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REVIEW

THERAPEUTIC APPROACHES TO NOCTURNAL BRUXISM – A SYSTEMATIC REVIEW

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Abstract

Introduction. The term "bruxism" defines the friction or "grinding" of the teeth and affects a large part of the population. The early diagnosis of bruxism is of great importance for its treatment and prevention.
The objective of the study was to conduct a systematic review of the therapeutic approaches of nocturnal bruxism, including only randomized controlled clinical trials published in the scientific literature.
Materials and methods. We analysed data from the following three databases: PubMed, ScienceDirect and Google Scholar. The EndNote program was used to finalize the selection of articles and simplify the collection of Vancouver-style bibliographic references. Nine studies met the inclusion and exclusion criteria and were further analysed. Data collection was done by developing a database in Microsoft Excel. Each study underwent a qualitative assessment based on the Jadad scale for reporting randomized controlled clinical trials.
Results. Botulinum toxin A reduces the number of episodes of bruxism and the total bruxism time. Pramipexol did not reduce the intensity or severity

Résumé

Approches thérapeutiques du bruxisme nocturne – une revue systématique

Introduction. Le bruxisme est un terme qui définit le frottement ou "grincement" des dents. Elle touche une grande partie de la population. Le diagnostic précoce du bruxisme est d'une grande importance pour son traitement et sa prévention.
L'objectif de l'étude était de réaliser une revue systématique des approches thérapeutiques du bruxisme nocturne, incluant uniquement les essais cliniques contrôlés randomisés publiés dans la littérature scientifique.
Matériaux et méthodes. Nous avons analysé les données des trois bases de données suivantes : PubMed, ScienceDirect et Google Scholar. Le programme EndNote a été utilisé pour achever la sélection des articles et simplifier la collecte des références bibliographiques à la Vancouver. Neuf études remplissaient les critères d'inclusion et d'exclusion et ont été analysées plus en détail. La collecte des données a été effectuée en développant une base de données dans Microsoft

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of nocturnal bruxism. Proton pump inhibitors have moderate effects of reducing the number of episodes of nocturnal bruxism. Biofeedback splint significantly reduces the activity of bruxism. The use of a stretching device led to an increase in the number of episodes of bruxism. Massage and Tray therapy reduces the symptoms of pain. Mandibular advancement device and maxillary occlusal splint reduce the number of bruxism episodes.

Conclusions. The physical methods of therapy can reduce the number of bruxism events, their duration, and may alleviate the pain of the masticatory muscles. Pharmacotherapy has proven low efficiency. Botulinum toxin type A is an effective therapeutic option for controlling the nocturnal bruxism.

Keywords: nocturnal bruxism, treatment, botulinum toxin A.

List of abbreviations:
BoNT-A – botulinum toxin A
PPX – pramipexol
PPI – proton pump inhibitors
BTB – biofeedback splint
MAD – mandibular advancement device
MOS – maxillary occlusal splint
SB – sleep bruxism

Excel. Chaque étude a fait l'objet d'une évaluation qualitative basée sur l'échelle de Jadad pour rapporter les essais cliniques contrôlés randomisés.

Résultats. La toxine botulique A réduit le nombre d'épisodes de bruxisme et la durée totale de bruxisme. Le pramipexol n'a pas réduit l'intensité ou la sévérité du bruxisme nocturne. Les inhibiteurs de la pompe à protons ont des effets modérés de réduction du nombre d'épisodes de bruxisme nocturne. L'attelle de biofeedback réduit considérablement l'activité du bruxisme. L'utilisation d'un appareil d'extension a entraîné une augmentation du nombre d'épisodes de bruxisme. La thérapie de massage et de plateau réduit les symptômes de la douleur. Le dispositif d'avancement mandibulaire et l'attelle occlusale maxillaire réduisent le nombre d'épisodes de bruxisme.

Conclusions. Les méthodes physiques de thérapie peuvent réduire le nombre d'événements de bruxisme, leur durée et peuvent soulager la douleur des muscles masticateurs. La pharmacothérapie s'est avérée peu efficace. La toxine botulique de type A est une option thérapeutique efficace pour contrôler le bruxisme nocturne.

Mots-clés: bruxisme nocturne, traitement, toxine botulique A.

Introduction

Bruxism, especially night bruxism, is a topic extensively debated in the scientific literature. However, there is still not enough evidence to define and support a standard therapeutic approach for bruxism[1]. Although wide-spread among the population and repeatedly investigated, bruxism remains an insufficiently known disease whose aspects require further scientific evaluation[2-5]. Bruxism has variable clinical aspects, being difficult to diagnose[4].

The episodes of the disease are very variable from one patient to another. The duration of nocturnal dental clamping can be from 5 to 38 minutes as part of parafunctional activities. When measuring the resistance of the contact between the teeth, it can be three times higher than the normal functional activity of the masticatory system[2].

Bruxism is one of the most relevant, complex, and destructive dental disorders. It is a complex occlusal parafunction that can hardly be placed in several different categories of parafunction. It can be classified as a sleep disorder, according to the International Classification of Sleep Disorders, when teeth clenching at night occurs in combination with at least one of the following signs: tooth damage, bruxism-associated sounds, and muscle pain. The episodes of bruxism, their duration and intensity are different, individual for each patient. The appearance of bruxism can be observed in 6-20% of the population, at any age, starting with the age of the eruption of deciduous teeth[2,3].

