International Journal of Innovative Technologies in Social Science

e-ISSN: 2544-9435

Scholarly Publisher
RS Global Sp. z O.O.
ISNI: 0000 0004 8495 2390

Dolna 17, Warsaw,
Poland 00-773
+48 226 0 227 03
editorial_office@rsglobal.pl

ARTICLE TITLE	RESTLESS LEG SYNDROME AS A REASON OF CHRONIC INSOMNIA
ARTICLE INFO	Jakub Jędrychowski, Natalia Pacocha, Natalia Karpowicz, Julia Kaszucka, Justyna Popczyńska, Agnieszka Raczyńska, Małgorzata Krzyżanowska, Marta Zgierska, Kinga Kosiec, Oliwia Krzemień. (2024) Restless Leg Syndrome as a Reason of Chronic Insomnia. *International Journal of Innovative Technologies in Social Science*. 4(44). doi: 10.31435/ijitss.4(44).2024.3040
DOI	https://doi.org/10.31435/ijitss.4(44).2024.3040
RECEIVED	15 November 2024
ACCEPTED	24 December 2024
PUBLISHED	30 December 2024
LICENSE	The article is licensed under a **Creative Commons Attribution 4.0 International License.**

RESTLESS LEG SYNDROME AS A REASON OF CHRONIC INSOMNIA

Jakub Jędrychowski *(Corresponding Author)*
Faculty of Medicine, Medical University of Warsaw, Poland
ORCID ID: 0009-0002-8496-292X

Natalia Pacocha
Faculty of Medicine, Medical University of Warsaw, Poland
ORCID ID: 0009-0001-3370-9521

Natalia Karpowicz
Faculty of Medicine, Medical University of Warsaw, Poland
ORCID ID: 0009-0000-6636-9546

Julia Kaszucka
Faculty of Medicine, Medical University of Warsaw, Poland
ORCID ID: 0000-0002-9017-3604

Justyna Popczyńska
Faculty of Medicine, Medical University of Warsaw, Poland
ORCID ID: 0009-0008-7654-932X

Agnieszka Raczyńska
Faculty of Medicine, Medical University of Warsaw, Poland
ORCID ID: 0000-0002-0423-3325

Małgorzata Krzyżanowska
Faculty of Medicine, Medical University of Warsaw, Poland
ORCID ID: 0009-0003-6287-5777

Marta Zgierska
Faculty of Medicine, Medical University of Warsaw, Poland
ORCID ID: 0009-0007-4472-0631

Kinga Kosiec
Faculty of Medicine, Medical University of Gdańsk, Poland
ORCID ID: 0009-0008-8756-3012

Oliwia Krzemień
Faculty of Medicine, Medical University of Gdańsk, Poland
ORCID ID: 0009-0003-1863-3025

ABSTRACT

Restless legs syndrome (RLS) is characterized by discomfort in the lower limbs with a strong need to move to bring relief. Based on the available literature and numerous studies on patient groups, we decided to summaries the aetiologias, risk factors, epidemiologies, and treatments for RLS. It is one of the most common causes of insomnia in both adult and child populations. Particularly at risk of developing RLS are people suffering from chronic renal failure, and pregnant women. Causes of RSL include mainly iron deficiency, and disturbances in dopaminergic transmission. Diagnosis is made primarily on the basis of the presence of symptoms, their severity, and frequency. Treatment first recommends non-pharmacological methods in the form of warm baths, massages, relaxation exercises, and avoidance of triggers. At a later stage, patients with more intractable symptoms are treated with oral iron supplementation, dopaminergic agonists, and alpha-2-delta ligands.

KEYWORDS

Restless Leg Syndrome, Insomnia, Dopaminergic Agents, Alpha-2-Delta Ligands, Ferritin, Iron, Limb Movements

CITATION

Jakub Jędrychowski, Natalia Pacocha, Natalia Karpowicz, Julia Kaszucka, Justyna Popczyńska, Agnieszka Raczyńska, Małgorzata Krzyżanowska, Marta Zgierska, Kinga Kosiec, Oliwia Krzemień. (2024) Restless Leg Syndrome as a Reason of Chronic Insomnia. *International Journal of Innovative Technologies in Social Science*. 4(44). doi: 10.31435/ijitss.4(44).2024.3040

Introduction.

Restless legs syndrome (RLS) is characterised by an unpleasant sensation in the lower limbs with a strong urge to move, including walking bringing relief. It occurs at rest and intensifies at night causing sleep problems. Restless legs syndrome can be primary (idiopathic) or secondary, associated with chronic renal failure, iron deficiency or occurring during pregnancy. In most patients, the disorder is mild severity. In such cases, non-pharmacological treatment methods, e.g. massage, hot baths, are usually satisfactory (Gossard, Trotti, Videnovic & St Louis, 2021). 1.5%-2.7% of sufferers have symptoms 2 or more times a week. In these patients, treatment may consist of pharmacotherapy with dopamine receptor agonists or Alpha-2-delta ligand (Silber et al, 2021).

