

SLEEP-RELATED MOVEMENT DISORDERS

Denis Martinez^{1,2*}, Maria do Carmo Sfreddo Lenz²

1. *Cardiology Unit – Hospital de Clínicas de Porto Alegre – Universidade Federal do Rio Grande do Sul, Brazil*

2. *Sleep Clinic – Rio Grande do Sul, Brazil*

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*Correspondence:

Serviço de Cardiologia

Hospital de Clínicas de Porto Alegre

Universidade Federal do Rio Grande do Sul

Rua Ramiro Barcelos, 2350 - Porto Alegre, RS - Brasil - 90035-903

E-mail: dm@ufrgs.br

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ABSTRACT

Movement disorders or disturbances (MD) comprise an important subset of sleep medicine. Among the known types of MDs, two are considered to be of great importance: disorders related to periodic limb movements in sleep (PLMS) and restless leg syndrome (RLS), which usually occur during sleep or at the transition between waking and sleep. These two problems tend to be associated and are frequently referred to by the common acronym RLS/PLMS. In addition to these, sleep related cramps, sleep bruxism and rhythmic movements make up the range of sleep-related movement disorders listed in the International Classification of Sleep Disorders. The present paper reviews the epidemiological, etiological, diagnostic and therapeutic aspects of these diseases.

Keywords: sleep; sleep disorders; movement disorders; restless legs syndrome; periodic limb movements.

INTRODUCTION

Sleep disorders are common but often neglected causes of human suffering. Due to the structuring of the sleep medicine and sleep societies spread throughout the world, there have been international efforts to analyze the mounting literature on the subject. The second edition of the International Classification of Sleep Disorders has recently been completed and published (ICSD-2). Periodic Limb Movement Disorder (PLMD) and Restless Legs Syndrome (RLS) are the primary themes of the chapter dealing with sleep-related movement disorders (SRMD).

Today, there are 72,027 articles containing the word “sleep” indexed in the ISI Web of Science. Among the 50 most frequently cited articles is one that for the first time defined the criteria for

diagnosing RLS in operational terms, with almost 500 citations (1). The present paper offers a review of the diagnostic and therapeutic aspects of SRMD.

PERIODIC LIMB MOVEMENT DISORDER

Originally termed nocturnal myoclonus, this disorder was described by Symonds (2) in 1953 as a manifestation of epilepsy. In 1972, Lugaresi and collaborators (3) recorded the first map of periodic limb movements (PLM) using polysomnography (PSG).

These events are characterized by periodic, stereotyped movements, similar to the Babinski reflex. They involve stretching of the great toe, generally associated with a partial flexion of the foot

and leg, occasionally reaching the thigh and hip. Such movements primarily involve the legs, although less frequently they may also affect the arms and trunk. The movements may vary from night to night, simultaneously involving both legs, but may be predominant in one limb or the other.

The periodicity of the movements is quite marked, suggesting the existence of some underlying mechanism, such as a pacemaker. Four burst in a sequence is necessary to characterize PLM. The interval between the movements varies between 5 and 90 seconds, but 70% occur at intervals of 30 seconds or less (Figure 1). Each contraction lasts from 0.5 to 5 seconds and induces a pronounced increase in the electromyographic register at least five times above the baseline.

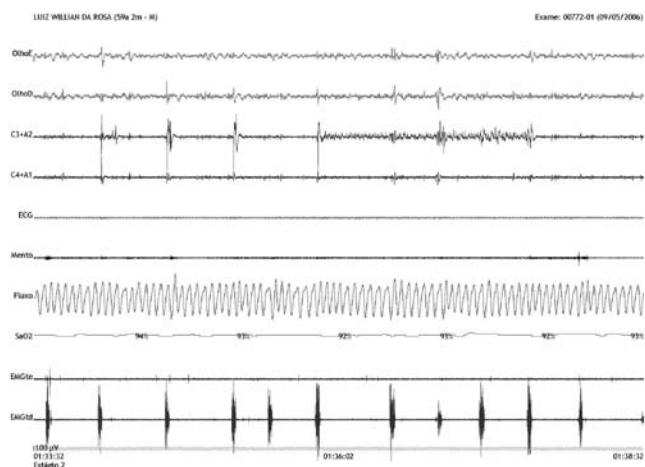


Figure 1. PLMS polysomnographic register during 5 minutes with predominance of the right anterior tibial muscle in the electromyography (EMGtd).