After an international consensus meeting (March, 2017, San Francisco, CA, USA), Lobbezoo et al.[4] published in 2018 a new definition of bruxism: a. *sleep bruxism* is a masticatory muscle activity during sleep that is characterized as rhythmic (phasic) or non-rhythmic (tonic) and is not a movement disorder or a sleep disorder in otherwise healthy individuals and b. *awake bruxism* is a masticatory muscle activity during wakefulness that is characterized by repetitive or sustained tooth contact and/or by bracing or thrusting of the mandible and is not a movement disorder in otherwise healthy individuals. During the same meeting, the researchers proposed a new grading system of the bruxism; it was emphasized that bruxism should be considered as a behaviour that can be a risk factor for certain clinical conditions rather than a disorder in otherwise healthy individuals[4,5].

Although the high variability of its prevalence is likely due to a lack of standardized diagnostic methods, epidemiological studies have shown that

prevalence rates among adults can range from 10% to 13% for nocturnal bruxism and 22-31% for diurnal bruxism[1]. However, in younger populations bruxism may be more common, affecting up to 40-50% of studies participants[1].

Global epidemiological data on bruxism reported a prevalence of nocturnal bruxism of 15.9% and of diurnal bruxism of 23.8%[3]. In Turkey, the prevalence of nocturnal bruxism in adults is 28.2% and of combined bruxism is 38.8%[6]. Other authors have reported an adult prevalence of daytime bruxism between 22.1% and 31% and nighttime bruxism of 12.8%[3,6,7].

A study in children reported a higher prevalence of bruxism (51.3%) whenever one parent reported a history of nocturnal bruxism, as opposed to children whose parents had no history (30.6%)[3]. Similarly, Michalowicz et al. evaluated 494 monozygotic and dizygotic twins through questionnaires and clinical tests and estimated the presence of signs and symptoms of bruxism. These authors did not find significant differences in clenching or gnashing of teeth, whether the twins had grown together or separately[3].

The aetiology of bruxism is not completely elucidated, because there is not a single factor responsible for its appearance. Many authors confirm that the aetiology of bruxism is multifactorial. It is also obvious that there is no effective generalized treatment to eliminate or reduce its occurrence[2].

Several studies focused on the relationship between allergies and intestinal parasites with bruxism. There is a close relationship between IgE levels, high eosinophilia, and the appearance of oral manifestations. The main pathophysiological mechanisms are thought to play an important role in nocturnal bruxism. In addition, psychological factors such as stress and anxiety appear to exacerbate the symptoms of nocturnal bruxism[2].

The early diagnosis of bruxism is of great importance both for its treatment and prevention. The diagnosis should focus on identifying the signs and symptoms reported by the patient or dentist during the clinical examination[2]. It is important to obtain a differential diagnosis based on the aetiology and clinical signs observed during the patient's clinical examination, including the symptoms detected in the history. Parafunctional forces directly affect the enamel on the teeth, which can be observed due to its abnormal wear. This sign is the most common evidence of the presence of bruxism. This wear can be limited to one tooth or the entire dentition. Radiological analysis may show changes in the periodontal space, which may disappear or may be associated with increased resorption of the tooth root, a fracture ,or changes in the dental pulp, sometimes with the appearance of pulp stones[2,7].

The diagnosis of bruxism is usually made clinically and is based on the patient's history and the presence of typical signs, including tooth mobility and damage, masseter hypertrophy, tongue indentation, hypersensitive teeth, and masticatory muscle pain. Temporo-mandibular joint cracking or blocking may occur[2,3,6].

Bruxism as an isolated condition cannot cause tooth damage. Another possible reason for the damage is acid erosion, which can occur in people who drink acidic juices or in people who have frequent vomiting or regurgitation of gastric acid. The presence of tooth damage only indicates that it has occurred at some point in the past and shows that the loss of tooth substance does not progress. People who grind their teeth and apply minimal parafunctional pressure on them do not show any damage to the teeth[2].

The diagnosis of bruxism usually involves the exclusion of dental, temporomandibular disease, and rhythmic movements of the jaw resulting from seizure-associated disorders. This usually includes dental examination and possible electroencephalography; in case you need to diagnose the attack of the disorder. Tooth damage can be perceived during a routine dental examination[2].

The standard reference for the diagnosis of nocturnal bruxism is polysomnography (PSG) with audio-video recordings. Other methods that measure the activity of masticatory muscles during sleep are PSG without audio-video recordings or electromyography (EMG) recorded with portable devices. Criteria for nocturnal bruxism include one or more signs: sounds of grinding teeth during sleep, tooth wear, maxillomandibular pain, or fatigue. Moreover, pain intensity can be assessed by a visual analog scale (VAS)[8].

Treatment for bruxism requires a multidisciplinary approach, including psychology, psychotherapy and speech therapy. Therapy planning should be done with rigorous attention to detail. The goal is to reduce physical and mental stress by treating the signs and symptoms. Early treatment involves reducing psychological stress by using relaxation methods such as exercise, massage, and physiotherapy. This treatment reduces the symptoms but does not eliminate the cause. The habit can be reactivated when the patient's tolerance to occlusal changes decreases[2].

