

# SLEEP BRUXISM TREATMENT

Flávio Alóe\*

*Centro de Distúrbios Vigília-Sono, Instituto de Psiquiatria, Universidade de São Paulo. São Paulo, SP.*

\*Correspondence

Flávio Alóe

Rua Joaquim Floriano, 871 - conjunto 43

04534-013 - São Paulo | SP, Brazil

E-mail: piero.ops@terra.com.br

Received May 29, 2008; accepted December 26, 2008

## ABSTRACT

SB treatment is based on a combination of behavioral treatment, pharmacological treatment, and dental treatment according to the carrier's profile. Secondary SB treatment should be tailored to the specific cause, in addition to any necessary procedures described below.

Behavioral treatment encompasses drugs suppression, sleep hygiene measures, relaxation techniques, and behavioral treatment for anxiety.

Primary and secondary SB pharmacology employs dopaminergic agonistic drugs, anxyolytic benzodiazepinics, clonidine, buspirone, non-benzodiazepinic hypnotics (zolpiden), muscle relaxers, antidepressants, such as mirtazapine, trazodone, and antiepileptic drugs, such as gabapentine. Local application of botulinic toxin to the masseter and temporal muscles may be used in cases of secondary bruxism or severe SB.

Association of behavioral strategies and dental protection appliances seem to be the most adequate therapeutic measures for mid- and long-term bruxism treatment.

**Keywords:** sleep bruxism, behavioral treatment, pharmacological treatment, dental treatment

## SLEEP BRUXISM TREATMENT

At present there is not a single treatment regimen or strategy that results in the remission of SB. A few years ago, the objectives of primary SB treatment aimed to prevent damage to orofacial structures and relieve complaints of pain. Today, primary SB treatment is also based on the physiopathological mechanisms of the condition(1,2).

Evaluation of SB treatment results is difficult for several reasons. There is a broad inter- and intra-individual variability in the intensity and frequency of SB medical and odontological objectives and subjective symptoms. In addition, there are no well delimited clinical rates, such as standardized scales or questionnaires for post-treatment reassessment (2-4). Utilization of the golden standard, that is, videopolysomnography, is technically limited, economically prohibitive in some contexts, restricted by local availability, in addition to the abovementioned limitation

related to inter- and intra-individual variability in the intensity and frequency of polysomnographic markers. SB treatment utilizes a combination of behavioral treatment, dental and pharmacological treatment according to the carrier's profile (1-3,5). Secondary SB treatment should focus on the specific cause, coupled with the measures described below whenever these are also indicated.

### 1. General Measures

Avoidance of medications that trigger SB, such as antipsychotic dopaminergic neurotransmission antagonists, serotonin reuptake inhibitor antidepressants, and calcium channel blockers and inhibitors (6-13).

### 2. Behavioral Treatment

Behavioral treatment includes sleep hygiene measures, bio-feedback, relaxation techniques, stress control techniques, and hypnotherapy.

### 2.a. Sleep hygiene

Sleep hygiene is a set of instructions which aims to correct personal habits and environmental factors that interfere with sleep quality (14). These instructions are as follows:

1. Avoid consumption of coffee, tea, stimulants, chocolate, and medications containing caffeine.
2. Avoid drinking alcohol at least six hours before bedtime.
3. Avoid smoking for at least six hours before bedtime.
4. Avoid eating heavy meals before bedtime.

### 2.b. Biofeedback

Biofeedback is a relaxation technique with concomitant monitoring of certain physiological variables, such as electromyography, skin temperature, cardiac frequency, blood pressure, and electrodermal activity. The patient receives specialized training with the objective of teaching them how to relax. More specifically, the patient observes and controls the physiological functions that are monitored by equipment. The positive effects of the treatment are generally only observed during the treatment period (15) – the beneficial effects are generally not observed after the treatment ends (11).

### 2.c. Relaxation techniques

Relaxation techniques include (1) specific methods for relaxing mandibular muscles, such as relaxing the jaw with the lips closed and separated several times a day and (2) voluntary clenching and subsequent unclenching of the teeth for five seconds each; this exercise should be repeated for a total of five times per series with six series per day over a two-week period (11,16,17).

