

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.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

**Hitaishi Mehta, Tarun Narang, Sunil Dogra,
Bhushan Kumar¹**

Department of Dermatology, Venereology & Leprology, Postgraduate Institute of Medical Education & Research, Chandigarh, ¹Department of Dermatology, Shalby Hospital, SAS Nagar, Punjab, India

Corresponding author:

Dr. Tarun Narang,
Associate Professor, Department of Dermatology, Venereology & Leprology, Postgraduate Institute of Medical Education & Research, Chandigarh, India.
narangtarun@yahoo.co.in

References

1. Lugão HB, Savarese LG, Silva S, Nogueira-Barbosa MH, Foss NT, Frade MAC. Methylprednisolone pulse therapy for leprosy neuritis: A retrospective study with sensory testing and peripheral nerve ultrasonography correlation. *Indian J Dermatol Venereol Leprol* 2021;88:114–6.
2. Richardus JH, Withington SG, Anderson AM, Croft RP, Nicholls PG, Van Brakel WH, et al. Treatment with corticosteroids of long-standing nerve function impairment in leprosy: A randomized controlled trial (TRIPOD 3). *Lepr Rev* 2003;74:311–8.
3. Walker SL, Nicholls PG, Dhakal S, Hawksworth RA, Macdonald M, Mahat K, et al. A phase two randomised controlled double blind trial of high dose intravenous methylprednisolone and oral prednisolone versus intravenous normal saline and oral prednisolone in individuals with leprosy type I reactions and/or nerve function impairment. *PLoS Negl Trop Dis* 2011;5:e1041.
4. Rao PS, Sugamaram DS, Richard J, Smith WC. Multi-centre, double blind, randomized trial of three steroid regimens in the treatment of type-I reactions in leprosy. *Lepr Rev* 2006;77:25–33.
5. Mahajan VK, Sharma NL, Sharma RC, Sharma A. Pulse dexamethasone, oral steroids and azathioprine in the management of erythema nodosum leprosum. *Lepr Rev* 2003;74:171–4.

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,

How to cite this article: Lugão HB, Savarese LG, Silva SRML, Nogueira-Barbosa MH, Foss NT, Frade MAC. Authors' reply. *Indian J Dermatol Venereol Leprol* 2023;89:295–7.

Received: April, 2022 **Accepted:** April, 2022 **Epub Ahead of Print:** June, 2022 **Published:** March, 2023

DOI: 10.25259/IJDVL_375_2022 **PMID:** 35841366

This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-Share Alike 4.0 License, which allows others to remix, transform, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

associated with nerve pain, paraesthesia or tenderness. We did not include patients with neuropathic pain. Additionally, this retrospective study only included patients that had undergone peripheral nerve ultrasonography and sensory testing before and after each cycle of pulse therapy. We would like to emphasize that, as routine, patients with leprosy reactions are submitted to a dermato-neurological examination by dermatologists and/or leprologists at least once a month and that the decision regarding the reduction of doses of anti-reactional treatment (prednisone and/or thalidomide) is guided by clinical evaluation considering both the cutaneous and the neurological manifestations of leprosy reaction.

Considering the comment in Table 1, unfortunately, the formatting for publication misconfigured the final lines and some important information were not presented properly. In the first mention of the expression “months of prednisone use before pulses,” the values refer to the sub-group that used only prednisone and in the second mention, the values refer to the subgroup that received prednisone + thalidomide.² We appreciate the opportunity to clarify this point.

We suggest the authors of the letter read our article again more carefully, as there was some misinterpretation that should be clarified.¹ In the third paragraph of our article it is evident that each patient only received three monthly pulses, and only four of the 21 patients included needed to repeat this 3-pulse cycle after 6–33 months.² Contrary to what the authors of the letter mentioned, we did not make any changes to the established pulse regimen and strictly followed the protocol recommended by the Ministry of Health of Brazil.³ No patient received 25 monthly pulses nor had “persistent need of pulse therapy for up to 33 months” as stated in the letter.¹ Furthermore, no patient maintained continuous use of prednisone at a dose of 80 mg for 72 months. Among the patients included, the maximum time of prednisone use before pulses in one patient was 72 months, but this patient used prednisone at variable doses during his follow-up. Only two patients were receiving 80 mg prednisone due to severe leprosy reaction when pulse therapy was started, but these patients were receiving the maximum dose for only one month before pulses and this dose was reduced immediately after the first infusion of methylprednisolone.

In routine follow-up for patients with leprosy reactions, whenever possible, the dose of prednisone is reduced and, if necessary, sparing agents such as azathioprine and methotrexate are used. Unfortunately, these and other steroid-sparing agents are difficult to access in our country, so pulse therapy stands out as an effective steroid-sparing therapy. Our results demonstrated that 87.5% of the patients had prednisone dosage reduced after pulses and eight patients discontinued prednisone use within six months, which is an impressive result considering that many of

these patients had been using prednisone chronically before pulses.²

Considering the potential side-effects of systemic steroids, all patients using oral steroids and/or pulse therapy were monitored for side-effects and received prophylaxis for disseminated strongyloidiasis, osteoporosis and peptic ulcer disease. The patients included in our article continue to be followed up in our outpatient clinic and none had major adverse events.