There are several treatment approaches for this disease, but the common goal is muscle relaxation. Studies suggest that treatment can be performed with oral devices, which appear to be effective in reducing the activity of nocturnal bruxism, with better resolution with devices that provide a large extension of mandibular advancement. The most common pharmacological approaches are botulinum toxin,

clonazepam, and clonidine, which may improve the symptoms of nocturnal bruxism compared to placebo. Electrical stimulation of the masseter muscles appears to be effective in reducing pain. However, there is insufficient evidence to define and support a standard approach to the treatment of nocturnal bruxism[2].

The objective of this study was to conduct a systematic review of the therapeutic approaches used to treat nocturnal bruxism, including only randomized controlled clinical trials (RTCs) published in the scientific literature.

This systematic review aims to provide a comprehensive overview of the multiple therapeutic methods of nocturnal bruxism, to evaluate the efficacy and acceptability of therapies in adult patients, to provide information on potential treatments that alleviate this parafunction, and to compare findings.

Materials and methods

To highlight the need for a systematic review on the types of treatment of nocturnal bruxism, the formulation of the research question according to the PICOS model was made. "P" – representing the population or disease, "I" – the intervention or variable of interest, "C" – the comparison, "O" – the result, and "S" – the type of study.

The eligibility criteria applied, which were selected using the PICOS qualitative analysis tool, are represented in the present study by the following:

- P – the target population being represented by all adults over 18 years of age, of any sex and of any ethnicity, suffering from nocturnal bruxism;
- I – the variable of interest being represented by the treatment methods of nocturnal bruxism;
- C – shows the desire to make a comparison between the different methods of treatment of nocturnal bruxism that exist, such as: chemical treatments such as botulinum toxin injection, drug treatments of various kinds and mechanical treatments such as gutters;
- O – highlights the effectiveness of each treatment and which of them has the highest efficiency among the target population, taking into account criteria such as: reducing pain, improving quality of life, reducing episodes of nocturnal bruxism;
- S – select only randomized controlled trial (RTC) studies.

Finally, the research question turned into the following purpose: Comparative evaluation of the results of various therapeutic methods of nocturnal bruxism in the adult population.

Bibliographic source search strategy

This systematic review was conducted in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) model for drafting a systematic review and meta-analysis and with the guidelines in the Cochrane Handbook for Systematic Reviews of Interventions (Cochrane Handbook for Systematic Reviews) of interventions).

The literature used in the elaboration of this paper was collected using the following three sources of electronic bibliographic data: PubMed, ScienceDirect and Google Scholar. All searches for methods of treating nocturnal bruxism were performed using a combination of subject titles and free-text terms, but the final search strategy was determined by several preliminary searches.

To ensure a sensitive search strategy, the following terms have been introduced in the search engines of the three databases: sleep bruxism (SB), treatment or therapy. The combined use of keywords facilitated a more precise search of the subject, which offered the possibility to cover a whole range of treatments for nocturnal bruxism.

In the PubMed database, the selection of specific filters from the filter menu was made, which helped to concentrate the search area of the articles for the last 10 years, as follows: „Publication Date10 years". We also tried to obtain these articles in "Free Full Text" format, that could be fully downloaded in their original format. When the search was performed in the Google Scholar database, the date of the articles was subsequently selected manually, after they corresponded to the four terms used for the initial search.

Eligibility criteria for the selection of scientific articles

The more in-depth selection of scientific articles was made by applying the inclusion and exclusion criteria. These criteria had to be met for the items initially selected to be further included in the present study.

Inclusion criteria:

- randomized clinical trials (RTC);
- studies written in English and published in specialized journals;
- studies published between 2011 and 2021;
- studies evaluating the methods of treatment of nocturnal bruxism;
- studies on adults over 18 years;
- in vivo experimental studies.

Only randomized clinical trials (RTCs) performed on adults over 18 years of age with a clinical diagnosis or a standard clinical diagnosis of nocturnal bruxism were selected, regardless of whether they had sleep disorders.

