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Original Article

Current Practice and Challenges with the Use of Multidrug Therapy (MDT) in the Management of Pediatric Leprosy Patients: An Expert Perspective from India

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The management of pediatric leprosy patients in India remains challenging. An expert panel was assembled and through a pre-event survey and virtual discussion, current challenges were discussed and recommendations to address these issues were made. Delayed diagnosis of leprosy in pediatric patients was identified as a major obstacle. The lack of readily available treatment for this patient population, due to lack of scoring of tablets in available multi-drug treatment packs and limited availability of liquid formulations affects successful management of leprosy in pediatric patients. The expert panel recommended additional training for healthcare professionals on timely diagnosis of leprosy in children, as well as dose adjustment strategies for patients under the age of 10 years.

Key words : Pediatric Leprosy, Clofazimine, Dapsone, Rifampicin

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Introduction

Advances in the management of leprosy, especially with the implementation of multi-drug treatment (MDT), have altered the course of the disease. Therapeutic options for adults via MDT in India are provided through the National Leprosy Eradication Program (NLEP) and individual components (rifampicin, dapsone and clofazimine) are available as generics, but the lack of child-friendly formulations results in challenges in the management of pediatric patients. This report summarizes consolidated expert opinion related to treatment approaches for the management of pediatric leprosy patients collected during a virtual advisory board conducted by Novartis in India.

Methodology

A pre-event survey was shared with the expert panel to gather information on incidence and management of pediatric leprosy in India over a 5-year period (2016 – 2020).

The following open-ended questions were shared with the expert panel prior to the virtual discussion.

Questions to healthcare professionals

1. How many new pediatric patients with leprosy did you diagnose and treat over the last 5 years (2016 – 2020)?
2. What are the current trends of prevalence of pediatric leprosy (increasing or decreasing) in your territory over the last 5 years (2016-2020)? Please specify below the details in percentages, if available.
3. Please provide the break-down of approximately total number of patients in last 5 years within various age groups: 0 – 2 years; 3 – 6 years; 7 – 12 years; 13 – 18 years.
4. Please provide the break-down of approximately total number of patients in last 5 years for two types of leprosy: multibacillary and paucibacillary.
5. How do you commonly confirm leprosy in pediatric patients?
6. For leprosy management in pediatric patients, which treatment guidelines do you follow?
7. How do you treat pediatric patients with leprosy infection in your clinical practice? Do you use the MDT therapy provided by WHO/ Novartis or do you use other drug regimens?
8. What are the challenges with the administration of existing dosage forms/strengths of primary drugs including MDT in pediatric patients especially in younger age group?
9. Please identify the challenges with each MDT drug component in the treatment of pediatric leprosy patients:
    a. Unavailability of MDT blister pack formulation specifically for children below the age of 10 years and less than 40 kg body weight
    b. Inaccuracy in precise dosing while scoring tablet or capsule
    c. Taste and palatability
    d. Unavailability of specific lowest strengths
    e. Compliance
10. Do you see a need to improve formulation/ method of administration of MDT drugs in pediatric patients?
11. In situations when there are challenges in administering available formulations of MDT pack in children, are you willing to consider administering these formulations by mixing the contents with soft food such as yogurt or apple sauce?

12. What percentage of "treatment non-compliance" is associated with poor adherence to MDT treatment (as per WHO guidelines) due to difficulties in administering primary drugs?

Questions to representatives from patient advocacy groups:

1. What are the primary complaints from patients or accompanying parent of a child related to leprosy?
2. For how long does the complaint(s) exist before the child himself/herself or accompanying parent of the child decide to visit physician?
3. Did patients take any over-the-counter medications or any remedies (if at all) for their complaints before consulting physician? If yes, please specify the medicine name.

Subsequently, a virtual discussion was held in November 2021 where results from the survey were discussed, and recommendations were formulated to address the identified challenges.

Outcome and Recommendations

A panel of eight Physicians with specialties including dermatology, surgery, and public health, with healthcare experience ranging from 21 to 41 years participated in this activity. In addition, two representatives from the patient advocacy groups operating in India, the Lepra Society and The Leprosy Mission Trust, participated to provide a perspective on the pediatric leprosy patient's experience. Discussions and recommendations are based on the clinical experience of the expert panel in managing leprosy in India.

Conventionally, pediatric patients are defined as patients 18 years and younger. However, as per the World Health Organization (WHO) treatment guidelines, pediatric patients in the context of leprosy and in this report are defined as patients up to the age of 14 years (WHO 2018). Discussions related to pediatric formulations are relevant to children under the age of 10 years.