We included four patients with diabetes mellitus. The possibility of impaired glycemic control in patients with diabetes during methylprednisolone infusions should be considered. Therefore, these patients underwent pulses in a hospital setting with glucose monitoring and received insulin correction when necessary. Despite the small number of patients with diabetes included, our experience with pulse therapy allowed for the use of lower daily doses of prednisone, thus contributing to better long-term glycemic control. Interestingly, the diabetic patients showed results similar to the whole group, with small frequencies of poor cross-sectional area and poor sensory outcomes, underlining the effect of intravenous methylprednisolone in leprosy neuritis, since pulse therapy would not improve diabetic neuropathy.²

Considering the comment about the apparent disagreement between the reduction of hypervascularity not accompanying the reduction in nerve diameter, there is already evidence that the neural enlargement that occurs in leprosy may not be completely reversed with the treatment of the reaction or even with the antimicrobial treatment.⁴ Neural thickening may persist as a result of the chronic changes and fibrosis due to leprosy neuropathy.^{4,5} The Doppler signal, on the other hand, can be considered as a marker of intraneural inflammatory activity and its reduction seems to indicate control of neuritis, which may be an indicator to guide steroid tapering.^{4,5}

Although the cutaneous manifestations may be evident during the reactional episodes, neuritis may lead to acute nerve function deterioration and is the main factor responsible for disabilities and deformities. Therefore, during the follow-up of patients with leprosy reactions, an assessment of nerve function should be performed at all visits. Our data indicate that methylprednisolone pulse therapy is effective for patients with leprosy reactions, especially patients with severe neuritis, recalcitrant neuritis and patients without control of cutaneous and neural manifestations of leprosy reactions with oral steroids.

Thus, returning to the question raised in the title of the letter,¹ and considering all the challenges related to the diagnosis and management of leprosy and its reactions, our work emphasizes the importance of not focusing only on the dermatological (morphological) manifestations based on the “logical

way,” as a simple disease of primary healthcare. Our paper reinforces the importance of introducing new technologies to improve the quality of care for leprosy patients. In addition, it encourages health professionals and students to think about the “rationale” of the pathophysiological diagnosis of leprosy and its reactions, emphasizing the importance of thorough follow-up of neurological manifestations (functional and morphological). The care of patients with leprosy should be provided according to the complexity of each case. Our group advocates that patients with leprosy reactions, especially those with neuritis, are patients at a higher risk of disability and therefore, should receive care adequate to the complexity of their pathology.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms.

Financial support and sponsorship

Dr. Lugao received research funding from FUNADERSP - Brazilian Society of Dermatology (Grant number: 62/2017; <https://www.sbd-sp.org.br>) and from FIOTEC - Fiocruz (Grant number: PRES-009-FIO-20; <https://www.fiotec.fiocruz.br/en>). Dr. Frade received research funding from Ministério da Saúde/Fundação de Apoio ao Ensino, Pesquisa e Assistência do Hospital das Clínicas da Faculdade de Medicina de Ribeirão Preto da Universidade de São Paulo (MS/FAEPA-FMRP-USP). Grant numbers: 749145/2010 and 767202/2011; www.faepe.br.

Conflicts of interest

There are no conflicts of interest.

***Helena Barbosa Lugão, Leonor Garbin Savarese²,
Stephenie Rharissa Moraes Libório Silva²,***

***Marcello Henrique Nogueira-Barbosa²,
Norma Tiraboschi Foss¹,
Marco Andrey Cipriani Frade¹***

Dermatology Division, Department of Internal Medicine, Ribeirão Preto Medical School, University of São Paulo, ¹National Reference Center in Sanitary Dermatology focused on Leprosy of Ribeirão Preto Clinical Hospital (CRNDSHansen), ²Radiology Division, Department of Medical Imaging, Hematology and Clinical Oncology, Ribeirão Preto Medical School, University of São Paulo, Ribeirão Preto, São Paulo, Brazil.

Corresponding author:

Dr. Helena Barbosa Lugão,
Dermatology Division, Department of Internal Medicine, Ribeirão Preto Medical School, University of São Paulo, Ribeirão Preto, São Paulo, Brazil.
helenalugao@hotmail.com

References

1. Mehta H, Narang T, Dogra S, Kumar B. Intravenous pulsed corticosteroids for leprosy neuritis: Logical or irrational?. *Indian J Dermatol Venereol Leprol* 2023;89:294–5
2. Lugão HB, Savarese LG, Silva SRML, Nogueira-Barbosa MH, Foss NT, Frade MAC. Methylprednisolone pulse therapy for leprosy neuritis: A retrospective study with sensory testing and peripheral nerve ultrasonography correlation. *Indian J Dermatol Venereol Leprol* 2021;88:114–6.
3. Brasil. Ministério da Saúde. Diretrizes Para Vigilância, Atenção e Eliminação da Hanseníase Como Problema de Saúde Pública: Manual Técnico-operacional. Ministério da Saúde, Brasília, DF, Brazil; 2016. Available from: <http://www.portalarquivos2.saude.gov.br/images/pdf/2016/fevereiro/04/diretrizes-eliminacao-hansenia-4fev16-web.pdf>. [Last accessed on 2021 Jun 20].
4. Lugão HB, Frade MA, Marques W Jr, Foss NT, Nogueira-Barbosa MH. Ultrasonography of leprosy neuropathy: A longitudinal prospective study. *PLoS Negl Trop Dis* 2016;10:e0005111.
5. Jain S, Visser LH, Praveen TLN, Rao PN, Surekha T, Ellanti R, *et al.* High-resolution sonography: A new technique to detect nerve damage in leprosy. *PLoS Negl Trop Dis* 2009;3:e498. 19668356 10.1371/journal.pntd.0000498