Treatment of Early Neuropathy in Leprosy.

No registrations found.

Ethical review	Positive opinion
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON22418

Source
Nationaal Trial Register

Brief title
TENLEP

Health condition

neuropathy, neuritis, leprosy

Sponsors and support

Primary sponsor: Royal Tropical Institute
Amsterdam
Source(s) of monetary or material Support: NLR
Turing Foundation
ALM
GLRA
Ordre de Malta

Intervention

Outcome measures

Primary outcome

Trial 1:

Proportion of patients developing clinical neuropathy as defined by MFT/VMT change.

Trial 2:

Proportion of patients with restored nerve function as measured by MFT/VMT (all nerves).

Secondary outcome

Trial 1:

1. Proportion of patients with recovered nerve function (all nerves, absence of SC-NFI);

2. Proportions of patients with improved, unchanged or deteriorated SC NFI scores respectively (not back to normal WDT and/ or NCV);

3. Proportions of patients with recovered, improved, unchanged or deteriorated score of a given nerve;

4. Proportion of patients with serious adverse events/ other complications leaving the trial;

5. Spontaneous recovery of nerve function as assessed by nerve conduction or thermal testing (placebo group).

Trial 2:

1. Proportion of patients with adverse effects or other complications, prompting removal from the trial;

2. Proportion of patients with ‘recovered’ improved, ‘unchanged’ or deteriorated function of a given nerve (e.g ulnar nerve);

3. Proportion of patients with changed (improved, unchanged, deteriorated) composite nerve scores;

4. Proportion of patients with changed reaction severity scores;

5. Proportion of patients with ‘changed’ SALSA and PP scale scores.

Study description

Background summary

The TENLEP Trials proposal builds on the findings of the INFIR Cohort Study and the recommendations of the NLR-funded international Workshop on Neuropathology in Leprosy in the Netherlands in 2007. At this workshop, several key research questions were prioritised. These included:

1. How effective is steroid treatment of sub-clinical neuropathy detected at diagnosis in reducing the proportion of patients with sensory and/or motor NFI one year after the start of MDT?

2. What is the optimal steroid treatment regimen for patients with clinical sensory and/or motor NFI of recent onset (<6 months)?

The TENLEP Trials will use a randomised double-blind controlled trial design to answer the above questions in 2 integrated trials. We have the following hypotheses:

Trial 1: Steroid treatment (20 weeks) of sub-clinical neuropathy detected at diagnosis will significantly reduce the proportion of patients with sensory and/or motor nerve function impairment 18 months after the start of MDT.

Trial 2: Steroid treatment of 32 weeks duration is more effective than treatment of 20 weeks duration in restoring nerve function in patients with clinical sensory and/or motor NFI of recent onset (<6 months).

All patients newly registered at the participating centres will be asked to consent to take part in the study. After consent, they will be enrolled in one of the two trials described above, depending on their nerve function status. They will then be randomised into a treatment or placebo group for Trial 1 or into one of two treatment arms for Trial 2. Patients who are not already in Trial 1 and who develop new NFI during the first 3 months of MDT will also be eligible for Trial 2. Outcomes will be assessed at the end of steroid treatment, and at 12 and 18 months after the start of MDT using monofilament test (MFT) voluntary muscle test (VMT), nerve conduction (NC), warm detection thresholds (WDT) and SALSA scale measurements. All nerve function assessment (NFA) will be blinded with regard to treatment status. Occurrence of all new or additional NFI events and leprosy reactions will be recorded. Outcomes will be compared between treatment groups with regard to nerve function, activity limitation, incidence of nerve function impairment events, and reactions and need of prednisolone treatment during follow-up.

The countries in which the study will take place are India, Bangladesh, Nepal, and Indonesia.

Study objective

The TENLEP Trials proposal builds on the findings of the INFIR Cohort Study and the recommendations of the NLR-funded international Workshop on Neuropathology in Leprosy in the Netherlands in 2007. At this workshop, several key research questions were prioritised. These included:

1. How effective is steroid treatment of sub-clinical neuropathy detected at diagnosis in reducing the proportion of patients with sensory and/or motor NFI one year after the start of MDT?

2. What is the optimal steroid treatment regimen for patients with clinical sensory and/or motor NFI of recent onset (<6 months)?

The TENLEP Trials will use a randomised double-blind controlled trial design to answer the above questions in 2 integrated trials. We formulated the following hypotheses:

1. Trial 1:

Steroid treatment (20 weeks) of sub-clinical neuropathy detected at diagnosis will significantly reduce the proportion of patients with clinical sensory and/or motor nerve function impairment 18 months after the start of MDT.

2. Trial 2:

Steroid treatment of 32 weeks duration is more effective than treatment of 20 weeks duration in restoring nerve function in patients with clinical sensory and/or motor NFI of recent onset (<6 months).

