

ILEP review on evidence base for treatment of T1R and ENL

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T1R and neuritis

- Common problem
- Affects 30% of MB patients
- Causes disability
- Difficult to diagnose
- Difficult to treat
- May be recurrent
- Management, training and health service challenge

T1R

- Steroids first line
- Assess outcome
 - Skin signs
 - Nerve damage - VMT, Sensory testing (MF)
- Cochrane review 2007 (Van Veen)
- Comprehensive review 2007 (Walker and Lockwood)
- Paucity of good trials
- CR only 3 trials adequate- all on steroids
 - Indian trial comparing 3 regimens dose & duration
 - Old nerve damage
 - Mild sensory loss
 - Conclusion- no evidence for the long term benefit of steroid treatment

T1R- Steroids – Measurement Problems

- 3 studies showed a benefit for steroid treatment
- Improvement about 50%
- Difficulties in comparing studies
 - Entry criteria
 - Outcome measures
 - Ballpoint pen, MF, no hard endpoint
 - Unvalidated scales, no scales
- Doses of steroids
- Duration of steroid treatment

Prospective randomised studies on steroids in T1R and NFI

Country, Year & Type of study*	Entry criteria	No.	Intervention	Outcome measures	Conclusion
BRAZIL (Garbino, 2008) R C	T1R / ENL or ulnar neuropathy	21	Pred 120mg daily vs. 60mg daily. Tapered variably.	Clin. Score and MNC	Non-comparable groups. Clin. Score not validated. T1R and ENL analysed together.
INDIA (Rao, 2006) DB, R C, Parallel	“Severe” T1R	334	3 pred regimens: 3.5g 20 wks 2.31g 20 wks 2.94g 12 wks	Extra pred req	20 wk regimens equally effective, less additional pred required
NEPAL (Marlowe, 2004) R C	T1R	40	12 wks aza and 8 wks pred vs. 12 wks pred	Skin signs, NT, sensory and motor testing, extra pred req	Equally effective
BANGLADESH (Richardus, 2003) R P C, DB	NFI 6-24 mo	92	16 wk std pred	Sensory and motor test scores	No difference
BANGLADESH (Van Brakel, 2003) R P C, DB	Mild sensory NFI	75	16 wk std pred	MF scores	No difference

* R C = Randomised controlled; R P C = Randomised placebo controlled; DB = Double-blind

T1R- Steroids

- Relapse rates
 - Often starts when steroid dose reduced
 - Marlowe study 50%, Sundar Rao study 30- 50%
 - Can the patients at risk of relapsing be identified?
- Dose of steroid- very little data
- Duration – probably longer is better
- 12 weeks high relapse rate
 - Sundar Rao study
 - Marlowe 42% relapse rate
 - Shetty (Lep Rev 2010) no difference in NCS rates after 12 weeks steroid treatment

T1R- Improving on steroids

- Methyl prednisolone
 - 50% had improved nerve function, 50% in both groups required further steroids
- Vital to do well designed studies on dose and duration with well defined outcomes
- Women under-represented
- No quality of life assessments

T1R –Second Line agents

- Needed for patients who do not respond to steroids
- Patients who have adverse effects from steroids
- Azathioprine
 - RCT in India currently recruiting (placebo, 24, 36 or 48 weeks aza)
- Cyclosporin
 - RCT in Ethiopia about to start
- HIV- Lep co-infected patients

T1R Summary

1. Large studies on dose and duration of steroids.
2. To include Africa, Brazil and Asia
3. Standardised scales for comparability
4. Identifying patients at risk of reactions
 1. More sensitive tests
 2. Genotyping
5. Second line treatments
6. HIV and leprosy- defining regimens

Erythema Nodosum Leprosum (ENL)

- Still important
 - Referral centres, 50% LL patients, under-diagnosed (INFIR study)
 - Immuno-suppression
- Chronicity
- Steroids
- Thalidomide
- Cochrane review (Van Veen 2009)
- Comprehensive review (Walker & Lockwood 2009)
- Very poor quality of studies
 - Small numbers of patients
 - No scales
 - Most done 30-40 years ago

ENL

- Cochrane review 13 studies
 - Steroids, Thalidomide, clofazimine, pentoxifylline, betamethasone, indomethacin, levamisole.
- Outcomes important
 - Control of symptoms initially important
 - Preventing further episodes then important
- Outcomes 3 studies showed benefit for thalidomide and clofazimine. Further reactions, treatment success, fewer relapses.
- Only 2 studies done on Thalidomide since introduction of MDT
 - Villahermosa 2005, compared doses of Thalidomide
 - Sales 2005, compared Thalidomide vs Pentoxifylline
- No studies comparing Thalidomide versus prednisolone
- BPRC, Hyderabad
 - 104 steroid dependent patients switched to Thalidomide as out-patients. No formal assessments.
- Evidence gap

ENL

- Second line agents
 - Cyclosporine, azathioprine, methotrexate, zafirlukast, infliximab.
 - All need assessing in large studies using validated scales
- Women under-represented
- Quality of life

ENL- Research Recommendations

1. Development of scales for international use.
2. A trial comparing prednisolone and Thalidomide in leprosy out-patients.
3. Then develop treatment guidelines.
4. Develop second line drugs- azathioprine, cyclosporine
5. Identifying patients at risk of ENL
6. develop safe and effective alternatives to steroids and Thalidomide.

Summary T1R and ENL

1. Absence of evidence
2. Studies needed on dose and duration of steroid treatment
 1. No dose / weight studies done
3. Role of steroids and thalidomide in ENL needs evidence
4. Second line treatments in both T1R and ENL needed
5. Studies needed in Africa, Asia and Brazil