Letter in Response to Previous Publication

Intravenous pulsed corticosteroids for leprosy neuritis: Logical or irrational?

Sir,

We read with interest the letter by Lugão *et al.* "Methylprednisolone pulse therapy for leprosy neuritis: A retrospective study with sensory testing and peripheral nerve ultrasonography correlation",[1] describing the successful use of suprapharmacological dose of methylprednisolone given intravenously for leprous neuritis. We critically reviewed this publication and the existing literature to discern whether this was a prudent therapeutic choice.

The publication is unclear about the inclusion criteria. Five patients were administered steroid pulse as the initial treatment, two received it after two months and several others after up to 72 months of oral steroid therapy. However, in Table 1 "months of prednisolone use before pulses" has been mentioned twice with varying figures.

It is imperative to know which signs/symptoms the authors wished to ameliorate and how were they monitored. It is very important to fix the duration of therapy- the 'end point'- and not–up to 72 months of oral steroids and then with an average of 25 pulses- making a total duration of eight years.

In the absence of this information, at least the signs reflected by sensory testing worsened significantly in 20% of the patients. The observed reduction of hypervascularity on ultrasonography in the nerve strangely did not reflect the corresponding reduction in its diameter.

Neuropathy in leprosy is the basic pathology that needs corticosteroids only during the pain of acute neuritis or significant nerve function impairment of recent onset. Continuation of high doses of oral steroids up to 80 mg/day for as long as 72 months without considering dose reduction or any steroid-sparing agent defies all pharmacological recommendations and also those of any leprosy expert group. In patients with prolonged neuritis as in those with persistent reaction, other causes of recalcitrance like drug resistance should have been considered.

Claimed reduction in the dose of thalidomide may not be relevant as thalidomide is not recommended for the treatment of leprosy neuritis. That the maximum dose of 200 mg given for patients with erythema nodosum leprosum is inadequate is another issue that needs attention.

Adverse effects are associated with prolonged steroid use, especially adrenal suppression, and the I/V administration of steroids restricts this approach to only specialised centres. Further, the use of pulse therapy in patients with neuropathy associated with diabetes may be imprudent, as steroids worsen diabetes and subsequently neuropathy. So, the inference that reduction of steroid dose after pulse therapy in diabetics may be beneficial based on the observations on only four patients may be too premature. The authors also used an arbitrary modification of the established pulse regimen without giving any valid reason.

In the TRIPOD-3 study, systemic corticosteroids did not significantly impact the course of nerve function impairment because of spontaneous improvement.[2] A randomized controlled double-blind trial comparing methylprednisolone pulse therapy and oral steroids showed no lasting difference between the two regimens by day 337.[3]

The biological half-life of methylprednisolone is 12–36 hours, hence the administration of pulse provides suprapharmacological levels for three days and ineffective levels during the rest of the month. Rao *et al.* compared three steroid regimens in leprosy patients having type 1 reaction with neuritis and concluded that a longer duration was more effective than the higher dose.[4] Mahajan *et al.* administered dexamethasone pulse therapy in three patients of erythema nodosum leprosum, unresponsive to oral prednisolone at 80 mg daily.[5] However, early remission of reaction had to be maintained with oral azathioprine, suggesting that the action of pulse is short-lived. The persistent need for pulse therapy for up to 33 months in the present study further undermines its real utility.[1]

It is important to remember that neuritis is not the sole manifestation of leprosy reactions, hence choosing therapy only on the basis of this one manifestation is not a judicious approach. It would be very informative to know how the authors continued labelling these patients as 'pure leprous neuritis', and did not consider 'neuropathic pain', long

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after the completion of multidrug therapy in any of them. While oral prednisolone given for short periods appears to be mostly safe in relation to reactivation of leprosy, similar safety data is unavailable for their long-term use in high doses.

In conclusion, current literature does not support the use of pulsed corticosteroids in leprosy neuritis.

Declaration of patient consent

Patient's consent not required as there are no patients in this study.

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Conflicts of interest

There are no conflicts of interest.

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Authors' reply

Sir,

We would like to thank the authors of the letter "Intravenous pulsed corticosteroids for leprosy neuritis: Logical or irrational?" for their interest in our article and we also appreciate the opportunity to use this space to clarify some points that might not have been clear.[1,2]

Initially, we would like to underline that the study was carried out in a national reference hospital, which is an important research centre about leprosy in Brazil. Our reference centre has leprologists with many years of experience in the care of highly complex patients. In our service, all patients with prolonged neuritis or persistent reaction are extensively investigated to assess the possibility of relapse, treatment failure and drug resistance. The evaluation includes a complete dermato-neurological exam and complementary diagnostic tests, as indicated for each case (slit skin smears, skin biopsy, *M. leprae*-specific repetitive element deoxyribonucleic acid polymerase chain reaction for *Mycobacterium leprae*, molecular investigation of resistance genes, nerve ultrasonography, electroneuromyography and, more recently, ribonucleic acid reverse transcription polymerase chain reaction).

The major inclusion criterion in our study was the presence of neuritis, defined as new nerve function impairment (sensory testing and/or voluntary muscle testing) of recent onset,

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