MECHANISMS

Frequently, each PLM is followed by a cortical excitation visible in the sleep electroencephalogram (EEG) or by a short autonomic activation. This excitation in the EEG can be expressed as short cortical awakenings, with the emergence of alpha waves for 3 to 15 seconds, micro-awakenings, K-complexes, K-alpha complexes (4) and delta wave surges. The autonomic activation is expressed as an increase in cardiac and respiratory frequency. In sporadic cases, PLMS is associated with light or fragmented sleep (5), as well as complaints of insomnia. Intense movements can promote full arousal, with restoration of consciousness and occasionally difficulty in returning to sleep, thus leading to insomnia.

Changes in the sleep EEG can match the movement, follow it or precede it. This variety of temporal associations suggests the existence of a central process that generates the cortical excitation and the movement, e.g., a pacemaker. PLM, therefore, instead of being the reason for sleep instability, may just be an epiphenomenon of the normal periodic excitation process which is observed in the sleep EEG, termed cyclic alternating pattern (CAP) (6). CAP is characterized by a recurrent sequence of excitatory activity (phase A) and inhibitory activity (phase B) in the EEG in cycles of

20 to 40 seconds.

Terzano and Parrino state that CAP is the expression of a basic excitation modulator. Such a modulator emerges in normal non-REM (NREM) sleep, causing the emergence of K-complexes and other excitatory phasic events in the EEG, coupled with autonomic excitation represented by fluctuations in blood pressure and cardiorespiratory frequency (7). In normal individuals, up to 50% of NREM sleep can show CAP. Increases in the percentage of NREM sleep with CAP have been linked to sleep instability (8,9). Phase A of CAP would represent “permission” for the occurrence of PLM. It was observed that in twelve cases of PLMS followed by complaints of insomnia, 94% of the contractions occurred during the excitation cycles in the EEG in phase A, most at an interval of one second from the onset of the excitation period. Nevertheless, PLM episodes were not always concomitant with phase A. Thus, it can be concluded that phase A allows the occurrence of a PLM episode but does not cause it. The effect of sleep upon the PLM generator seems to be inhibitory. Spinal cord dissection, either partial or full, prevents central inhibition from reaching the legs and increases the probability of a PLM episode, both in paraplegic (10) individuals and in models of spinal cord injury in rats (11). In cases of PLMS, subjects show a reduction in the sleep period and greater sleep fragmentation. In addition, NREM sleep duration in the presence of CAP is 15% longer than in controls. The fact that CAP is responsible for PLM periodicity but does not induce contractions leads to the conclusion that the causes of the contractions are the same as those underlying RLS, including changes in iron metabolism (12).

EPIDEMIOLOGY

In adults, the prevalence of PLMS varies from 5% to 11%; in elderly people, it may reach as high as 30% (13). In children, the prevalence is around 6%, but this increases in children with associated diseases. PLMS can occur as an isolated condition or associated with other sleep disorders. RLS is followed by PLMS in 80-90% of the cases, and such a high degree of co-occurrence has led some authors to raise the hypothesis that RLS/PLM is a single disorder, where PLMs represent the painless form fruste – or precursor – of RLS (14).

The prevalence of PLMS increases with age, regardless of its association with other sleep disorders. When other sleep disorders are present, the prevalence may reach 80%, as happens among RLS sufferers. Greater prevalence is also observed in patients with narcolepsy, REM behavioral disorders (70%) (15) and sleep apneas. PLMs may occur either associated with apneas or as independent episodes. In patients suffering from severe apnea associated with a significant number of PLMs, apnea should be treated before evaluating the clinical relevance of the PLMD (16).