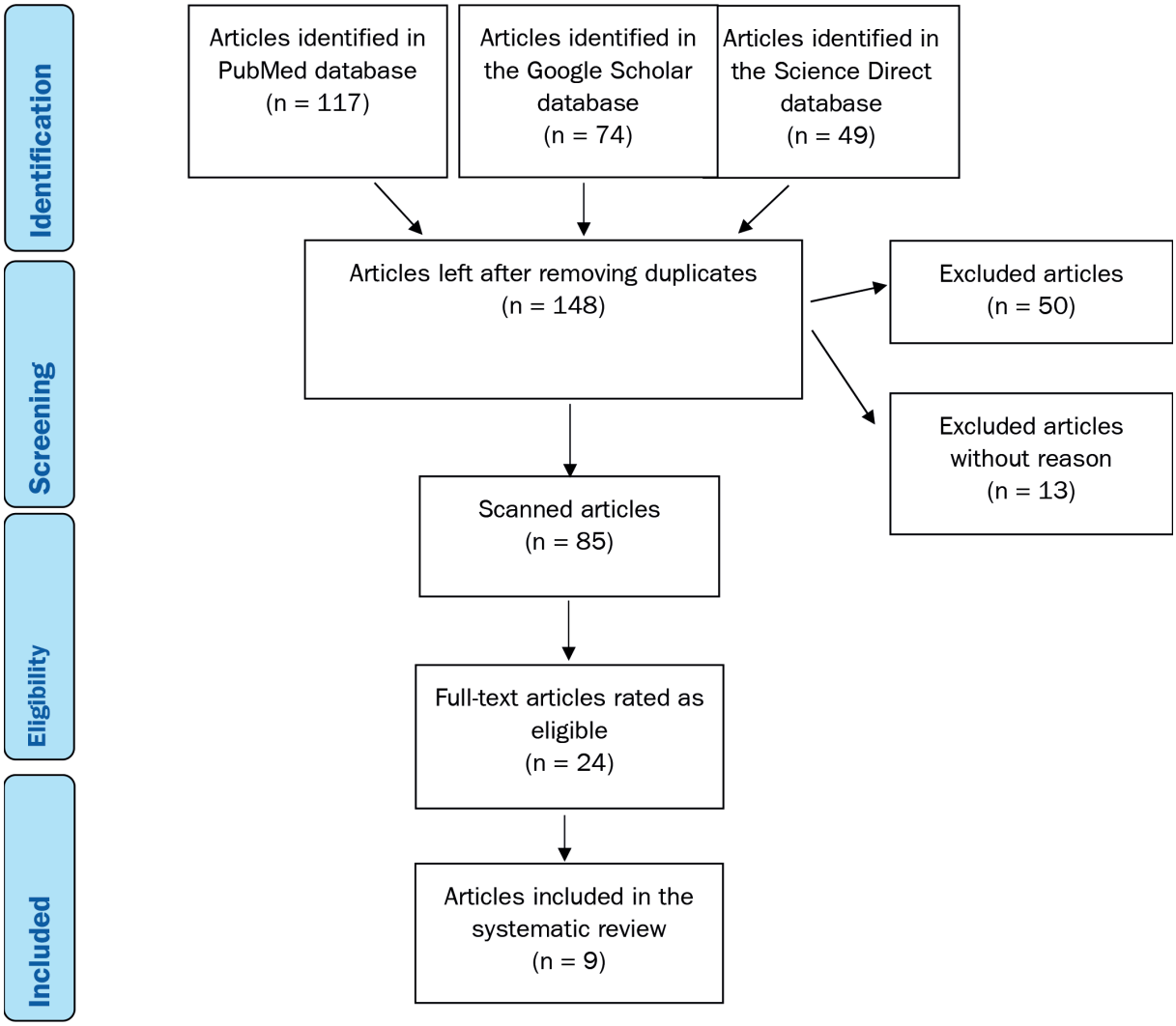

Figure 1. Systematic search diagram based on the PRISMA scientific writing guide of systematic reviews and meta-analyses

Exclusion criteria:
- studies older than 10 years;
- ongoing studies;
- studies on children under 18;
- cohort studies;
- non-randomized comparative studies;
- transversal studies;
- case-control studies;
- systematic reviews;
- author or editorial summaries and debates;
- studies showing a lack of efficient statistical analysis
- studies showing the lack of standardized measures for the evaluation of bruxism;
- studies in patients with systemic diseases and syndromes or neurological and psychiatric disorders.

Stages of data collection

The EndNote program was used to achieve the selection of articles and simplify the collection of Vancouver-style bibliographic references. The evaluation of the studies was done initially by reading all the titles and abstracts, to exclude the articles that do not meet the inclusion criteria, after which the works were read in their entirety. After reading the titles, out of a total of 240 articles, 98 were excluded because they were not relevant to the chosen topic or were duplicated during the collection, then out of the 148 articles evaluated from the abstract point of view, only 85 of them. Finally, the full text of each of the 24 articles was read and only a total of 9 articles met the inclusion criteria, which became eligible for the study (Fig. 1).

Data analysis

The selected studies that met the inclusion and exclusion criteria – 9, were analysed and described, and data collection was done by developing a database in Microsoft Excel which included bibliographic reference:
- the author;

Table 1. Caption: * A study receives a score of 1 for "yes" and 0 for "no"**. A study receives a score of 0 if no description is provided, 1 if the method is described appropriately, –1 if the method is improperly described.

	Bergmann et al, 2020[9]	Shim et al, 2020[11]	Ondo et al, 2018[12]	Gouw et al, 2018[13]	Cahlin et al, 2016[14]	Ohmure et al, 2016[15]	Gomes et al, 2015[8]	Singh et al, 2015[16]	Gomes et al, 2014[10]
Described as randomized *	1	1	1	1	1	1	1	1	1
The description of the randomization method was made according to **	1	0	1	1	1	1	1	1	1
Described as blind or double-blind *	1	1	1	0	1	1	1	0	1
The description of the blind or double-blind method was made according to **	0	1	0	0	0	0	1	0	0
Description of withdrawal of subjects *	1	1	1	1	1	1	1	1	1
Score	4	4	4	3	4	4	5	3	4

- year of publication;
- type of study;
- the title;
- the sample;
- duration of the study;
- intervention;
- results;
- conclusions.

The analysis of the collected data was done by comparing the results of each study.

Results

Selection of studies

The search strategy performed by electronic and manual screening, identified 240 potential articles: 117 from the PubMed database, 74 from Google Scholar and 49 from Science Direct (Fig. 1). After removing the duplicates, 148 articles were analysed in terms of title, and 50 of them were deleted. Subsequently, another 13 articles were removed because they were not relevant to the subject of the study. Reading the abstracts of the remaining 85 articles, led to the elimination of another 61. The last stage in the selection of studies, found in full reading and application of inclusion and exclusion criteria on the remaining 24 articles, and in the end, only 9 of them were corresponding to be included in the systematic review.