### 2.d. Anxiety behavioral treatment

Personality profile, stress and anxiety are major factors in SB. Nevertheless, no controlled studies determining the effectiveness of anxiety behavioral treatment for clinical SB symptoms have been developed. Cognitive behavioral psychotherapy, cognitive relaxation techniques for managing stress and anxiety coupled with changes in lifestyle have been suggested (1,16).

### 2.e. Hypnotherapy

Hypnotherapy or self-hypnosis is a specific relaxation technique. A study conducted by Clarke et al. with 8 SB carriers demonstrated that hypnotherapy produced objective and subjective improvements in SB symptoms during a 36-month follow-up period (18).

## 3. Pharmacological Treatment

No specific pharmacological treatment for primary SB or diurnal bruxism (DB) has reported long-term effectiveness (1-3,16). A range of drugs have been suggested for pharmacological treatment, but only a few controlled studies that have evaluated efficacy, pharmacological safety and corresponding effects upon SB have been conducted (13,16) (Table 1).

Table 1. Drugs and sleep bruxism

Pharmacological agents	Efficacy
<b>Muscle relaxants, sedatives, anxiolytics:</b>	
Diazepam	Reduction
Clonazepam	Reduction
Metocarbamol, baclofen	?
Zolpiden	?
<b>Dopaminergic agents:</b>	
L-dopa	Reduction
Bromocriptine	Without studies
Pramipexole / Ropirinoles	Without studies
Pergolide	?
<b>Beta-adrenergic agonists:</b>	
Clonidine	Reduction
<b>Antidepressants:</b>	
Amitriptyline	Exacerbation
SSRI	Exacerbation
Venlafaxine	Exacerbation
Mirtazapine	Without studies
Trazodone	Without studies
Agomelatine	Without studies
<b>Others</b>	
Buspirone	Reduction
Botulinum toxin A	Reduction

### 3.a. Zolpiden

Zolpiden (5-10 mg per dose) is a non-benzodiazepine non-anxiolytic agonist hypnotic of the imidazopyridine class that selectively binds to the omega-1 GABA-benzodiazepine receptor complex. This drug has a short half-life (2 to 3 hours) and is used for treating acute insomnia and comorbid chronic insomnia (14).

Zolpiden is also marketed in a second format, with two release phases: one quick phase (30 minutes) for sleep induction, and one slower phase with a half-life of approximately 6 hours.

Clinical studies reporting zolpiden's positive effects upon sleep have been conducted. Such studies involved patients with Parkinson's disease, supranuclear progressive paralysis, restless leg syndrome, and REM sleep behavioral disorders. Significant motor symptom improvements for these four hypodopaminergic conditions were observed in these studies (19-23).

The reason for improvement in cases of Parkinson's disease, progressive supranuclear paralysis, and restless leg syndrome are likely due to the high density of zolpiden receptors in base ganglions (24). Thus, according to hypodopaminergic evidence in SB genesis, the positive effects of zolpiden on diseases that involve dopaminergic alterations may indicate similar improvement in sleep bruxism. In addition, zolpiden would also likely act positively upon arousals that occur before abnormal masticatory muscle activity (14,25). This is, however, an untested hypothesis; clinical studies for the treatment of SB using zolpiden in either of its two presentation modes have not yet been developed.

### 3.b. Antidepressants

A double-blind study of amitriptyline (25 mg per dose) conducted in a study population of ten female SB carriers demonstrated

that amitriptyline did not reduce masseter electromyographic activity, nor did it increase the total sleep period in a statistically significant manner (26,27).

An antidepressant with an agonist dopaminergic profile, such as amineptine or bupropion, may be useful for the treatment of SB, pursuant to the hypothesis that dopaminergic deregulation is important in SB (28,29).

