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Short-course multi-drug therapy for paucibacillary patients in Guyana: preliminary communication

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As from 1 December 1981 the WHO short-course multidrug regimen[1] was introduced into the Guyana Hansen's Disease Control Programme. It is too early yet to review results of treatment of multibacillary patients but this preliminary report describes the progress of 303 paucibacillary patients who had completed treatment by 31 May 1983.

Previous management of paucibacillary patients

Prior to December 1981, paucibacillary patients were treated with dapsone monotherapy (100 mg daily) until clinically inactive and, thereafter, maintained on dapsone at full dosage for periods ranging from 2 years for TT to 5 years for BT patients. About 30 patients were released from treatment annually until 1981 when 64 patients were released from control. Relapses were not seen. Patients attended the clinic monthly at first and subsequently every 2–3 months.

New treatment regimen

All patients moved on to the new regimen at their next, routine clinic appointment after 1 December 1981 so that by the end of February 1982 most of the paucibacillary patients remaining in touch were on a regimen consisting of a single, monthly dose of rifampicin 600 mg plus dapsone 100 mg given under supervision at clinic, together with a daily dose of dapsone 100 mg to be taken at home. Although not specifically advised in the WHO study, it has been found important, for psychological reasons, that a dapsone tablet is given under supervision along with the rifampicin at the monthly clinic. Otherwise there is a

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danger that both patients and staff will underestimate the value of dapsone and conclude that because of the emphasis given to them, only the coloured capsules are essential for cure.

Evaluation

In evaluating this field trial of a new treatment regimen the following points were considered: Is the treatment acceptable to patients? Is the treatment acceptable to and manageable by the nursing staff? Are results comparable with those previously obtained? Are there unacceptable side-effects or unacceptable reactions?

Patient appeal

Patients definitely prefer the new regimen. Much time was spent explaining it to each patient and their very positive response is reflected in the small number of missed appointments—only 8% having to extend their treatment period over a seventh month because of a missed, single dose of rifampicin (a further 4% missed more than one appointment). It had been anticipated that the biggest problem would be the provision of support for patients anxious to continue treatment because of the presence of incompletely resolved lesions. However, this did not prove as big a problem as had been anticipated. Extra time was spent in counselling these patients and they were assured that they could attend clinic whenever they wanted to. The only patient who needed further support was a young man who became inappropriately worried over a few, faint stains sometime after his very obvious facial BT lesions had faded. It subsequently transpired that he was planning to emigrate.

Acceptable by nursing staff

The necessity for all patients to attend clinic monthly produced a rise of 120% in the number of patients seen at clinic in 1982. This tremendous increase in workload was cheerfully accepted by the clinic nurses once they understood the reasons for the change. As we move through 1983/84, many multibacillary patients will come to the end of their treatment and we shall move onto surveillance with a reduction in the clinic workload.

Results

Patients can be grouped into those who were active at the start of the new

treatment and those who were already inactive but who had not yet completed the previously accepted norm of post-activity treatment. As expected, the latter remain inactive but will be under surveillance for a minimum of 2 years. Active patients can be divided into TT and BT groups, the former consisting of patients with either a single macule or a single enlarged nerve. These TT lesions have either cleared completely or continue to regress at a satisfactory rate. No relapses have been seen so far. Active BT lesions, as expected, have taken longer to resolve but most continue to improve steadily. Two patients have presented as relapses—both within 8 months of completing treatment. One is a women in her mid-seventies and the other a teenage girl who became pregnant and in whom there was certainly an inadequate drug intake. These figures give a relapse rate of 1% of 192 BT patients at risk.

Side-effects

Rifampicin is given as near to the monthly due date as possible so as to avoid the well-documented dangers of too closely spaced, intermittent rifampicin. In fact only one patient was adversely affected by this drug. A middle-aged woman (TT) experienced a typical cutaneous syndrome[2] with an irritating erythematous and oedematous rash developing over face, scalp and neck about 1 hour after rifampicin. She was given an oral antihistamine and the rash gradually subsided over the next hour. As this patient was inactive and already within a few months of completing the normal span of dapsone monotherapy she was removed from the project and completed her treatment on dapsone alone. Later in the year a young woman with multibacillary disease (this group will be reported in a later publication) experienced a similar rash—beginning with an intense irritation of the palms and developing into a maculo-papular rash of small urticarial-type weals distributed mainly over the upper half of the body and most thickly over the head and neck. As with the previous patient the rash settled with re-assurance and antihistamine alone. There is no doubt that these rashes must be attributed to rifampicin as they were identical in type, no other drugs were being taken and in the second patient the rash recurred on challenge with rifampicin alone. It has been possible to desensitize this patient[3] and she has continued her treatment without mishap.

