Effect of Prophylactic Corticosteroids on the Incidence of Reactions in Newly Diagnosed Multibacillary Leprosy Patients

TO THE EDITOR:

Leprosy reactions, including reversal reactions and episodes of neuritis, are known to occur in leprosy patients most frequently in the first few months after starting multidrug therapy (MDT), especially in cases with multibacillary (MB) disease([2, 5, 7, 8, 10, 12]). Such reactions can lead to impairment of nerve function, and subsequent deformity and disability. That this can occur in leprosy patients who present without any nerve function impairment (NFI) at diagnosis is a discouraging phenomenon for both the patient and the doctor or health worker.

It is an axiom of modern leprosy control that early case detection and treatment with MDT can prevent much NFI by halting the multiplication of the leprosy bacillus, and that this is the single most important activity in the prevention of NFI([9]). So far, little attention has been focused on the prevention of NFI after starting MDT, although there is some evidence that clofazimine has a prophylactic role in preventing type 2 reactions([6]) and even reversal reactions([1]). It is generally accepted that corticosteroids are an effective treatment for reactions, and that they may reverse the effects of nerve damage([3, 4]). Since this is the case, can they also be used to prevent reactions if given prophylactically at the time of registration and commencement of MDT?

The incidence of reactions after the start of MDT is known to be higher in MB patients than PB([11]), with around 30% of MB patients experiencing a leprosy reaction after treatment commences. We felt that a reduction in the proportion of MB patients experiencing a reaction by about 50% would be a worthwhile result, and may be widely applicable for leprosy treatment. We decided to conduct an uncontrolled study to investigate the hypothesis that prophylactic corticosteroids can prevent the occurrence of reactions in newly diagnosed MB leprosy patients.

The study was based at the Danish-Bangladesh Leprosy Mission (DBLM) in Nilphamari, Bangladesh. DBLM operates a vertical leprosy program and has a field-based system of treatment of leprosy reactions([4]). A prospective cohort study was started there in 1995 to investigate the epidemiology of NFI in leprosy patients, the Bangladesh Acute Nerve Damage Study (BANDS). This study has recruited 2664 new leprosy cases who are being regularly followed up for signs of reaction and NFI. It was decided to use MB patients from among the BANDS cohort to act as historical controls in this trial.

The selection criteria for including patients in the treatment group and the control group were as follows: MB classification (>5 skin lesions and/or skin-smear positive); no acute reaction present at diagnosis needing treatment; age 15–50; weight >35 kg; not pregnant; no contraindications to prednisolone. In addition, informed, written consent was obtained from patients receiving prophylactic corticosteroid treatment.

Ninety-two new MB leprosy patients fulfilling the above criteria were recruited into the study during a 10-month period from May 1997 to February 1998. These patients were given prednisolone 20 mg/day for 3 months, tapering to zero in the fourth month. Patients were normally recruited at registration, and given their first dose of prednisolone at the same time as their first MDT dose. However, a few cases initially classified as PB were reclassified as MB when their skin smears were found to be positive. These cases were included in the study if their prednisolone was started within 2 weeks of their first MDT dose.

All patients were followed up monthly with sensory testing using a ballpoint pen applied to 12 standard points on each palm and 11 on each sole, and Medical Research Council (MRC) motor strength testing to one movement of each of the facial, ulnar, median, radial and lateral popliteal nerves. The trial outcome was defined as the proportion of patients developing one or more of the following signs of reaction: a) the loss of 2 or more points in the sensory score, or b) the loss of 2 or more MRC grades for one nerve's function, or c) severe nerve pain, or d) 1 point sensory or motor loss combined with moderate pain in the nerve of supply, or e) a severe type 1 reaction in the skin.

Patients developing a type 2 reaction were excluded from the calculations. The proportion of patients developing a reactive phenomenon was then compared with an historical cohort of 200 MB patients drawn from the BANDS cohort matched for Ridley-Jopling classification using random numbers to exclude or include. Patients recruited at the start of the study have completed 12 months of follow up; those recruited in the last months have received only 4 months.

Among the 200 control patients, there were 53 events of reaction as defined above during 77,316 days at risk, a proportion of 0.265. Among the 92 treatment patients, 14 reactive events occurred during 20,937 days at risk, a proportion of 0.152. The odds ratio is 2.01 (95% CI 1.05 to 3.85), indicating that there is a prophylactic effect of prednisolone in preventing type 1 reactions/NFI in MB patients of about the order sought.

The results must be interpreted with caution, however, since follow up is not complete among the trial patients recruited toward the end of the study. Further, this is an open trial and numbers are relatively small. However, the results do indicate that there is an effect worth investigating more thoroughly.

A randomized, double-blind, controlled trial to investigate the effectiveness of prophylactic corticosteroids in the prevention of reactions in MB leprosy patients has been designed by this study group, and is one of a trio of trials aimed at investigating the prevention of disability in leprosy. These are known as the TRIPOD (Trials in Prevention of Disability) Trials and are currently running in six centers in Bangladesh and Nepal.

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