DIAGNOSIS

Since PLM episodes occur during sleep, they usually are not noticed by the patient. The search for a diagnosis occurs mainly as a function of the close association with RLS. PLMS diagnosis

is conducted primarily in the PSG, but screening for cases can be performed using actigraphy (17). The severity of the disorder is given by the PLM index (PLMI; Table 1), which is obtained by dividing the number of PLMs by the number of sleeping hours observed in the PSG. Non-periodic movements, PLMs inducing to awakening and PLMs during wakefulness, which may indicate the presence of RLS, are also reported in the PSG.

Table 1. PLMS severity indices

DISORDER DEGREE OF SEVERITY	NUMBER OF PLMS PER HOUR
Normal	up to 5/hour
Mild	from 5 to 24/hour
Moderate	from 25 to 50/hour
Severe	More than 50/hour

TREATMENT

Since many patients with PLMS are asymptomatic, the need for treatment is controversial. PLMS can be an incidental finding in the PSG, and treatment will not always resolve the symptoms that motivated the investigation, typically insomnia or excessive diurnal sleepiness. One of the reasons for the persistence of symptoms despite treatment might be the fact that PLMS occurs as an epiphenomenon of excessive central excitability, with awakenings and EEG activation in phase A of CAP (18). Thus, eliminating PLMs would not eliminate either awakenings or the sleep instability shown by the increased CAP; thus, it would not result in any symptomatic improvement. Since no criteria have been established in clinical studies to determine which cases should be treated, the decision depends on clinical judgement. When PLMS is associated with sleep obstructive apnea-hypopnea syndrome, treating apneas with CPAP masks reduces PLMI (19). Treatment for PLMS is the same as for RLS and effectively reduces PLMI. Upon performing a therapeutic test, evaluation of the symptomatic benefits obtained with a reduction in PLMI should guide the decision about proceeding with treatment for PLMS.

RESTLESS LEG SYNDROME

Restless leg syndrome (RLS) is a common neurological condition that involves motor and sensory symptoms that follow a circadian pattern. It is characterized by an almost irresistible urge to move the legs and is associated with countless unpleasant symptoms that are engendered or exacerbated by rest and relieved by walking or moving the legs. In 1672, RLS was described by Thomas Willis (20), but only in 1945 was the condition understood as it is today. Karl Ekbom (21) observed that 5% of patients showed restless leg symptoms and described the characteristics of the syndrome. Even so, until the 1990's it was considered an uncommon disorder.

EPIDEMIOLOGY

In 1994, Lavigne and Montplaisir (22) published data on 2,019 Canadians showing a prevalence of 12% and confirming that RLS was indeed a common disorder, though not frequently diagnosed. The percentage of RLS was substantially larger among French Canadians compared to British Canadians, suggesting a genetic component. Most studies on prevalence have been conducted only in recent years, and it has been found that prevalence varies widely as a function of population characteristics and the methods applied. Studies conducted in other countries show that prevalence is estimated between 7% and 11%.

Most surveys show that the prevalence of RLS increases with age. Nevertheless, a bimodal distribution has been observed: the onset of RLS symptoms usually occurs before the patient is 30 years old when a genetic component is present, but later in the absence of such a component (23). In addition, the prevalence is higher among females (24-26). Studies have also demonstrated that during pregnancy, the prevalence of RLS ranges from 19% (27,28) to 26% (29). The prevalence of RLS in children has not been well demonstrated. It has been observed that RLS is prevalent in adults who experienced childhood pains; in addition, the parents of children who have experienced childhood pains show a higher prevalence of RLS than control parents (30).

ETIOLOGY

Despite progress in studies related to RLS and advanced methods that can be used to study the disorder, the cause for the disorder still remains unexplained in most cases. In view of this, the syndrome has been classified as follows:

1. Idiopathic

It is estimated that 60-80% of the cases are classified as idiopathic or cryptogenic and that half of them are hereditary in nature. In a study conducted with twelve pairs of monozygotic twins, it was seen that the RLS symptoms were concurrent in 10 pairs (31). Despite the high rate of concurrence, the age of onset of symptoms and the severity of such symptoms varied among the pairs. In all likelihood, the syndrome is not caused by a single genetic fault, but by a hereditary complex, as seen in other disorders like Alzheimer's disease.