Type I reaction

Three instances of Type I reaction[4] occurred in BT patients during the period under review. All three patients already had a moderately severe reaction on diagnosis—there were no instances of reaction occurring in patients who were reaction-free at diagnosis. The reactions were handled in a routine manner and

did not present any unusual difficulties. Clinical details of the first case are as follows (the other two patients are still undergoing treatment and will be described in a later publication). Reaction involving large skin lesions scattered over body recurred after changing to the new regimen but settled under prednisolone without nerve damage. The presenting reaction had fluctuated over the previous 9 months' treatment but was reasonably well controlled at the time of the change. Chemotherapy was continued throughout and for 6 months after withdrawal of prednisolone. There is nothing to indicate that the use of rifampicin contributed to the severity of this reaction. We have seen equally severe reactions developing with patients on dapsone monotherapy. In this respect it is particularly interesting that no reaction occurred except in those patients who were already reacting on presentation and, so far, no reaction has been seen in any patient after completion of treatment.

Patients taking alternative therapy

During the 18 months under review there were three patients who failed to complete the recommended monotherapy. (i) The middle-aged woman with a cutaneous syndrome reaction to rifampicin (see above), who completed her treatment on dapsone monotherapy. (ii) A teenaged boy with an indeterminate facial lesion who developed infectious mononucleosis (not a dapsone drug reaction) after 6 months on dapsone monotherapy. On recovery he refused dapsone but agreed to take thiambutosine. When the programme changed to dapsone and intermittent rifampicin this patient received thiambutosine and intermittent rifampicin, as he remained unwilling to take dapsone. (iii) A young woman with very early BT lesions developed an extensive, irritating papular rash 2 weeks after starting treatment. The rash settled with corticosteroid ointment and an oral antihistamine but recurred with her second month's treatment, accompanied by facial oedema which required prednisolone for control. Challenge with rifampicin alone was uneventful but challenge with dapsone produced severe facial oedema. Daily dapsone was, therefore, replaced by daily clofazimine 50 mg but the patient subsequently refused this on the grounds of 'skin irritation'. Challenge did not support this complaint but as the patient had had a very uncomfortable experience it was thought wiser to maintain her on monthly, supervised drugs only—rifampicin 600 mg together with clofazimine 300 mg.[5] No further adverse effects were noted and the patient was on the verge of inactivity on completing treatment.

Discussion

Two hundred and forty-six of the 303 patients under review completed treatment

during 1982 and 57 during the first 5 months of 1983. It is certainly too soon for a comprehensive review of results but on the evidence available so far the WHO recommendations for paucibacillary patients are effective. There have been neither relapses nor reactions among three indeterminate (I) and 108 TT patients at risk and a relapse rate of 1% amongst the 192 BT patients is acceptable. However, these 192 patients include many who had already had some previous treatment and it is possible that the relapse rate may rise in the future when all patients are 'new' patients.

The crucial factor here is surely time. The earlier the treatment is given the lower the incidence of reactions, nerve damage and relapse—and conversely, the longer treatment is delayed the more likelihood there is of complications. The identification of early cases is, therefore, a matter of the highest priority. The introduction of a short-term treatment regimen for paucibacillary patients has reduced our gross caseload in Guyana to below 60% of its previous level. This gives us valuable time in which to expand and to concentrate on health education and contact tracing in a determined effort to reach more patients and to treat them earlier in the course of their illness. Experience so far suggests that there is no need to fear that patients released from treatment will not report back on deteriorating; on the contrary, patients frequently return for treatment of incidental skin complaints and for reassurance where macules, though fading, are still present. Perhaps one of the most important benefits to be expected from the new regimen is that the release of large numbers of satisfied patients, after such a relatively short period of treatment, will have a tremendously beneficial impact on case finding. A further account of progress in the treatment of paucibacillary, and also multibacillary cases, will be published later.

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