Characteristics of the studies

The studies included in the systematic review were published between 2014 and 2020 and are exclusively represented by randomized, controlled clinical trials (RCTs). Also, they were performed only on adult subjects, over the age of 18, with no upper age limit.

Recruitment of study subjects was generally based on questionnaires[8], clinical evaluations[9], electromyography[10] and polysomnography[11] or by the combined use of all the methods listed[12-16]. Randomization of participants in intervention programs was performed using a computer-generated randomization sequence[12-14], sealed opaque envelopes[8,9,16,17], or both combined[15].

Quality assessment

Each study was subjected to a qualitative evaluation, based on the Jadad scale for the reporting of randomized controlled clinical trials, the evaluation criteria being shown in Table 1.

According to this scale, the quality of all included clinical trials was assessed based on 5 questions that analyse the randomization process, experimental blindness, and dropout rate, in patients who were lost to follow-up. This scale provides a total score that can range from 0 to 5, where 0 is a low-quality study and 5 is the highest possible quality. A study is considered of good quality when it obtains a score of at least 3.

According to the results from this table, all 9 studies included in the systematic review met a score of at least 3, so they had a good quality. However, only one of them reached the highest score.

Risk of bias

To avoid the risk of bias in the randomization phase of the intervention program, the grouping of

Table 2. Bias risk summary: authors' judgments on each element of bias risk for each study included.

Risk of bias	*Bergmann et al, 2020*[9]	*Shim et al, 2020*[11]	*Ondo et al, 2018*[12]	*Gouw et al, 2018*[13]	*Cahlin et al, 2016*[14]	*Ohmure et al, 2016*[15]	*Gomes et al, 2015*[8]	*Singh et al, 2015*[16]	*Gomes et al, 2014*[10]
Random sequence generation	+	+	+	+	+	+	+	+	+
Hiding the randomization sequence	+	+	?	+	+	+	+	+	?
Blindness of participants and staff	–	+	–	–	?	?	+	–	?
Blindness of outcome evaluation	–	+	–	+	+	–	–	–	–
Incomplete result data	+	+	?	?	?	?	+	+	+
Selective reporting of results	+	+	+	?	+	?	+	+	+
Other sources of bias	–	+	+	?	–	+	+	–	+

Legend: + – low risk of bias ? – risk of unclear bias – – high risk of bias

participants by sex and age groups was performed[13]. Also, to avoid the risk of bias in the manufacturing stages of studies that used occlusal devices such as maxillary splints, they were made for all subjects before randomization[9]. When two different types of splints are used, the risk of bias may be increased due to the difference in the vertical occlusion size recorded between the two models[9]. In addition, the increased risk of bias may also be due to participants' emotional biases that favour some occlusal devices such as maxillary occlusal gutters (MOS) instead of mandibular advancement devices (MAD) that generate discomfort and dental sensitivity that influence oromotor activity[16].

The limitations of studies that may induce the risk of bias are the recruitment of subjects from an area of patients with orofacial pain1[4] or from tertiary hospital care institutions1[6], instead of being recruited from the general community population. Also, the values of the study results could be influenced in the absence of a corresponding blindness[9,13].

To properly assess the risk of bias, the Cochrane Collaboration Tool was used to assess the risk of bias in randomized trials. The results are presented in Table 2.

Although all studies are randomized, two of them were unclear in the correct highlighting of the randomization sequence[12,17]. Also, blinding of study participants and staff was not performed properly in four of them[9,12,13,16], and three others left unclear[14,15,17]. Blindness assessment of the outcome was not performed at all or was not specified in six studies [8,9,12,15-17] and other sources of bias were found in only three of them[9,14,16].

Results

One of the 9 selected studies evaluated the effect of muscle stretching in the management of nocturnal bruxism, associated with sleep hygiene tips, practices and habits that can promote improved sleep quality[13]. In the intervention group that performed the static muscle stretching exercises with a stretching device for 10 days, there was a tendency to increase the episodes of bruxism compared to the control group. This can be explained by the fact that intensive / forced stretching of the muscles can lead to muscle injuries, which in turn can lead to increased muscle activity due to a protective reaction. In addition, the duration, number of repetitions and type of stretching exercises may affect the therapeutic effect on bruxism[13]. Static muscle stretching also led to a maximum amplitude of pain-free opening of the mouth and a decrease in the pain threshold at muscle pressure[13]. The authors conclude that stretching the masticatory muscles was not effective in reducing nocturnal bruxism in the absence of pain or other dysfunction[13].

Two studies published one year apart by the same lead author, Gomes et al., looked at the effect of massage and the use of occlusal splints as a therapy to improve sleep quality and reduce pain caused by nocturnal bruxism[8,17]. One difference between the two is that the first study conducted in 2014, uses subjects with severe temporomandibular dysfunction, while

the other excludes them. Both have four groups: the massage group, the group with conventional Michigan-type occlusal splints, the group of conventional massage and occlusal splints and a final control group[8] or the group of vacuum silicone occlusal splints formed of 3 mm polyvinyl sheets[17]. Those in the massage group underwent 3 massage sessions per week, for 4 weeks, bilaterally at the level of the anterior masseter and temporal muscles. Those in the splint group received treatment with maxillary occlusal splints, and those in the combined group received both treatments for the same period. It has been found that massage can lead to an improvement in mandibular function, as well as a reduction in the frequency and intensity of bruxism and the symptoms of temporomandibular dysfunction[17]. The authors believed that massage therapy on masticatory muscles in combination with occlusal splints also lead to improvements in quality-of-life indicators[8]. However, significant changes occurred only in the group that used splint therapy. Isolated use of gutters provides greater protection against tooth aggression caused by nocturnal bruxism[8]. An occlusal splint does not cure temporo-mandibular dysfunction or nocturnal bruxism, but it can help improve quality of life, improve the ability of the oral cavity to open maximum, and reduce myofascial pain[17].