2. Secondary

Association with several health conditions (e.g., pregnancy, uremia, iron deficiency or polyneuropathies) leads to classification of the disease as secondary RLS. There are at least two proven causal mechanisms (Chart 1):

2.1. Alterations in iron metabolism in the CNS

Iron metabolism can play an important role in RLS secondary to pregnancy, anemia, gastric surgery and renal disease, and under these conditions the symptoms usually recede with iron supplementation (32). A clear relationship has been observed between low concentrations of ferritin and symptoms of RLS, particularly when ferritin levels are measured in the cerebrospinal fluid. Anal-

ysis of the substantia nigra in cases of RLS submitted to autopsy compared to that of controls without RLS shows a complex pattern of abnormalities: iron, H-ferritin and two primary iron carriers are reduced, while ferritin levels are increased, as expected in cases of iron deficiency. Nevertheless, the number of transferrin receptors is reduced, contrary to the expected response to iron deficiency (33). This suggests that in the presence of RLS, iron deficiency in the substantia nigra is likely to be associated with abnormalities in regulation of the transferrin receptor.

Chart 1. Causes of Secondary RLS

Uremia (34)
Diabetes
Anemias
Sleep disorders
- Periodic limbs movements
- Narcolepsy (35)
- REM sleep behavior disorders
- Sleep apneas (36)
- Insomnia
- Hypersomnia
Reumathoid arthritis (37)
Iron deficiency (38,39)
Ferritin deficit (40)
Folate deficit
Myelopathies
Polyneuropathies (41)
Radiculopathies
Multiple sclerosis
Fibromialgies (42)
Parkinson's Disease
Post-polio Syndrome
Neoplasias
Attention-deficit hyperactivity disorder (43-46)
Peripheral vascular insufficiency
Peripheral venous insufficiency
Drugs
- Caffeine
- Alcohol (47)
- Antidepressants
- Dopamine inhibitors (48)
- Lithium carbonate
- Neuroleptic agents

2.2. Dopaminergic neurotransmission

The optimal response to treatment of RLS with dopaminergic medication indicates the involvement of both the dopamine neurotransmitter and dopaminergic receptors in RLS pathophysiology. Iron is an important cofactor for tyrosine hydroxylase, an enzyme that inhibits dopamine synthesis and plays an important role in the functioning of D₂ receptors.

Worsening of RLS symptoms in the evening seems to be modulated by circadian factors. At night, a reduction in dopamine levels can be observed (49). Nevertheless, the only circadian marker

significantly correlated with RLS so far is melatonin. Apparently, melatonin exacerbates symptoms in the evening and at night due to its inhibitory effect on central dopamine secretion (50).

CLINICAL PICTURE

Patients experience a unilateral or bilateral unpleasant sensation, which is many times impossible to describe, but is sometimes described as twinges, shocks, electrical current, burning, paresthesias or pain. At the onset of the episode, discomfort is felt mainly deep inside the calf. As the disorder progresses, the feet, ankles and knees are also frequently affected. Other parts of the body (51), such as the arms (52), trunk and face, may also be impaired (53). Another characteristic of RLS is that rest, even in wakefulness, evokes motor and sensory symptoms. The concept of rest includes both physical immobility and reduction of alertness levels. Over 80% of patients have difficulty in falling and/or remaining asleep.

Circadian factors and immobility are RLS facilitators. Thus, going to bed in an attempt to fall asleep triggers discomfort. Moving the legs relieves the symptoms, if not completely, then at least partially or temporarily. Patients with RLS usually sleep better at daybreak. A large number of patients with RLS complain about fatigue and sleepiness and report that they do not have refreshing sleep. On the other hand, other do not have any complaints about fatigue or sleepiness. Results of studies conducted by Allen and collaborators (54) suggest that high levels of hypocretin in the CNS of patients with this disorder maintain the alert state, but their findings have not been confirmed in subsequent studies (55). Depression and anxiety symptoms, difficulty sleeping with a partner sharing the same bed and deterioration of quality of life are frequently reported by these patients (56).