Pediatric leprosy in India: Prevalence and Trends

During the period 2016 to 2020, the panel jointly diagnosed 270 cases of pediatric leprosy in their clinics. Considering age distribution of pediatric patients using age bands of 0-2, 3-6; 7-12 and 12-18 years respectively, most pediatric leprosy cases are diagnosed among 13 – 18 years old patients (66% of cases), while approximately 30% of patients diagnosed are between the ages of 7 – 12 years old. Grade II disability is mostly seen in the 13 – 18 years age group. It is postulated that the lack of deformities/disabilities in younger patients is related to the long incubation period of leprosy.

Diagnosis of pediatric leprosy cases

Diagnosis of leprosy in the pediatric population in tertiary care centers is mostly based on clinical examination and the results of a slit-skin smear test. Skin biopsies and polymerase chain reaction (PCR) tests are rarely used but provide more accurate diagnostic results. Diagnosis of leprosy is often delayed due to inability of younger patients to communicate symptoms; further complicated by the limited number of skin patches on presentation, challenges in detecting nerve function impairment, misdiagnosis, and limitations in further investigations. According to the expert panel, the delay in seeking medical attention after experiencing initial symptoms was varied, with a delay of more than 12 months reported for 12% of pediatric patients in northern India region while a similar delay was reported for 80% of pediatric patients in southwestern India region. Field diagnosis of leprosy in children by frontline workers often becomes a challenge for these reasons.

Data collected during the survey indicated that multibacillary (MB) leprosy is diagnosed more frequently than paucibacillary (PB) leprosy (64.4% vs 35.6%) in pediatric patients. In contrast, published data suggest an equal split between MB and PB diagnosis in the pediatric population (Darlong et al 2017, Ghunawat et al 2018). Regional differences in patient presentation, rates of early diagnosis and availability of tertiary care centers with advanced diagnostic facilities where medical experts can support diagnosis of atypical pediatric cases may contribute to this disparity.

Challenges with treating pediatric leprosy in India and potential recommendations

WHO recommended treatment of pediatric leprosy patients are rifampicin, clofazimine and dapsone (WHO 2018). While these treatments are widely available as MDT packs, management of patients under the age of 18 is complicated by the ambiguity in the definition of 'pediatric' in the context of leprosy. Specific packs are available for patients aged 10 – 14 years old, but treatment options for patients younger than 10 years are limited.

Syrup formulations of rifampicin are available as a convenient option in the pediatric population and is frequently substituted for the rifampicin capsules in MDT packs. Doses of dapsone (50 and 100 mg) available in MDT packs are inappropriate for use in patients younger than 10 years of age, and as these tablets are not scored, inaccurate dosing may occur. Similarly, dose adjustment on mg/kg basis in patients younger than 10 years old and/or with body weight below 40 kg for clofazimine is challenging as it is only available as soft gelatin capsules (50 and 100 mg).

Furthermore, compliance to the treatment remains a challenge. While four of the expert panel members reported the difficulties in administering primary drugs resulted in less than 10% non-compliance to treatment, one advisor noted 11-20% non-compliance and two advisors reported >30% non-compliance for the same reason. This is exacerbated by the extended treatment duration, intolerable taste, required storage conditions of medicines, availability of MDT, misinformation regarding effectiveness of the treatment and treatment-related skin discoloration due to clofazimine.

Experts recommend that formulations specific for children, preferably a palatable liquid form, is developed for dapsone and clofazimine. However, it is acknowledged that development and large-scale manufacturing is challenging due to the low number of pediatric leprosy patients globally. As an alternative, the appropriate use of readily available soft food vehicles is recommended for these medicines.

Conclusion

Current challenges in the effective management of leprosy in pediatric patients in India stem from the delay in diagnosis as well as the practical difficulties in pharmacological management. Recommendations include additional training of healthcare professionals on timely and accurate diagnosis of leprosy and appropriate dose adjustment strategies in the pediatric patient population. Availability of recommended therapy in child-friendly formulations or the suitability of readily available food vehicles warrant further investigation.

Conflicts of interest

Rakesh Chugh, Hardik Pathak, Parag Borde, Jagannath Kota and Sunil Modali are employed by Novartis Healthcare Pvt. Ltd. Gangadhar Sunkara is employed by Novartis Pharmaceuticals Corporation.

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