Materials and Method.

A review of the literature available in the "PubMed" databases was conducted. The search was performed by using the following keywords: rapid legs syndrome, insomnia, alpha-2-delta ligand, dopamine agonist, sleep disorders.

Results and Discussion.

Restless legs syndrome is a common disorder leading to chronic insomnia at any age. It occurs in approximately 7-10% of adults. It is more common in women. Most studies show that the incidence of RLS increases after the age of 65 years (Gossard et al, 2021). Children and adolescents are also a diseased group with the prevalence of the syndrome ranging between 1-4% (Gossard et al, 2021; Silvestri & DelRosso, 2021], also more common in girls (Silvestri & DelRosso, 2021). Interestingly, only 1-3% of patients experience persistent, intractable symptoms. Particularly in younger patients, a familial occurrence of up to 87-90.9% has been proven (Silvestri & DelRosso, 2021).

The International Restless Legs Syndrome Study Group (IRLSSG) has set out the criteria necessary for the diagnosis of the syndrome (Allen et al, 2014):

1. The desire to move the legs, which is usually, but not always, accompanied by uncomfortable and unpleasant sensations in the legs, or which is felt to be caused by such sensations.

2. The urge to move the legs and the accompanying uncomfortable sensations start or increase during periods of rest or inactivity, such as lying or sitting.

3. the urge to move the legs and any accompanying unpleasant sensations are partially or completely relieved by movement, such as walking or stretching, at least as long as the activity continues.

4. The urge to move the legs and any accompanying unpleasant sensations during rest or inactivity occur or are worse in the evening or at night than during the day.

5. the presence of the above features is not solely a primary symptom of another medical or behavioural condition (e.g. muscle pain, venous stasis, leg swelling, arthritis, leg cramps, position-related discomfort, habitual foot tapping).

The most common cause of restless legs syndrome (RLS) is iron deficiency. It remains questionable whether central iron levels or peripheral iron levels have a greater influence on the occurrence of symptoms. The current prevailing theory is that brain iron deficiency is the key biological factor leading to RLS. This hypothesis explains the presence of symptoms due to peripheral tissue hypoxia (Gossard et al, 2021). The most important indicator besides serum iron concentration is ferritin concentration. Studies have shown that the determination of ferritin can be helpful in the diagnosis of RLS, as its decrease is an important risk factor for the syndrome (Li, Yeh & Hsu, 2023). It has also been shown that iron substitution in patients with iron deficiency can not only alleviate the symptoms of restless legs syndrome, but also reduce the risk of its onset (Li, Yeh & Hsu, 2023).

A second risk factor for restless legs syndrome (RLS), is chronic renal failure. A number of studies have shown that chronic dialysis patients suffer significantly more often than people in the general population. Up to 15-30% of dialysis patients have been shown to suffer from RLS (Safarpour, Vaziri & Jabbari, 2023). Also very often in this group, RLS occurred together with depressive disorders (Szentkiralyi et al, 2009). Furthermore, it has been shown that patients reporting RLS symptoms during haemodialysis, after renal transplantation, reported resolution of symptoms within a maximum of 21 days (Winkelmann, Stautner, Samtleben & Trenkwalder, 2002; Azar, Hatefi & Talebi, 2007).

An increased prevalence of restless legs syndrome has been observed in women during pregnancy (Grover, Clark-Bilodeau & D'Ambrosio, 2015); Nowakowski, & Meers, 2019). Studies have shown that up to 20% of pregnant women suffer from RLS, which is the third most common cause of sleep disorders in pregnancy (Nowakowski, & Meers, 2019). Most commonly, RLS symptoms were reported by women in the third trimester (Tuna Oran, Yuksel & Ruzgar, 2021). The hypothesis for this relationship focuses on the increased secretion of prolactin during pregnancy, which decreases dopamine levels which increases the risk of RLS symptoms (Grover, Clark-Bilodeau & D'Ambrosio, 2015).

A particular group of patients at risk of RLS are post-stroke patients. Moreover, despite the lateralisation of other symptoms resulting from stroke, RLS symptoms usually occur bilaterally and are detected much later than in the general population (Woo, Lee, Hwang, & Ahn, 2017).

Polysomnography can be a useful test in the diagnosis and assessment of the course and severity of restless legs syndrome (Liang et al, 2024). However, it is not recommended in the routine diagnosis of patients (Becker, 2015).