DIAGNOSIS

1. Medical history

Diagnosis demands a description of the clinical history of sensory symptoms experienced by the patient. In 1995, the essential criteria for diagnosis were standardized by the international group of studies on RLS (IRLSSG). In 2003 (57), the IRLSSG reviewed and updated these criteria. The essential criteria should be utilized to confirm diagnosis, but ancillary criteria also provide useful clues (Chart 2). Diagnosis in children has its own peculiarities in view of the difficulty that children usually have in describing the sensations experienced in their legs (Chart 3).

Chart 2. Criteria for diagnosing RLS in adults (58)

ESSENTIAL CRITERIA

1. Urge to move the legs (with or without an unpleasant sensation; other parts of the body may also be involved, such as the arms).
2. Rest triggers or worsens symptoms.
3. Movement makes the unpleasant sensation vanish.
4. Symptoms get worse in the evening or at night.

ANCILLARY CRITERIA

1. Family history (50% of the idiopathic cases have a positive family history).
2. Response – at least at the beginning of treatment – to levodopa or dopamine receptor agonists at doses significantly lower than those used to treat Parkinson's disease.
3. Periodic limb movements during wakefulness or during sleep occur in at least 85% of patients with RLS.

ASSOCIATED CRITERIA

1. Variable clinical course, but typically chronic and progressive.
2. Normal physical tests in idiopathic/familial forms.
3. Sleep disorder is a common complaint in most patients affected.

Chart 3. Criteria for diagnosing RLS in individuals under 12 years of age

1. Criteria are the same as those for adults, as long as the child is able to clearly explain the uncomfortable symptoms felt in the legs.
2. If the child shows the essential criteria as those for adults but has difficulty in reporting the sensation of discomfort in the legs, then at least two of the following findings must be confirmed:
 - a. Disturbed sleep for his/her age
 - b. Parents or siblings with well defined RLS
 - c. Periodic limb movements registered in the PSG at a rate of 5 or more PLMs per hour.

2. Lab tests

The most useful lab tests are those involving iron metabolism. Serum ferritin is the primary indication that low iron reserves participate in RLS genesis. Another important aspect is the evaluation of renal function for detection of renal insufficiency and glycemia, in order to confirm the presence of diabetes mellitus.

3. Immobilization test

This test was developed for the purpose of inducing and exacerbating RLS motor and sensory manifestations in wakefulness, thus allowing their quantification. The test is run for one hour, before the patient's main sleep period, usually before the PSG. Motor manifestations are obtained through a register of the electromyography run on the right and left anterior tibial muscles. A high rate of periodic limb movements corroborates RLS diagnosis.

4. Polysomnography

RLS diagnosis is based primarily on the patient's clinical his-

tory. PSG, however, may contribute to detect the presence of PLMs, which occur in 80-90% of cases. The movements are measured through electromyography of the anterior tibial muscles. For the activity to be considered periodic, it should occur in sequences of at least four contractions lasting from 0.5 to 5 seconds, with a minimum interval of 5 seconds and a maximum interval of 90 seconds. Some publications, however, accept intervals between 4 and 120 seconds.

5. Actigraphy

The actigraph is worn on the wrist, like a watch, and registers the presence or absence of movements every minute for periods that may extend for weeks. Periods of immobility are correlated with sleep. The validity of the method for PLMS diagnosis, however, has not been well established.

DIFFERENTIAL DIAGNOSIS

Among the several manifestations that can be confounded with RLS are positional discomfort, cramps, "painful legs and moving toes syndrome," pains in the legs, acathisia induced by neuroleptic agents, intermittent vascular claudication, peripheral neuropathy and myelopathy.