Bergmann et al. compared maxillary occlusal splints with biofeedback type splints. These special "bruXane" splints use a pressure sensor integrated in the occlusal surface that vibrates when it detects that an episode of bruxism has been triggered and additionally presents an audible alarm[9]. Thus, biofeedback is triggered directly by the applied occlusal force, and the delivery of biofeedback stimuli is done intrabuccally at the time and location of the target activity, i.e. directly at the starting point of bruxism, in the form of two stimuli (vibration and sound), so two senses were approached[9]. Biofeedback splint therapy used for 3 months, obtained a statistically significant reduction in the activity of bruxism during the treatment phase, in terms of number of events and, in particular, their duration[9]. The biofeedback splint measurement feature can help identify the causes of the patient's bruxism and the extent to which the reported symptoms are due to bruxism[9]. It has also been observed that this biofeedback system seems to work effectively at the subconscious level (does not wake the patient)[9]. Moreover, the results suggest that biofeedback gutters reduce the level of bruxism-related stress on the stomatognathic system, having the potential to prevent other disorders resulting from the application of bruxism-related forces[9]. Biofeedback gutters provide a statistically significant improvement in the general well-being of patients compared to conventional gutters[9]. Treatment with biofeedback gutters led to a statistically significant reduction in pain felt in the facial muscles compared to the control group[9]. Biofeedback splints seem safe for their therapeutic use and offer considerable benefits to patients such as tooth protection[9]. By reducing the duration of outbreaks and the pathological load on the masticatory system, biofeedback gutters additionally offer additional positive therapeutic effects in terms of prophylaxis and in reducing the symptoms related to buxism[9].

By comparing maxillary advancement devices with conventional occlusal gutters, Singh et al. demonstrated that both methods have led to a significant improvement in sleep quality and a reduction in the number of episodes of bruxism per hour. The main mechanism behind the positive effects of mandibular advancers is the forward advancement of the mandible, which widens the airspace and reduces the occurrence of bruxism episodes, and in contrast, conventional occlusal gutters reduce masseter and temporalis muscle activity by improving muscle balance[16].

Two other studies use botulinum toxin type A for the management of nocturnal bruxism. Shim et al. revealed that the injection of 25 units (U) of botulinum toxin type A (BoNT-A) into the masseter muscles cannot control the genesis of rhythmic masticatory muscle activity (RMMA), but rather represents a control management option, intensity of masticatory muscles during nocturnal bruxism and protects orofacial structures from excessive forces[11]. In the study conducted by Ondo et al., a quantity of 60 U of botulinum toxin type A, was injected both in the masseter muscles and in the bilateral temporal muscles[12]. Thus, type A onatobotulin toxin (BoNT-A) improved the symptoms of bruxism, as demonstrated by significant improvements in overall clinical impression (CGI) and visual analog scale (VAS)[12]. It was also observed that the total sleep time tended to improve in the BoNT-A group, and the total bruxism time decreased from 13.13 to 10.32 in the test group, increasing from 7.26 to 18.8 in the control group[12]. The effect of BoNT-A on nocturnal bruxism is to reduce the intensity of contractions in the injected muscles, and it is maintained for at least 12 weeks[11].

The last two studies included in the systematic review study the pharmacotherapeutic effect of dopamine agonist[14] and proton pump inhibitor[15] on patients with nocturnal bruxism. Cahlin et al., uses the substance called paramipexole (PPX) administered to subjects in titrated form over a period of 3 weeks in various doses modified as follows: 0.9 mg on days 1-4, 0.18 mg on days 5-7, 0.36 mg on days 8- 14 and finally 0.54 mg on days 15-21[14]. Pramipexole is an agonist of D2 L and S, D3 and D4 receptors with affinity for

some serotonin and andrenergic receptors[14]. It was recorded that the number of awakenings and the percentage of awakenings after the onset of sleep were higher after PPX administration compared to the control group, suggesting sleep fragmentation[14]. Also, the proportion of sleep in the state with rapid eye movement was lower after PPX[14]. Triggers of bruxism episodes and episodes (total, phasic, tonic, and mixed) remained unchanged after PPX, so the authors concluded that the involvement of the dopamine system in the aetiology of bruxism is unlikely and that dopamine agonist administration reduced neither the intensity nor severity of nocturnal bruxism[14]. Ohmure et al., use rabeprazole for 24 days for the treatment of nocturnal bruxism, which is a proton pump inhibitor (PPI) with the strongest acid inhibitory effect among the top 3 PPIs approved in Japan. There was a 20% decrease in outbreaks or episodes of bruxism achieved with PPI, but as for the frequency of swallowing events, no significant difference was observed between placebo and PPI[15]. PPI administration significantly reduced the frequency of RMMA episodes and electroliographic triggers (EMG)[15]. However, the effect of PPI was only moderate and varied widely between patients, especially in terms of grinding sound, and the frequencies of post-administration RMMA episodes and EMG outbreaks were higher than those present in healthy individuals[15].