The basis for relieving the symptoms of restless legs syndrome are non-pharmacological methods. These include avoiding alcohol, caffeine, nicotine, and stimulant antidepressants. Taking warm baths, massages, and relaxation exercises are recommended. It is also necessary to maintain sleep hygiene with avoidance of falling asleep at all costs. However, acupuncture, cryotherapy or vibrating devices have not been shown to be effective during exercise (Vlasie, Trifu, Lupuleac, Kohn, & Cristea, 2022).

The first step in the pharmacological treatment of patients suffering from restless legs syndrome is oral iron supplementation. It has been shown that it can significantly reduce the severity of symptoms especially in patients with peripheral iron values < 75ug/dL (During, & Winkelman, 2019; Vlasie et al, 2022).

If intractable, frequent RLS symptoms are present, it is recommended to implement therapy with dopaminergic agonists. Long-term therapy with levodopa has been shown to be effective in reducing the frequency and severity of symptoms with relatively few side effects. Unfortunately, tolerance to treatment has been demonstrated, resulting in the need to increase doses during therapy (Vlasie et al, 2022; Comella, 2014).

If treatment with dopamine agonists is ineffective, therapy should be changed to treatment with an Alpha-2-delta ligand like gabapentin or pregabalin (Vlasie et al, 2022; Klingelhoefer, Bhattacharya, & Reichmann, 2016; Comella, 2014).

An alternative treatment is the use of carbamazepine preparations, but despite the proven efficacy there are many side effects of such therapy. Lamotrigine and topiramate are also used to treat RLS symptoms (Vlasie et al, 2022).

In Europe, a formulation containing a combination of oxycodone and naloxone is possible in patients who do not achieve the expected effects of the above-mentioned therapies. Some patients have been shown to respond positively to such treatment (Comella, 2014).

A number of trials of magnesium supplementation to alleviate the symptoms of RLS are known; unfortunately, the efficacy of this treatment has not been proven and it is not recommended (Marshall et al, 2019).

Conclusions.

Restless legs syndrome (RLS) is one of the most common causes of insomnia, which can lead to chronic fatigue, mood disorders including depressive disorders. RLS can occur at any age regardless of gender. Patients with chronic renal failure, especially those on dialysis, peripheral iron deficiency and pregnant women are particularly at the highest risk. Diagnosis is mainly based on the patient's physical examination, taking into account the frequency and severity of symptoms. The mainstay of treatment is still non-pharmacological methods with an emphasis on sleep hygiene in combination with iron supplementation in those with iron deficiency. In most cases of RLS of mild severity, such methods are satisfactory for patients. For moderate to severe cases of the syndrome, treatment with dopaminergic agonists or Alpha-2-delta ligand is recommended.

Conflict of Interest Statement.

No conflicts of interest to declare.