Positional discomfort may occur when a patient is lying in bed, but may be relieved by changing position, without the need for making repetitive movements or wandering around. Cramps may be exacerbated at night and relieved with movement, as happens in RLS, but since they are localized and painful, they are usually easy to differentiate. In the "painful legs and moving toes syndrome," described in 1971 (59), the pain is typically intense (similar to that experienced in causalgia), affecting one or both feet and causing a burning sensation and frequent movement of the toes. Such symptoms may occur any time of the day and are not relieved by walking around. Several pains in the legs must be distinguished from RLS, such as neuropathic, vascular and traumatic pains. RLS can be triggered by dopaminergic antagonists, as well as by neuroleptic-induced acathisia. In acathisia, however, the difference lies in the absence of a circadian pattern and in relief with levodopa.

TREATMENT

Treatment of RLS can be pharmacological or not, and should be individualized according to the situation when the syndrome occurs also in subjects with no comorbidity. When the patient has an ongoing condition such as pregnancy, breast-feeding or any other condition associated with end-stage renal disease, treatment of RLS demands specific approaches.

1. Non-Pharmacological

Before anything else, it is essential to investigate and exclude manageable medical conditions that induce RLS and also ensure that the patient is not using antidopaminergic or antidepressant agents.

Adequate measures concerning sleep hygiene should be imple-

mented before starting the pharmacological treatment. Patients should avoid consuming caffeine, alcohol, nicotine and substantial meals right before bedtime; they should also maintain a regular bedtime schedule and gradually reduce night activities (60).

If the serum ferritin concentration is below 45–50 mcg/L, iron levels should be restored. In these cases, a combination of ferrous sulfate and vitamin C is indicated. Iron levels should be monitored through the control of ferritin levels every 3 or 4 months.

2. Pharmacological

Four categories of drugs are normally prescribed to treat RLS: dopaminergic agents, anticonvulsive agents, opioid substances and benzodiazepines.

2.1. Dopaminergic drugs

2.1.a) Dopaminergic precursors

Levodopa or levodopa-benserazide. Levodopa was the first dopaminergic agent used to treat RLS and is still the initial choice. Nevertheless, its side effects with prolonged use are such that they make the use of levodopa as a standard drug impracticable.

2.1.b) Dopaminergic agonists

Dopaminergic agonists may be ergotaminic or non-ergotaminic. Ergotaminic agonists (e.g., bromocriptine, pergolide and cabergoline) are associated with frequent side effects. Non-ergotaminic dopaminergic agonists (e.g., such as ropinirole and pramipexol) are currently considered first line drugs for treating RLS, as they are more effective and do not cause as many side effects as dopamine precursors.

Pramipexol has high affinity for the D3 dopamine receptor and shows sustained efficacy in over 90% of patients with RLS (61). Nausea and orthostatic hypotension on the first day of administration are common side effects. Ropinirole, a dopaminergic agonist similar to pramipexol, is well tolerated by patients and has a 24-hour half-life. It is metabolized in the liver, and is therefore indicated in cases of RLS caused by renal insufficiency.

2.1.c) Side effects of dopaminergic drugs

Dopaminergic precursors are effective, although many times they can trigger side effects that make their use impracticable. Among these effects are nausea, vomiting, tachycardia, postural hypotension, rebound and symptom exacerbation.

Morning rebound is characterized by recurrence of RLS symptoms in the morning period as a result of the drug having been taken the previous night at bedtime. It occurs while the circulating drug is eliminated, which happens within a time period comparable with the drug half-life.

Augmentation (exacerbation) (62) is an increase in symptoms, an intriguing phenomenon that is peculiar to RLS. This term is used to describe the occurrence of exacerbated symptoms over a larger period, that is, two or three hours prior to the time when the symptoms used to emerge prior to taking the drug started, in at least five out of seven days. Augmentation is less prevalent with the use of dopaminergic agonists than with levodopa; even so, the phenomenon can be observed in more than 32% of patients undergoing long term treatment with the drug (63).

