Case No. C. 619. On admission in November 1967 this young boy of 11 was a case of lepromatous leprosy with tender ulnars. He had marked infiltration of the ear lobes and eyebrows. His skin smear was 80% solids to 20% fragments with a BI of 6 on admission. He was given 100 mg of B. 663 and in two weeks the ulnar neuritis disappeared. Pigmentation was obvious in four weeks but he had no other systemic side effect. By four months the MI was negative for solids and the boy tolerated the drug very well. Pigmentation was pronounced by sixteen weeks but the patient cooperated well in continuing the drug. No signs of any drug resistance was encountered.

The anti-mycobacterial property of B. 663 was not in question and our experience confirms the impressions elsewhere that this drug is effective against *M. leprae*. The total duration of treatment and the least effective dose are to be established after more detailed study. Effective fragmentation of the bacilli within four months was an indication that B. 663 would be a very useful and effective anti-leprosy drug.

Conclusion

The experiences with B. 663 at the R.C.B.M. Hospital during the past six months indicate that B. 663 possibly exerts an anti-inflammatory effect on patients with chronic reactions. The dose required to suppress an episode of reaction and in the maintenance of a no-reaction state seem to vary greatly and it is our impression that each patient needs to be evaluated separately. An average of 200 mg seems adequate but further observations are necessary. There may, however, be cases of ENL that either do not respond to B. 663 or become refractory after a period of therapy.

B. 663 definitely has a place in treating nerve swellings that accompany neuritis. B. 663 effectively controls the swelling as well as relieves the pain and discomfort of the patient. We had convincing experience that patients with neuritis respond very well to B. 663.

In our limited experience we were able to evaluate favourably the effect of B. 663 in cases of untreated lepromatous leprosy. Pigmentation is a side effect and cosmetically objectionable. We could not, however, assess if B. 663 would prevent reaction in patients who are prone to this syndrome.

We confirm the reports in other parts of the world that the major side effect is the deep pigmentation. We have had patients from many racial groups and not all of them necessarily get hyperpigmented. While 300 mg daily confers a very deep pigmentation, a dose of 100 mg seems to render the skin uniformly stained, thus in fact improving the "look" of the patient. This fact of pigmentation with B. 663 was not an obstacle in the acceptance of patients who desired recovery from pain, ulcers and suffering. It has been reported that pigmentation is temporary and that it is a reversible change. We are awaiting answer in this direction and if this be true, there would be no difficulty in asking patients to

accept this drug to tide them over the crisis that they encounter in the course of treatment for leprosy.

It is our impression that there is a place for the regular use of B. 663 in leprosaria both to treat patients with chronic reaction and to evaluate the optimum dosage that would give maximum clinical improvement.

It must also be added that patients under therapy with B. 663 appeared cheerful and relieved. We could not say if this was due to any euphoric effect of the drug or whether this was because of the general well-being, free from further pain and suffering.

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References

AHRENS, TH. Personal communication

ATKINSON, A. J., SHEAGREN, J. N., BARBA RUBIO, J. & KNIGHT, V. (1967). Evaluation of B. 663 in human leprosy. — Int. J. Leprosy *35,* 119-127

BROWNE, S. G. (1965 a). B. 663 – Possible anti-inflammatory action in lepromatous leprosy. — Leprosy Rev. *36,* 9-11

BROWNE, S. G. (1965 b). Treatment of leprosy with B. 663. Appraisal of pilot trial after three years. — Leprosy Rev. *36,* 13-15. Abstract by J. R. Innes, Trop. Dis. Bull. *62,* 422 (1965)

BROWNE, S. G. (1965 c). Red and black pigmentation developing during treatment of leprosy with "B. 663". — Leprosy Rev. *36,* 17-20

BROWNE, S. G. (1966 a). B. 663 (Geigy) – Further observations on its suspected anti-inflammatory action. — Leprosy Rev. *37,* 141-145. Abstract by J. R. Innes, Trop. Dis. Bull. *63,* 1344 (1966)

BROWNE, S. G. (1967). The transient reappearance of morphologically normal *M. leprae* in patients under treatment. — Leprosy Rev. *38,* 82-86

BROWNE, S. G. & HOGERZEIL, L. M. (1962 a). B. 663 in the treatment of leprosy. Preliminary report of a pilot trial. — Leprosy Rev. *33,* 6-10. (Ref. in Practitioner, May 1962)

HASTINGS, R. C. & TRAUTMAN, J. R. (1968). B. 663 in lepromatous leprosy. Effect in erythema nodosum leprosum. — Leprosy Rev. *39,* 3-7

PETTIT, J. H. S. (1967). The treatment of erythema nodosum leprosum with B. 663. A controlled study. — Int. J. Leprosy *35,* 11-16

PETTIT, J. H. S., REES, R. J. W. & RIDLEY, D. S. (1967). Chemotherapeutic trials in leprosy. Pilot trial of rimino-phenazine derivative. B. 663 in the treatment of lepromatous leprosy. — Int. J. Leprosy *35,* 25-33

WARREN, A. G. (1968). A preliminary report on the use of B. 663 in the treatment of Chinese leprosy patients with chronic reaction. — Leprosy Rev. *39,* 61-66

WILLIAMS, T. W. et al. (1965). Experience with B. 663 in the treatment of leprosy. — Int. J. Leprosy *33,* 767-775