Discussion

In two studies[8,10], Gomes et al. aimed at the effectiveness of muscle massage, occlusal splints or both combined treatments in the treatment of nocturnal bruxism. Massage therapy and occlusal splints are used to stimulate local blood flow and nutrient transport, to restore normal muscle status, to prevent hyperactivity and to reduce pain[8]. Although the effect of occlusal splints, including silicone ones, indicated to control parafunctional activity, is to improve quality of life and reduce pain, it is not maintained for a long time due to the adaptive mechanisms of the muscles[8]. Therefore, the benefits appear to be temporary and non-cumulative, and daily use is necessary to maintain the effect, which explains the results obtained, as the evaluations were performed only before and after 4 weeks from the cessation of the use of gutters[17].

Manfredini et al. suggest in his systematic review that almost any type of occlusal splint is somehow effective in reducing SB activity , and this hypothesis can be supported by the observation that intermittent use of occlusal splinters is more effective in reducing bruxism. nocturnal (SB) than their continuous use[18].

Singh et al. discuss the efficacy of mandibular advancement devices (MAD) compared to conventional occlusal gutters (MOS), noting a significant improvement in sleep quality and a significant reduction in hourly bruxism episodes in both groups[16]. Although MAD has provided a greater degree of improvement in nocturnal bruxism indices, MOS remains the treatment of choice because its benefits outweigh its adverse effects in patients with nocturnal bruxism[16].

Bergmann et al., report as limitations of his study, the very low number of subjects who reported specific symptoms of bruxism and emphasize that conclusions should be drawn with caution[9]. A relevant clinical finding of this study is that the body is effective in the subconscious response to biofeedback therapy[9]. Biofeedback splint therapy achieved a statistically significant reduction in bruxism activity during the treatment phase, in terms of the number of events and, in particular, their duration and there were no adverse effects[9]. Although this treatment does not address the underlying causes of patients' bruxism, it appears to be an effective and safe tool in treating nocturnal bruxism[9]. Because biofeedback therapy is a „training process" in which patients have to „unravel their behaviour", a greater post-treatment impact can be expected after a longer phase of treatment, possibly overcoming any achievable effect using a splint "passive"[9].

The results of the study conducted by Ondo et al. showed that injections with BoNT-A in the masseter and temporalis muscles, may be a valid treatment option for patients with nocturnal bruxism, since they lead to improved symptoms of bruxism[12]. Shim et al. also confirm that, although BoNT-A cannot control the genesis of RMMA, the toxin is an option for controlling the intensity of masticatory muscles during nocturnal bruxism, which decreases during the 4 weeks of use[11].

However, these studies are not exempt from limitations, as most samples are too small[11,12] to allow statistically significant results. There are also no clear guidelines for quantifying bruxism, i.e. the number of events, their total duration and intensity[12] and the evaluation of the BoNT-A effect focused on the efficacy and objective findings of polysomnography (PSG). Another limitation was that the recruitment of subjects was slow, in principle because they were not sent to a clinic dealing with such disorders[12] or because their selection was made from subjects with nocturnal bruxism who already used occlusal gutters[11]. It was thought that these patients had a moderate to high frequency of nocturnal bruxism, but PSG showed high variability in the first nights with low frequencies[11].

Finally, budgetary constraints led to the limitation of polysomnographic records which were reduced so that multiple evaluation nights had to be abandoned[11,12].

Table 3. Pharmacotherapeutic methods of nocturnal bruxism.

Article, Author, Year	*Affection, Sample*	*Intervention*	*Result*
Shim et al, 2020[11]	Bruxism at night, 30	Test group: 25 U BoNT-A injected into the masseter muscles Placebo group: 25 U saline injected into the masseter muscles	BoNT-A – reduces the intensity of contractions in the injected muscles
Ondo et al, 2018[12]	Bruxism at night, 31	Test group: 60 U BoNT-A injected into the masseter muscles and 40 U into the temporalis muscles Placebo group: 60 U placebo solution injected into the masseter muscles and 40 U into the temporalis muscles	BoNT-A – reduces no. episodes of bruxism and total bruxism time; improves total sleep time
Cahlin et al, 2016[14]	Bruxism at night, 20	Test group: pramipexole (PPX) 0.18 mg, oral tablets for 3 weeks Control group: placebo	PPX – did not reduce the intensity or severity of nocturnal bruxism
Ohmure et al, 2016[15]	Bruxism at night, 12	Test group: rabeprazole 10 mg orally, for 2 cycles of 5 days each, separated by a washout of at least 14 days. Control group: placebo	PPI – moderate effect of reducing the frequency of nocturnal bruxism episodes and electromyographic triggers

Abbreviations: BoNT-A = botulin toxin type A, PPX = pramipexole, PPI = proton pump inhibitor.

Although commonly, botulinum toxin type A (BTX-A) is used to treat various diseases in the oro-maxillofacial region, Nunez at al, conducted a systematic review in which it was observed that although BTX-A could decrease masticatory muscle strength, this effect is only temporary and normal function returns to normal when the effect of the toxin disappears[19]. Another review of Baat et al. highlights that the literature still has uncertainties about the necessary dosage of botulinum toxin[20]. Although it is a safe treatment for patients with nocturnal bruxism, an important note is a possible adverse effect consisting of bone loss in the condylar and alveolar regions of the mandible, which was demonstrated after treatment with botulinum toxin type A[20]. Probably bone loss develops due to localized paresis of the muscles that induce mineral density, a phenomenon called osteopenia[20]. Also, when recommending the use of BTX-A, attention should be paid to the side effects such as: asthenia, blepharoptosis, dysphagia, myasthenia, sore throat, visual disturbances, xerostomia and hyposalivation (medications and addictive)[20].