2.2. Anticonvulsants:

Within this category, the preferred drug is gabapentin, in view of its greater effectiveness and fewer side effects, including light sleepiness that can be desirable in cases of insomnia. It is most useful in managing the augmentation phenomenon. It is also the first choice in cases of RLS associated with painful neuropathy, as well as in patients that describe pain as an RLS sensorial component.

2.3. Benzodiazepines:

The effect of such drugs upon RLS symptoms is not significant, and they are typically used as a coadjuvant therapy to help sleep maintenance in patients with RLS. They are used when dopaminergic agents show stimulating effects that exacerbate insomnia. Clonazepam is preferred in view of its extended half-life.

2.4. Opioids:

Opioids are classified into two groups according to their potency: low potency opioids (e.g., codein and tramadol) and high potency opioids (e.g., morphine, methadone and oxycodone). Opioids are well tolerated, and their efficacy lasts for extended periods. Addiction and abuse are quite rare, even in the case of methadone, which is used in cases of RLS associated with painful diabetic neuropathy (64).

THERAPEUTIC SCHEMES

Symptom regularity and severity may vary depending on the patient, indicating the need for individualized control (65). Therapeutic approaches can be devised for three levels of RLS (Chart 4):

- *Intermittent*: when symptoms cause a degree of discomfort sufficient to require treatment, but their occurrence is not frequent enough to justify daily use of medication.
- *Daily*: when symptoms cause a degree of discomfort sufficient to require treatment and are so frequent that they require daily use of medication.
- *Refractory*: when the patient under treatment with a dopaminergic agonist shows one or more of the following reactions:
 - a) inadequate initial response despite dose adequacy;
 - b) inadequate response over the course of time despite an increase in dosage;
 - c) intolerable side effects;
 - d) side effects, like augmentation, which are not controlled with preventive additional doses.

Chart 4. Approach of RLS.

	Non-Pharmacological	Pharmacological
Intermittent	<ul style="list-style-type: none"> • Sleep hygiene • Assessment and treatment of primary disease • Withdraw of alcohol, caffeine, nicotine. • Withdraw of drugs witch cause RLS. • Iron replacement when necessary 	<ul style="list-style-type: none"> • Dopaminergic agonists • Dopaminergic precursors • Benzodiazepines • Low potency opioids
Daily	<ul style="list-style-type: none"> • Sleep hygiene 	<ul style="list-style-type: none"> • Dopaminergic agonists • Gabapentin • Low potency opioids
Refractory	<ul style="list-style-type: none"> • Sleep hygiene 	<ul style="list-style-type: none"> • Change between dopaminergic agonists • Change dopaminergic agonists by gabapentin • Keep dopaminergic agonists and add gabapentin • Add low potency opioids • Change to high potency opioids

CONCLUSION

Not much attention has been given to RLS, but it is a disease that may impair quality of life and must, therefore, be treated. The use of dopaminergic agonists has simplified control of this disease.

Sleep-Related Cramps

Sleep-related cramps are characterized by painful sensations caused by sudden and intense involuntary contractions of muscles, usually in the calf, occurring during sleep. The cramp can be relieved by strongly stretching the affected muscle and sometimes by local massage, application of heat or movement of the affected limb. Nearly every adult over the age of 50 has experienced cramps at least once in their lifetime. Both the prevalence and frequency of the number of nights in which such episodes occur usually increase with age. Among children and adolescents, about 7% have been reported to have sleep-related leg cramps, but children under 8 almost never experience this kind of discomfort. Among older people, 33% above the age of 60 and 50% above the age of 80 report experiencing cramps at least once every two months, and 6% of adults above the age of 60 experience cramps every night (66). In studies conducted in the city of São Paulo in 1987 and 1995, it was found that the prevalence of nocturnal cramps ranged from 2.6% to 5.8% in samples comprising 1,000 adults, but frequency was not studied (67). Predisposing factors are: diabetes mellitus, peripheral vascular disease and metabolic diseases. The disorder is associated with prior vigorous exercise, electrolytic disorders, endocrine diseases, neuromuscular diseases and medications such as oral contraceptives. Sleep-related cramps

occur in about 40% of pregnant women and generally resolve after delivery. No familiar pattern is known. Complications include muscular pain, insomnia and occasional diurnal fatigue. A large majority of cases of nocturnal cramps seems to be idiopathic, with no relation to other diseases (68). RLS registers intense non-periodic electromyographic activity of the gastrocnemius muscle. The episodes occur during sleep, and no specific physiologic changes are observed.