An antidepressant with an 5HT<sub>2A</sub> postsynaptic receptor blocker antagonist profile, such as mirtazapine (7.5-30 mg per dose), trazodone (50-100 mg per dose), ritanserine (5-10 mg per dose), or agomelatine (25-50 mg per dose), increases the amount of slow wave sleep in both normal volunteers and individuals suffering from depression (28-30). These agents are alternatives to be considered in SB treatment, as abnormal oromandibular activity is less plentiful and intense in deep sleep or delta sleep stages, and an increase in delta sleep quantity would play a protective role against SB (1,2,3,23,28). Another effect of the blocking action performed by the 5HT<sub>2A</sub> postsynaptic receptor is increased dopaminergic neurotransmission in the prefrontal cortex (29).

Despite these associations, a controlled study of mirtazapine, trazodone, ritanserine, mianserine, or agomelatine for the treatment of SB has not yet been conducted. Agomelatine, a melatonin receptor agonist with antidepressant activity and a 5HT<sub>2A</sub> antagonist profile shows the best potential among antidepressants for the treatment of SB.

### 3.c. Bupirone

Bupirone is a partial agonist serotonergic agent used for the treatment of generalized anxiety. Bupirone shows a pharmacological profile, with activity on 5-HT<sub>1</sub> postsynaptic receptors and 5-HT<sub>2A</sub> receptor antagonist activity (7).

A report of four bruxism cases indicates that patients administered sertraline felt subjective relief of SB after introduction of a 10 mg bupirone night dose. Bupirone (10-40 mg per dose) can be particularly useful for treating SB when co-administered with a selective serotonin reuptake inhibitor antidepressant and duals agents, such as venlafaxine (7,13).

### 3.d. Anticonvulsant agents

Some anticonvulsant agents (ACA), such as gabapentine, topiramate, tiagabine, and pregabalin, promote sleep stability in epileptic subjects (31). In addition to this effect, such agents promote a reduction in arousals and increases in delta and REM sleep in healthy individuals, epileptic subjects, and patients suffering from insomnia (31).

Gabapentine, a GABAergic agonist, is indicated as a coadjuvant agent in the treatment of generalized anxiety, essential tremors, as a central painkiller in postherpetic pain, diabetic peripheral neuropathy or trigeminal neuralgia, and for treating restless leg syndrome and nocturnal myoclonus (14,19,31). Anxiety and pain are frequently associated with SB. The frequency decrease of arousals and the increase of delta sleep associated with central painkillers in addition to the ansiolytic effects and an improvement of restless leg syndrome and nocturnal myoclonus treatment make gabapentine an attractive option for treating SB. Gabapentine (1200 to 1800 mg/day) is quite effective for treating restless leg syndrome

and nocturnal myoclonus, which are comorbid conditions that are associated with approximately 10% of SB cases (19).

A previous study has demonstrated the therapeutic effect of gabapentine (300 mg per dose) administered at bedtime to a patient carrying secondary bruxism relative to treatment with venlafaxine. Another study has demonstrated benefits achieved with tiagabine (9,32). So far, no studies assessing the therapeutic effect of topiramate, pregabalin, valproic acid or lamotrigine for SB have been conducted.

### 3.e. Clonazepam

Clonazepam is a benzodiazepine ansiolytic with an extended half-life. It is used for treating anxiety disorders, epileptic syndromes and involuntary movement disorders (tremors). It is also used as a muscle relaxer and as a hypnotic agent for treating acute insomnia or comorbid chronic insomnia. In addition, clonazepam is used as a coadjuvant agent for the treatment of restless leg syndrome and nocturnal myoclonus, which are related to a central dopamine deficiency (19). Clonazepam is the first choice treatment for REM sleep behavior disorders. REM sleep motor disorders are highly prevalent in Parkinson's syndrome (23). Clinical evidence of the effectiveness of clonazepam for controlling involuntary movements cause by hypodopaminergic syndromes, as well as its ansiolytic effects qualify clonazepam as an potentially effective and safe agent for the treatment of SB. In addition, clonazepam should also reduce arousals that occur before RMMA episodes (14).

