

Gabapentin versus Levodopa-c for the Treatment of Restless Leg Syndrome in Hemodialysis Patients: A Randomized Clinical Trial

BACKGROUND:

- Restless Leg Syndrome (RLS) symptoms occurs more frequently in hemodialysis patients than the normal population.
- Dopaminergic agonists (like levodopa-c) are the drugs of choice for treating RLS, whereas gabapentin has shown improved sensorimotor symptoms in RLS patients, reduced leg movements, and improved sleep architecture.

OBJECTIVE

- The study's objective was to compare the efficacy between gabapentin and levodopa-c for reducing the RLS symptoms and sleep problems in hemodialysis patients with RLS in a 4-week randomized clinical trial (after a 4-week wash-out period).

METHODS

- **Design:** Single site, double-blinded, randomized clinical trial; Duration: 4 weeks
- **Inclusion criteria:** presence of all four characteristics with a minimum score of 10 for the International Restless Leg Syndrome (IRLS) questionnaire, minimum time of hemodialysis of three months, an age more than 15 years, and no evidence of other cause on neurological examination.
- **Exclusion criteria:** psychotropic agents during the four weeks prior to the study, presence of another neurological disease comorbid with ESRD (such as CVA, MS, etc.), iron deficiency, and pregnancy.
- **Primary outcome measure:** Compare mean reductions in the IRLS total score from baseline between gabapentin and levodopa-c.
- **Secondary outcome measures:** compare sleep disturbances, duration, and latency between the 2 regimens.
- 82 patients (42 in gabapentin group, 40 in levodopa-c group) received either
 - Gabapentin 200 mg given three times weekly at the end of hemodialysis, 2 hours before night bedtime
 - OR
 - Levodopa-c 110 mg given as a single dose 2 hours before night bedtime
- A minimum sample size of 32 patients in each group with an expected standard deviation of less than five scores showed an alpha of 0.05, and a power of 0.90.
- Data handling method was exclusion-of-subjects (per protocol)

RESULTS

- **Primary outcome measure:** Gabapentin significantly improved the IRLS total scores (change from baseline to post-treatment ~-17) compared to levodopa-c (change from baseline to post-treatment ~-13) (P: 0.016).
- **Secondary outcome measures:**
 - Sleep disturbances: When comparing gabapentin and levodopa-c, gabapentin was significantly superior to levodopa for sleep disturbances (P< 0.0001).
 - Sleep duration: Both gabapentin and levodopa-c improved sleep duration compared with baseline (P<0.05).
 - Sleep latency: Both gabapentin and levodopa-c improved sleep latency compared with baseline (P<0.05). When comparing gabapentin and levodopa-c, gabapentin was significantly superior to levodopa for sleep latency (P<0.001).

- Sleep quality: Both gabapentin and levodopa-c improved sleep quality compared with baseline ($P < 0.05$). When comparing gabapentin and levodopa-c, gabapentin was significantly superior to levodopa for sleep quality ($P < 0.0001$).

Author's conclusion: The study shows that gabapentin (200 mg daily) is a safe and effective treatment over levodopa-c (110mg) for RLS in hemodialysis patients in the short term. Thus, this medication may be considered as an alternative or additive treatment to current therapeutic remedies for this conundrum.

STRENGTHS

- No conflicts of interest

LIMITATIONS

- Uncertain about blinding throughout trial
- Using questionnaires (subjective tests) to identify efficacy of the trial
- More likely to see AE with gabapentin. (Administered three times weekly vs. levodopa-c daily)
- Dosages between drugs are variable (Levodopa-c at minimum, and Gabapentin low).
- Duration of drugs may not have been long enough, especially for Levodopa-c
- Washout period may not have been significant enough
- No data provided to account for adherence
- Weak active control group

CONCLUSION

- Gabapentin may have a role in RLS symptoms in hemodialysis patients since gabapentin showed improvements in mean IRLS total score and sleep measurements, especially for daytime sleepiness. A bigger study and more research is needed to compare gabapentin vs. higher dosages of levodopa-c or other dopaminergic agonists for treating RLS symptoms.
- Future research
 - Further research is needed in this field. The study was found to be small and did not use objective tests to identify the efficacy for treatment between regimens. The study did not explain how the patients and research team were masked, if unblinding occurred, and the type of formulations the patients were given or if the patients were compliant with their regimen. Therefore, one can not justify that gabapentin is superior to levodopa-c in the treatment of RLS symptoms in hemodialysis patients.

Reference: Razazian N, Azimi H, Heidarnejadian J, Afshari D, Ghadami MR. Gabapentin versus levodopa-c for the treatment of restless legs syndrome in hemodialysis patients: a randomized clinical trial. Saudi J Kidney Dis Transpl. 2015; 26(2):271-8.

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