Sleep-Related Bruxism

Bruxism or nocturnal tooth grinding is characterized by grinding or clenching of the teeth during sleep, usually associated with sleep arousals. Contraction of masticatory muscles can be isolated and sustained, termed tonic contraction, or can occur through a series of phasic muscle contractions, termed rhythmic. Friction may lead to abnormal wear of the teeth, tooth pain, jaw muscle pain or temporal headache. Sleep-related bruxism may also result in sleep disruption. Severe cases usually lead to limitation of jaw movements. Bruxism may also occur during the waking period, but a correlation with sleep bruxism is not known. Bruxism is termed primary when there is not a clear triggering cause, and secondary bruxism may be associated with the use of psychoactive medications, recreational drugs or other diseases (e.g., infantile cerebral paralysis and mental retardation). There is a correlation between bruxism episodes and stressful situations or anxiety related to current life events. It seems to occur most frequently among highly motivated or vigilant individuals. The use of cigarettes and caffeine in hours before sleep contributes to increased tooth grinding.

Sleep-related bruxism is frequently reported in childhood but decreases with age; nevertheless, in some subjects tooth grinding may be observed every night across their life span. The prevalence in children ranges from 14% to 17%; in adolescents and young adults, it is around 12%; in adults, it is around 8%; and in older people, it is around 3%. Between 20% and 50% of subjects have at least one member in the family showing a history of bruxism.

Bruxism episodes are preceded by autonomic cardiac activation 4-8 minutes before the masticatory activity starts. Four seconds before that, an increase in cerebral activity is registered in the PSG and, in 90% of the cases, alpha waves with microarousings are registered in the EEG. One second before the onset of a bruxism episode, an increase in the cardiac frequency and in the suprahyoid muscular tonus occurs, followed by a contraction of the masseter muscles and tooth grinding (69). Electromyography of the masseter muscles shows either a phasic activity pattern with a frequency varying from 0.25 to 2 seconds, a sustained tonic activity lasting for more than two seconds or otherwise a mixed pattern. It could be said that a new episode of bruxism is distinguished when at least three seconds have elapsed without the occurrence of any muscular activity. Movements caused by tooth grinding can be video-monitored. Bruxism may occur during any sleep stage, but over 80% of typical episodes occur in stages 1 and 2 of NREM sleep, while less than 10% occur during REM sleep. Rarely is bruxism predominant in REM sleep. The disorder is diagnosed as bruxism when at least four episodes per hour of sleep or 25 individual surges of muscular activity per hour of sleep occur, with at least two audible tooth grinding episodes and no

abnormal activity being registered in the EEG.

Treatment remains controversial. The literature is concentrated mainly on the use of bite guards to avoid tooth wear, but evidence cited in an updated study performed by Cochrane in October, 2007, was considered insufficient to ensure that dental devices were effective for treating bruxism (70). Other therapeutic attempts remain inconclusive. Despite the success of dopaminergic agents for treating MDs, only one study so far has investigated their effect on bruxism, demonstrating that L-Dopa reduces the number and the intensity of masticatory episodes (71). In view of this lack of evidence, but based on experience with hundreds of cases, the authors think that bruxism can be considered to be another DM that adequately responds to dopaminergic medications, mainly pramipexol.

CONCLUSION

Knowledge about the mechanisms of the disorders reviewed here enables the prevention of undesirable effects caused by erroneous treatments (e.g., the use of hypnotic drugs to treat RLS), which may perpetuate and aggravate the suffering of individuals with misdiagnosed conditions.

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