The only reported randomized double-blind study conducted with clonazepam for the treatment of SB included ten subjects with SB showing anxiety and depression symptoms. These subjects were administered one dose of clonazepam (1 mg dose) 30 minutes before bedtime. This group showed positive results in anxiety and depression psychometric tests and improved subjective sleep quality. In addition, based upon polysomnographic rates, clonazepam administration resulted in improved sleep efficiency, sleep latency and total sleep period, and reductions in the number of lower limb periodic movements and bursts of masticatory muscle activity during sleep (33).

Benzodiazepine's neurocognitive effects, such as sedation and ataxia, should be considered before starting treatment. Moreover, extended use of benzodiazepines exposes the patient to risks concerning tolerance and dependence (14).

### 3.f. Dopaminergic agents

The association of restless leg syndrome and other dopaminergic disorders with SB suggests a therapeutic role of dopaminergic agents in SB (34). Literature regarding the efficacy of dopaminergic agents for SB is limited and inconclusive. The clinical double-blind study conducted by Lobbezoo et al. in 1997 with low L-dopamine doses and benserazide administered to primary SB carriers demonstrated only one attenuating effect upon 30% of bruxism symptoms (35).

Bromocriptine, a dopamine D<sub>2</sub> receptor agonist, was evaluated only one placebo-controlled double-blind study for the treatment of SB (36). Bromocriptine (7.50 mg dose) did not reduce the frequency of tooth grinding episodes during sleep, nor did it decrease the amplitude of masseter muscle contractions as evalu-

ated by polysomnography (36).

So far, no studies with other synthetic dopamine agonists (pergolide, cabergoline, pramipexole, or ropinirole) for the treatment of SB have been conducted.

### 3.g. Adrenergic agents

The hypothesis that deregulation of central mechanisms occurs with an increase in sympathetic tonus 3 minutes before a bruxism episode during sleep supports the use of sympatholytic agents for the treatment of SB (37,38). Two agents that act upon adrenergic transmission, propranolol and clonidine, have been evaluated for the treatment of SB. Since propranolol acts upon the peripheral autonomic nervous system, a central action agent may provide greater positive effects than propranolol (39). Clonidine, a central selective alpha-2 agonist (0.1-0.3 mg per dose), is used for the treatment of arterial hypertension, attention-deficit hyperactivity disorder, and restless leg syndrome, and as a central painkiller. Clonidine suppresses REM sleep and increases the quantity of NREM sleep at stage II, but does not increase the quantity of delta sleep (14,19).

It has been reported that propranolol (120 mg per dose) is effective for treating patients with primary SB, and also for treating patients with secondary SB who are medicated with an antipsychotic (30).

In a randomized, placebo-controlled cross-over study coupled with active treatment (propranolol 120 mg and clonidine 0.30 mg) conducted in 2006, it was demonstrated that clonidine, not propranolol, was clinically effective for treatment SB symptoms. Clonidine significantly (70% positive rate response) reduced abnormal masticatory activity and reduced the frequency of teeth grinding bursts and the sympathetic tonus one minute before each teeth grinding burst (39).

Clonidine side effects include dry mouth, constipation, reduced libido, sleepiness, cognitive deficit, and clinically limiting arterial hypertension for 4 hours after arousal. In the present study, propranolol with a 120 mg dose before bedtime was not shown to be clinically effective.

### 3.b. Muscle relaxers

Baclofen, a GABA type B agonist (10-60 mg per dose), can be utilized for the treatment of SB symptoms; however, no controlled studies of its efficacy for the treatment of SB have been reported (1).

### 3.i. Botulinum toxin

Botulinum toxin type A (TXB-A) is an effective treatment for certain neurological disorders (40). The mechanism of action of TXB-A is blockage of acetylcholine release into neuromuscular junctions, which establishes a chemical denervation with muscular focal paresia. TXB-A has been used for the treatment of secondary bruxism related to other movement disorders, such as cervical dystonia, oromandibular facial dystonia, and Huntington's disease (40).

The clinical effect of TXB-A upon secondary bruxism can be observed within 2 to 4 days after injection. Its beneficial effects last for approximately 4 months. It also promotes a reduction in daily symptoms and in masseter and temporal muscle hypertrophy

(41). Treatment with TXB-A is relatively safe, and occurrence of dysphasia and facial and masticatory muscle palsy is rare.