REFERENCES

1. Gossard, T. R., Trotti, L. M., Videnovic, A., & St Louis, E. K. (2021). Restless Legs Syndrome: Contemporary Diagnosis and Treatment. *Neurotherapeutics : the journal of the American Society for Experimental NeuroTherapeutics*, *18*(1), 140–155. https://doi.org/10.1007/s13311-021-01019-4
2. Silber, M. H., Buchfuhrer, M. J., Earley, C. J., Koo, B. B., Manconi, M., Winkelman, J. W., & Scientific and Medical Advisory Board of the Restless Legs Syndrome Foundation (2021). The Management of Restless Legs Syndrome: An Updated Algorithm. *Mayo Clinic proceedings*, *96*(7), 1921–1937. https://doi.org/10.1016/j.mayocp.2020.12.026
3. Silvestri, R., & DelRosso, L. M. (2021). Pediatric Restless Legs Syndrome. *Sleep medicine clinics*, *16*(2), 305–314. https://doi.org/10.1016/j.jsmc.2021.02.006
4. Allen, R. P., Picchietti, D. L., Garcia-Borreguero, D., Ondo, W. G., Walters, A. S., Winkelman, J. W., Zucconi, M., Ferri, R., Trenkwalder, C., Lee, H. B., & International Restless Legs Syndrome Study Group (2014). Restless legs syndrome/Willis-Ekbom disease diagnostic criteria: updated International Restless Legs Syndrome Study Group (IRLSSG) consensus criteria--history, rationale, description, and significance. *Sleep medicine*, *15*(8), 860–873. https://doi.org/10.1016/j.sleep.2014.03.025
5. Li, Y. S., Yeh, W. C., & Hsu, C. Y. (2023). Association of low serum ferritin levels with augmentation in patients with restless legs syndrome: A systematic review and meta-analysis. *Sleep medicine*, *112*, 173–180. https://doi.org/10.1016/j.sleep.2023.10.022
6. Safarpour, Y., Vaziri, N. D., & Jabbari, B. (2023). Restless Legs Syndrome in Chronic Kidney Disease- a Systematic Review. *Tremor and other hyperkinetic movements (New York, N.Y.)*, *13*, 10. https://doi.org/10.5334/tohm.752
7. Szentkiralyi, A., Molnar, M. Z., Czira, M. E., Deak, G., Lindner, A. V., Szeifert, L., Torzsa, P., Vamos, E. P., Zoller, R., Mucsi, I., & Novak, M. (2009). Association between restless legs syndrome and depression in patients with chronic kidney disease. *Journal of psychosomatic research*, *67*(2), 173–180. https://doi.org/10.1016/j.jpsychores.2009.05.004
8. Winkelmann, J., Stautner, A., Samtleben, W., & Trenkwalder, C. (2002). Long-term course of restless legs syndrome in dialysis patients after kidney transplantation. *Movement disorders : official journal of the Movement Disorder Society*, *17*(5), 1072–1076. https://doi.org/10.1002/mds.10231
9. Azar, S. A., Hatefi, R., & Talebi, M. (2007). Evaluation of effect of renal transplantation in treatment of restless legs syndrome. *Transplantation proceedings*, *39*(4), 1132–1133. https://doi.org/10.1016/j.transproceed.2007.03.097
10. Grover, A., Clark-Bilodeau, C., & D'Ambrosio, C. M. (2015). Restless leg syndrome in pregnancy. *Obstetric medicine*, *8*(3), 121–125. https://doi.org/10.1177/1753495X15587452
11. Nowakowski, S., & Meers, J. M. (2019). Cognitive Behavioral Therapy for Insomnia and Women's Health: Sex as a Biological Variable. *Sleep medicine clinics*, *14*(2), 185–197. https://doi.org/10.1016/j.jsmc.2019.01.002
12. Tuna Oran, N., Yuksel, E., & Ruzgar, S. (2021). Prevalence of restless leg syndrome and effects on quality of life during pregnancy. *Sleep & breathing = Schlaf & Atmung*, *25*(4), 2127–2134. https://doi.org/10.1007/s11325-021-02311-5
13. Liang, R., Zhu, W., Gao, Y., Zhao, C., Zhang, C., Xu, L., Zuo, Y., Lv, Y., Zhao, M., Li, C., Gao, J., Mei, J., Gong, X., Zhang, L., Shen, S., Yang, C., Ren, J., Liu, Y., Wang, Z., Wang, P., … Han, F. (2024). Clinical features, polysomnography, and genetics association study of restless legs syndrome in clinic based Chinese patients: A multicenter observational study. *Sleep medicine*, *117*, 123–130. https://doi.org/10.1016/j.sleep.2024.03.022
14. Becker P. M. (2015). Diagnosis of Restless Leg Syndrome (Willis-Ekbom Disease). *Sleep medicine clinics*, *10*(3), 235–xii. https://doi.org/10.1016/j.jsmc.2015.05.001

15. Woo, H. G., Lee, D., Hwang, K. J., & Ahn, T. B. (2017). Post-stroke restless leg syndrome and periodic limb movements in sleep. *Acta neurologica Scandinavica*, *135*(2), 204–210. https://doi.org/10.1111/ane.12582
16. During, E. H., & Winkelman, J. W. (2019). Drug Treatment of Restless Legs Syndrome in Older Adults. *Drugs & aging*, *36*(10), 939–946. https://doi.org/10.1007/s40266-019-00698-1
17. Vlasie, A., Trifu, S. C., Lupuleac, C., Kohn, B., & Cristea, M. B. (2022). Restless legs syndrome: An overview of pathophysiology, comorbidities and therapeutic approaches (Review). *Experimental and therapeutic medicine*, *23*(2), 185. https://doi.org/10.3892/etm.2021.11108
18. Klingelhoefer, L., Bhattacharya, K., & Reichmann, H. (2016). Restless legs syndrome. *Clinical medicine (London, England)*, *16*(4), 379–382. https://doi.org/10.7861/clinmedicine.16-4-379
19. Marshall, N. S., Serinel, Y., Killick, R., Child, J. M., Raisin, I., Berry, C. M., Lallukka, T., Wassing, R., Lee, R. W., Ratnavadivel, R., Vedam, H., Grunstein, R., Wong, K. K., Hoyos, C. M., Cayanan, E. A., Comas, M., Chapman, J. L., & Yee, B. J. (2019). Magnesium supplementation for the treatment of restless legs syndrome and periodic limb movement disorder: A systematic review. *Sleep medicine reviews*, *48*, 101218. https://doi.org/10.1016/j.smrv.2019.101218
20. Comella C. L. (2014). Treatment of restless legs syndrome. *Neurotherapeutics : the journal of the American Society for Experimental NeuroTherapeutics*, *11*(1), 177–187. https://doi.org/10.1007/s13311-013-0247-9