

Restless Legs Syndrome

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Oxford, UK.
November 1 2019

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Definition

1. An urge to move the limbs, usually associated with parasthesia/dyaesthesia
2. Motor Restlessness
3. Symptoms exclusively while at rest, with relief (completely or partially) with movement.
4. Symptoms worse at night.
5. Cannot be solely attributed to another cause.

International RLS Study Group – Definition of RLS (2012)

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Not all ESKD patients
with a disturbance of their legs
have Restless Legs Syndrome.

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Differential diagnosis

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- Leg cramps
- Peripheral neuropathy
- Osteoarthritis
- Pruritus
- Akathisia

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Associations

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Sleep disturbance

Daytime somnolence

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Premature cessation of dialysis sessions

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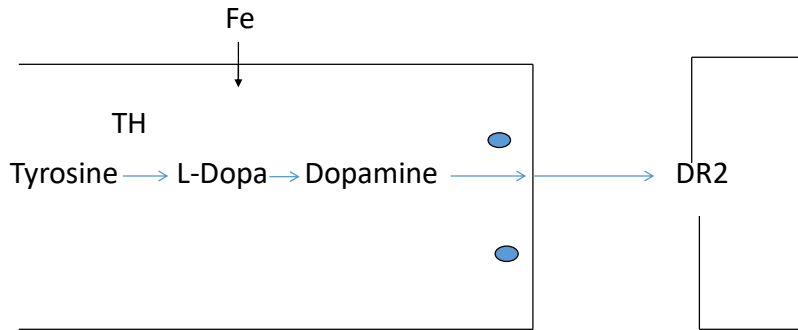
- Reduced QOL
- Hypertension
- New CVS events
- Mortality

Novak M et al.
Restless Legs Syndrome in Patients with CKD.
Sem. in Nephrology 2015; 35(4): 347-358.

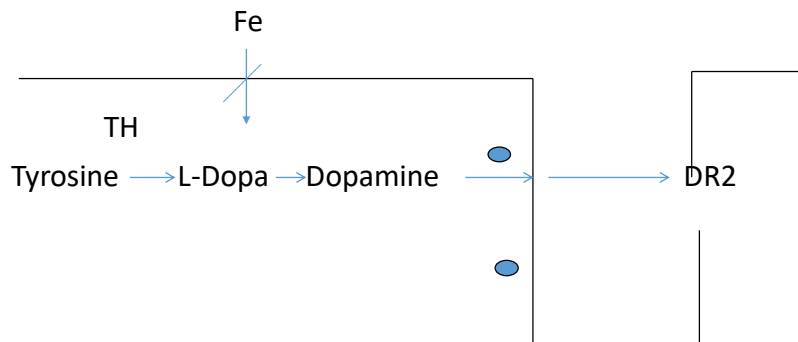
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Mechanism is not completely understood

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Management

Dopamine agonists

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- **Non-Ergot Dopamine Agonists (Pramipexole, Ropinirole, Rotigotine)**
- Ergot-Dopamine Agonists (Pergolide, Cabergoline) – not used.

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- Augmentation

- Rebound

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Gabapentinoids
($\alpha 2\delta$ calcium-channel ligands)

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Two RCTs have shown efficacy for Gabapentin in the treatment of RLS in Dialysis patients

1. Placebo controlled – Thorp et al (2001)
2. Gabapentin compared to Levo-dopa – Micozkadioglu et al (2004)

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Three RCT comparing Pregabalin, Pramipexole and placebo.

Heuber et al. *Neurology* 2013; 80: 738-742

Allen RP et al. *N Eng J Med* 2014; 370; 621-632

Garcia-Borroguero MD. *Sleep* 2014; 37(4): 635-643.

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Two found that Pregabalin was significantly more efficacious than Pramipexole and placebo in treating uraemic RLS.

Heuber et al. *Neurology* 2013; 80: 738-742

Garcia-Borroguero MD. *Sleep* 2014; 37(4): 635-643.

One found Pregabalin provided significantly improved treatment over placebo but not Pramipexole. Also Pregabalin caused statistically less augmentation.

Allen RP et al. *N Eng J Med* 2014; 370; 621-632

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Opioids

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Opioids have a protective effect on dopamine cells that have been subject to Fe deficit.

Sun YM et al. *J Neurol Sci* 2011;304:93-101

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Oxycodone

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Prolonged release oxycodone / naloxone
Severe, treatment-resistant RLS treatment
RCT, double blind, placebo –controlled.