A study that evaluated the use of TXB-A in 18 individuals that presented with teeth grinding refractory to other forms of clinical and odontological treatment was reported in 2000. According to the results of this study, TXB-A (25 to 100 MU per dose) effectively treated this SB symptom (42). TXB-A has been used for treating cases of secondary bruxism as well (41). No long-term studies of TXB-A efficacy for the treatment of primary or secondary bruxism have been reported.

### 3.j. Other medical treatments

It is important to treat gastroesophageal reflux in SB carriers, since the presence of gastroesophageal reflux and/ xerostomy are risk factors for development or progression of SB (43).

Approximately 3-5% of obstructive sleep apnea-hypoapnea syndrome carriers show SB. A study of this patient group indicated full remission of SB symptoms upon treatment of obstructive sleep apnea-hypopnea (44,45).

## 4. Dental Treatment

In cases of bruxism, dental alterations, as well as occlusal defects and dental restorations, should be duly treated (1,3,11).

Several types of intraoral appliances (dental plates) have been developed for the purpose of relieving local pain, preventing lesions in orofacial structures, and preventing temporomandibular articulation dysfunction (3).

The mechanisms of action of intraoral appliances and their effectiveness at reducing neuromuscular activity during sleep have not yet been well established (17,46).

The efficacy and safety of a non-occlusal intraoral appliance have been compared with those of a palatal control device in 9 bruxism carriers. Both devices led to 50% reductions in the frequency of teeth grinding episodes per hour of sleep. They also reduced the level of tooth grinding noise. No difference in the efficacy or safety of the two devices was observed (47). Recent studies that compared a stabilizer device and a palatal control device showed a reduction in masseter activity. Importantly, this reduction was transitory, as the device was used for just six weeks (48,49).

Long term adherence to treatment with dental plates is low – after one year, less than 20% of patients continue using the device (2). Moreover, data demonstrate that the number of respiratory pauses during sleep tends to increase with the use of non-occlusal intraoral appliances, including dental plates, in obstructive sleep apnea-hypoapnea syndrome carriers (50).

## REFERENCES

1. Alóe F, Gonçalves LG, Azevedo A, Barbosa RC. Bruxismo durante o sono. Rev Neurociências 2003;11:4-17.
2. Lavigne GJ, Manzini C, Kato T. Sleep Bruxism. In: Kryger MH, Roth T, Dement WC. Principles and Practice of Sleep Medicine. 4<sup>th</sup> edition. Philadelphia: WB Saunders, 2005. p. 946-59.