Study design

At intake, at the end of treatment, at 12 and at 18 months the following investigations will be done:

1. Nerve function assessment (NFA): Nerve Function Assessment will be done using the following methods:

A. History taking;

B. Motor nerve function:

i. Voluntary muscle testing (VMT) using the 0-5 modified MRC scale;

ii. Motor nerve conduction measurements (ulnar, peroneal, median);

C. Sensory nerve function:

i. Sensory testing using a standard set of 5 Semmes-Weinstein monofilaments (MFT);

ii. Warm detection testing WDT using the Thermal Sensory Analyzer II (ulnar, median, radial cutaneous, sural and posterior tibial);

iii. Sensory nerve conduction (SNC) measurements (ulnar, median, radial cutaneous, sural and posterior tibial).

2. Activities of daily living: A questionnaire-based ADL assessment will be done to evaluate possible consequences of neurological impairment at the activity level.

Intervention

Trial 1:

Patients receiving prednisolone will start at a dose of 1 mg/kg/day, taken in the morning. To allow better comparison of treatment outcomes, two weight groups are discerned, one less than 50 kg (average of 45 kg) and the other more than 50 kg (average 60). These two weight classes will receive a differing total dosage, allowing similar dosage per kg. The dose will be tapered down quickly with 5 mg weekly till a plateau is reached of 0,3-0,5 mg/kg/day. Final tapering down will be done in the last 3 weeks. In the treatment arm a therapeutic dose of more than 0,3 mg/kg/day will be maintained for 17 weeks. The total course will be of 20 weeks duration.

NB: Patients receiving placebo will follow the same scheme, but now using placebo tablets that will be a replica of those containing prednisolone.

Trial 2:

Patients will start at a dose of 1 mg/kg/day, taken in the morning. To allow better comparison of treatment outcomes, two weight groups are being distinguished, one less than 50 kg (average of 45 kg) and the other more than 50 kg (average 60). These two weight classes will receive a differing total dosage, allowing similar dosage per kg. The dose will be tapered down quickly with 5 mg weekly till a plateau is reached of 0,3-0,5 mg/kg/day. Final tapering down takes place in the last 3 weeks.

In arm 1 a therapeutic dose of more than 0,3 mg/kg/day will be maintained for 17 weeks. The

total course will be of 32 weeks, of which the first 20 weeks will be prednisolone and the remaining weeks will be placebo for the purpose of comparison with arm 2. To enable blinding of arm 1 and arm 2, patients in each arm will receive the same amount of tablets per day. In arm 1 this results in a combination of prednisolone tablets and placebo tablets (see figure).

In arm 2 a therapeutic dose of more than 0,3 mg/kg/day will be maintained for 29 weeks. The total course will be 32 weeks (see table 2).

Contacts

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Eligibility criteria

Inclusion criteria

Trial 1:

General: All newly diagnosed leprosy patients who can be followed will be eligible for inclusion in the trials.

The following groups of patients can be included in trial 1:

1. Any patient who has signs of sub-clinical sensory or motor impairment (see Annex);

2. Optional, if there is sufficient time available for testing at 1, 2 or 3 months after starting MDT: Patients who on initial tests have normal nerves, but who may develop subclinical NFI

within the first 3 months following diagnosis.

Trial 2:

All diagnosed leprosy patients, irrespective of MDT duration/status, who can be followed-up, will be eligible for inclusion in the trials.

The following groups of patients can be included in trial 2:

1. Any among the above who have signs of clinical sensory or motor impairment of recent onset (= < 6 months duration) (see diagnostic criteria);

2. Patients from trial 1 who had a clinical outcome in the first 3 months (and only those who have been in the placebo arm, as demonstrated by later decoding, will be taken into the analysis of trial 2).

Exclusion criteria

General exclusion criteria:

1. Any patient refusing informed consent;

2. Any patient with a single skin lesion on the trunk as the only sign of leprosy;

3. Any patient over 60 or under 15;

4. Women with known pregnancy at the time of diagnosis;

5. People with known other conditions that may affect the peripheral nervous system (e.g. diabetes, alcohol abuse, HIV/AIDS, carpal tunnel syndrome, peripheral nerve injuries);

6. Any patients for whom steroids would be indicated for reasons other than a recent nerve function impairment.

Trial 1, specific exclusion criteria:

1. Any patients with sensory or motor impairment by MFT or VMT in any nerve tested;

2. Any patient requiring steroid treatment for skin-only reversal reaction or ENL.

Trial 2, specific exclusion criteria:

1. Any patients with old (> 6 months duration) sensory or motor impairment by MFT or VMT in any nerve tested, and not having any recent nerve function impairment (MFT or VMT);

2. Patients with skin-only reactions or ENL;

3. Patients previously enrolled in Trial 1, who have been in the treatment arm of Trial 1 (this will become clear at the moment of analysis at the end of the trials).

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-10-2010
Enrollment:	1250
Type:	Anticipated

Ethics review

Positive opinion

Date:	28-04-2010
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL2176
NTR-old	NTR2300
Other	:
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results
N/A