Trenkwalder C et al. *Lancet Neurology* 2013; 12: 1141-1150.

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Prolonged release oxycodone / naloxone
Severe, treatment-resistant RLS treatment
RCT, double blind, placebo –controlled.

Dose oxycodone 5mg / naloxone 2.5 mg bd – adjusted.
Primary end point – change in RLS severity score at 12 weeks.

Trenkwalder C et al. *Lancet Neurology* 2013; 12: 1141-1150.

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Significant improvement in:

- Severity of RLS
- Subjective quality of sleep
- Overall QOL

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Significant improvement in:

- Severity of RLS
- Subjective quality of sleep
- Overall QOL

Withdrew due to adverse events in intervention group – 15 %
versus 7 % in placebo group.

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Methadone

Silver N et al. *Sleep Medicine* 2011;12:440-444

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Fe infusions

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IVI 1000mg Iron Dextran

Statistically improved RLS over placebo.
Effect faded at 4 weeks.

Sloand JA et al. *Am J Kid Dis* 2004; 43: 663-670.

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Intradialytic exercise

Giannaki CD et al. *BMC Nephrol* 2013; 14: 194.

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International Guidelines

European Federation of Neurological Societies (2012)

International RLS Study Group (2016)

International Parkinson and Movement Disorder Society (2018)

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International RLS Study Group (2016)

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Because of the issue of augmentation
we recommend
commencing Gabapentinoids first
before the dopamine agonists.

Garcia-Borreguero D et al. *Sleep Medicine* 2016; 21:1-11.

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If severe augmentation or
treatment-resistant
consider opioids – oxycodone, methadone.

Garcia-Borreguero D et al. *Sleep Medicine* 2016; 21: 1-11

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- Gabapentinoids
- Dopamine Agonists
- If severe augmentation or treatment-resistant consider opioids – oxycodone, methadone.

Garcia-Borreguero D et al. *Sleep Medicine* 2016; 21: 1-11

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The clinical experience
at St George Hospital, Sydney

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Between March 2009 and October 2019
596 patients completed a symptom survey at
their first
Renal Supportive Care service visit

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Of those 596 patients:

- 33% dialysis patients
- 55% conservatively managed patients
- 4% transplant patients
- 8% Undecided

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Following those patients
who had at least 3 clinic visits.

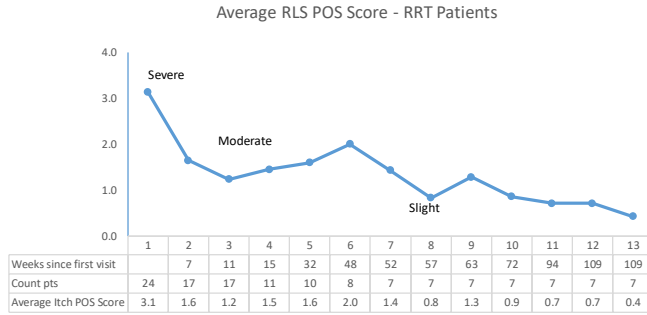
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Of those who presented at first clinic visit with RLS
that was reported as “severe” to “overwhelming”...
what happened over time ?

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RLS Score- patterns - (RRT) patients

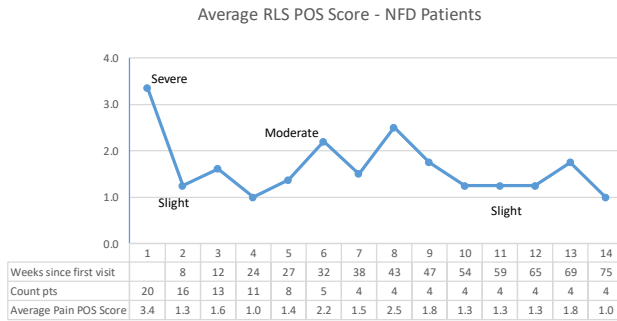
- for patients with more than one visit
- for patients that scored 3-4 for RLS on their first visit (**Severe to overwhelming**)
- for clinic visits where there were 5 or more patients



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RLS Score- patterns - Conservative (NFD)

- for patients with more than one visit
- for patients that scored 3-4 for RLS on their first visit (**Severe to overwhelming**)
- for clinic visits where there were 5 or more patients



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