3. Bader G, Lavigne GJ. Sleep bruxism; an overview of an oromandibular sleep movement disorder. *Sleep Medicine Reviews* 2000;4:27-43.
4. Lavigne GJ, Guitard F, Rompré PH, Montplaisir JY. Variability in sleep bruxism over time. *J Sleep Res* 2001;10:237-44.
5. Thompson BA, Blount BW, Krumholz TS. Treatment approaches to bruxism. *Am Fam Physician* 1994;49:1617-22.
6. Amir I, Heremesh H, Gavish A. Bruxism secondary to antipsychotic drug exposure: a positive response to propranol. *Clin Neuropharmacol* 1997;20:86-9.
7. Bostwick JM, Jaffe MS. Buspirone as an Antidote to SSRI-Induced Bruxism in 4 Cases. *J Clin Psychiatry* 1990;60:857-60.
8. Boutrel B, Koob GF. What keeps us awake: the neuropharmacology of stimulants and wakefulness-promoting medications. *Sleep* 2004;27:1181-94.
9. Brown ES, Hong SC. Antidepressant-induced bruxism successfully treated with gabapentin. *JADA* 1999;130:1467-9.
10. Ellison JM, Stanziani P. SSRI-Associated nocturnal bruxism in four patients. *J Clin Psychiatry* 1993;54:432-4.
11. Leo R. Movement disorders associated with the serotonin selective reuptake inhibitors. *J Clin Psychiatry* 1996;57:449-54.
12. Micheli F, Pardo MF, Gatto M. Bruxism secondary to chronic anti-dopaminergic drug exposure. *Clin Neuropharmacol* 1993;16:315-23.
13. Winocur E, Gavish A, Voikovitch M, Emodi-Perlman A, Eli A. Drugs and bruxism: a critical review. *J Orofac Pain* 2003;17:99-111.
14. Alóe F, Tavares S. Transtornos do Sono. In: Lopes AC, Neto VA (Eds). *Tratado de Clínica Médica. Volume II. São Paulo: Editora Rocca, 2006. p. 2524-53.*
15. Foster PS. Use of the Calmset 3 biofeedback/relaxation system in the assessment and treatment of chronic nocturnal bruxism. *Appl Psychophysiol Biofeedback* 2004;29:141-7.
16. Pierce CJ, Gale EN. A comparison of different treatments for nocturnal bruxism. *J Dent Res* 1988;67:597-601.
17. Sjöholm T, Lehtinen I, Helenius H. Masseter muscle activity in diagnosed sleep bruxists compared with non-symptomatic controls. *J Sleep Res* 1995;4:48-55.
18. Clarke JH, Reynolds PJ. Suggestive hypnotherapy for nocturnal bruxism: A pilot study. *Am J Clin Hypnosis* 1999;33:248-53.
19. Alóe F, Tavares SM. Síndrome das pernas inquietas. *Rev Neurociências* 2006;14:204-213.
20. Bezerra MLS, Matinez JVL. Zolpidem in restless legs syndrome. *Eur Neurol* 2002;48:180-1.
21. Daniele A, Albanese A, Gainotti G, Gregori B, Bartolomeo P. Zolpidem in Parkinson's disease. *Lancet* 1997;349:1222-3.
22. Daniele A, Moro E, Bentivoglio AR. Zolpidem in progressive supranuclear palsy. *N Engl J Med* 1999;341:543-4.
23. Schenck C, Mahowald M. REM sleep behaviour disorder, clinical, developmental, and neuroscience perspective 16 years after its formal identification in SLEEP. *Sleep* 2002;25:120-38.
24. Niddam R, Dubois A, Scatton B, Arbilla S, Langer SZL. Autoradiographic localization of [<sup>3</sup>H] zolpidem binding sites in the rat CNS: Comparison with the distribution of [<sup>3</sup>H] flunitrazepam binding sites. *J Neurochem* 1987;49:890-9.
25. Kato T, Rompré PH, Montplaisir JY, Sessle BJ, Lavigne GJ. Sleep bruxism: an oromotor activity secondary to micro-arousal. *J Dent Res* 2001;80:1940-4.
26. Mohamed SE, Christensen LV, Penchas J. A randomized double-blind clinical trial of the effect of amitriptyline on nocturnal masseteric motor activity (sleep bruxism). *J Craniomandibular Pract* 1997;15:326-32.
27. Raigrodski AJ, Christensen LV, Mohamed SE, Gardiner DM. The effect of four-week administration of amitriptyline on sleep bruxism. A double-blind crossover clinical study. *Cranio* 2001;19:21-5.
28. Moreno RA, Moreno DH, Soares MBM. Psicofarmacologia de antidepressivos. *Rev Bras Psiquiatria* 1999;21:24-40.
29. Wilson S, Argyropoulos S. Antidepressants and sleep. A qualitative review of the literature. *Drugs* 2006;66:927-47.
30. Aslan S, Isik E, Cosar B. The effects of mirtazapine on sleep: A placebo controlled, double-blind study in healthy young volunteers. *Sleep* 2002;25:666-8.
31. Sammaritano M, Sherwin A. Effect of anticonvulsants on sleep. *Neurology* 2000;54:16-24.
32. Kast RE. Tiagabine may reduce bruxism and associated temporomandibular joint pain. *Anesth Prog* 2005;3:102-4.
33. Saletu A, Parapatics S, Saletu B, Anderer P, Prause W, Putz H, et al. On the pharmacotherapy of sleep bruxism: placebo-controlled polysomnographic and psychometric studies with clonazepam. *Neuropsychobiology* 2005;51:214-25.
34. Lavigne GJ, Montplaisir J. Restless legs syndrome and sleep bruxism: prevalence and association among Canadians. *Sleep* 1994;17:739-43.
35. Lobbezoo F, Lavigne GJ, Tanguay R, Montplaisir JY. The effect of catecholamine precursor L-dopa on sleep bruxism: a controlled clinical trial. *Mov Disord* 1997;12:73-8.
36. Lavigne GJ, Soucy JP, Lobbezoo F, Manzini C, Blanchet PJ, Montplaisir JY. Double-blind, crossover, placebo-controlled trial of bromocriptine in patients with sleep bruxism. *Clin Neuropharmacol* 2001;2:145-9.
37. Huynh NT, Kato T, de Champlain J, Rocques P, Leblanc R, Montplaisir J, et al. Sleep bruxism is associated with a higher sympathetic and a lower parasympathetic tone before the onset of masticatory muscle activation. *Sleep* 2003;26(suppl):A320.
38. Lavigne GJ, Kato T, Kolta A, Sessle BJ. Neurobiological mechanisms involved in sleep bruxism. *Crit Rev Oral Biol Med* 2003;14:30-46.
39. Huynh N, Lavigne GJ, Lanfranchi PA, Montplaisir JY, de Champlain J. The effect of 2 sympatholytic medications--propranolol and clonidine--on sleep bruxism: experimental randomized controlled studies. *Sleep* 2006;29:307-16.
40. Berardelli A, Mercuri B, Priori A. Botulinum toxin for facial-oral-mandibular spasms and bruxism. In: Jankovic J, Hallett M, ed. *Neurological disease and therapy, therapy with botulinum toxin. New York: Marcel Dekker; 1994. p. 361-7.*
41. Ivanhoe CB, Lai JM, Francisco GE. Bruxism After brain injury: successful treatment with botulinum toxin-A. *Arch Phys Med Rehabil* 1997;78:1272-3.
42. Tan EK, Jankovic J. Treating severe bruxism with botulinum toxin. *J Am Dent Assoc* 2000;131:211-6.
43. Miyawaki S, Tanimoto Y, Araki Y, Akira KA, Akihito FA, Teruko TY. Association between nocturnal bruxism and gastroesophageal reflux. *Sleep* 2003;26:888-992.
44. Okeson JP, Phillips BA, Berry DTR, Cook YR, Cabelka JF. Nocturnal bruxing events in subjects with sleep-disordered breathing and control subjects. *J Craniomandib Disord Facial Oral Pain* 1991;5:258.
45. Oksenberg A, Arons E. Sleep bruxism related to obstructive sleep apnea: the effect of continuous positive airway pressure. *Sleep Med* 2003;3:513-5.
46. Lobbezoo F, Rompré PH, Soucy JP, Iafrancesco C, Turkewicz J, Montplaisir JY, et al. Lack of association between occlusal-cephalometric measures

- side imbalance in striatal D2 receptors binding in sleep-related oromotor activities. *J Orofac Pain* 2001;15:64-71.
47. Dube C, Rompre PH, Manzini C, Guitard F, de Grandmont P, Lavigne GJ. Quantitative polygraphic controlled study on efficacy and safety of oral splint devices in tooth-grinding subjects. *J Dent Res* 2004;5:398-403.
  48. Harada T, Ichiki R, Tsukiyama Y, Koyano K. The effect of oral splint devices on sleep bruxism: a 6-week observation with an ambulatory electromyographic recording device. *J Oral Rehabil* 2006;33:482-8.
  49. van der Zaag J, Lobbezoo F, Wicks DJ, Visscher CM, Hamburger HL, Naeije M. Controlled assessment of the efficacy of occlusal stabilization splints on sleep bruxism. *J Orofac Pain* 2005;19:151-8.
  50. Gagnon Y, Manzini C, Mayer P, Morisson F, Rompré PH, Lavigne GJ. Aggravation of sleep apnea by the use of occlusal stabilization splint in apneic patients: a pilot study. *Sleep* 2003;26(suppl):A223.