Cahlin et al., who used the dopamine agonist in the treatment of nocturnal bruxism, reported as limitations that the population from whom the subjects were selected was not without comorbidities, which explains the lack of drug power[14]. Although there were side effects of using pramipexole such as nausea, drowsiness, poor sleep and blurred vision, these effects were moderate and did not lead to discontinuation of the drug[14]. This study also suggests a possible association between low serum ferritin levels and a high intensity of some variables of bruxism, which requires a more detailed epidemiological study in order to be statistically confirmed[14]. It was concluded that the administration of the dopamine agonist, pramipexole, did not reduce either the intensity or the severity of nocturnal bruxism[14].

This conclusion was also confirmed by the review written by Baat et al., where several dopamine agonists were used and it was observed that bromocriptine did not exacerbate or reduce nocturnal bruxism, and pramipexole or levodopa did not had an attenuating effect on nocturnal bruxism[20].

The limitations of the study of Ohmure et al. are the low capacity of the sleep laboratory, which led to the electromyographic recording of the first two nights at home in subjects before using the PSG laboratory[15]. Also, because the microphone was placed with the video camera approximately 1.5 m above the patient's abdomen, it was difficult to differentiate the grinding sound from other sounds when the participant was sleeping in a lateral or inclined position[15]. It was observed that the calculated potency and clinical benefits of the proton pump inhibitor represented by rabeprazole were not adequately validated[15]. For insufficient and inconsistent efficacy, several causes are speculated, such as: differences between individuals make rabeprazole metabolism different, and the 10 mg dose may not be sufficient for some patients, failing to sufficiently reduce gastric acid inhibition[15].

The use of muscle stretching combined with sleep hygiene tips as a treatment for nocturnal bruxism increased the episodes of nocturnal bruxism in both the intervention and control groups, concluding that stretching the masticatory muscles was not effective in reducing nocturnal bruxism, thus the clinical effect is not relevant[13]. Gouw et al. reported

Table 4. Physical methods of treatment of nocturnal bruxism.

Article, Author, Year	*Affection, Sample*	*Intervention*	*Result*
Bergmann et al, 2020[9]	Bruxism nocturn, 41	Test group: biofeedback splitters (BFB) Control group: conventional occlusal splints (AOS)	BFB – significantly reduces the activity of bruxism (no. And duration of events; improves overall well-being and reduces facial muscle pain.
Gouw et al, 2018[13]	Bruxism nocturn, 24	Test group: sleep hygiene tips and static muscle stretching exercises with a stretching device for 10 days. Control group: sleep hygiene tips	Nr. of episodes of bruxism increased in both the intervention group and the control group. Muscle Stretching – Increases Maximum Opening Mouth (MMO)
Gomes et al, 2015[8]	Bruxism nocturn, 78	Massage group: massage 3 times a week 30 minutes for 4 weeks on the masticatory muscles Gutter group: treatment with splints for 4 weeks Massage and splint group: combined treatment Control group: no intervention	Massage therapy – reduces pain symptoms Gutter therapy – reduces muscle pain and increases functionality Combination therapy – improves the quality of life
Singh et al, 2015[16]	Bruxism nocturn, 28	Test group: mandibular advancement device (MAD) Control group: maxillary occlusal splints (MOS)	MAD and MOS – improve sleep quality, reduce no. average hours of bruxism episodes per hour (MAD – greater reduction of bruxism indices than MOS)
Gomes et al, 2014[10]	Bruxism nocturn, 60	Massage group: 3 massage sessions per week, for 4 weeks, bilaterally at the level of the masseter and anterior temporal muscles Gutter group: treatment with conventional occlusal splints for 4 weeks Massage and splint group: combined treatment Silicone gutter group: occlusal therapy with vacuum-formed silicone splints for 4 weeks	Massage therapy – increases mandibular function and reduces the frequency and intensity of bruxism and symptoms of temporomandibular dysfunction (TMD) Gutter therapy – insufficient to reduce muscle activity Combination therapy – reduces the intensity of signs and symptoms of DTM and nocturnal bruxism.

Abbreviations: BFB = biofeedback splints, AOS = conventional occlusal splints, MMO = maximum mouth opening, MAD = mandibular advancing device, MOS = maxillary occlusal splints, TMD = temporomandibular dysfunction.

that limiting the recruitment of subjects through advertisements and announcements, arguing that their intrinsic motivation to participate in the study would have decreased the chance of dropping out, but at the same time, each person's personality traits could have affected the results[13]. The 10-day study period was too short to observe significant differences, as the level of pain or muscle tension may initially increase for a short time before it decreases as a result of the long-term therapeutic effect[13]. The systematic review by Guaita et al. also recommends sleep hygiene rules such as: smoking cessation and drinking coffee or alcohol at night, limiting physical or mental activity before bed and ensuring good sleeping conditions (silence and darkness)[21].

The comparative analysis of pharmacotherapeutic treatments for nocturnal bruxism can be seen in Table 3.

The comparative analysis of physical treatments for nocturnal bruxism can be seen in Table 4.

Conclusions

All treatments using physical methods such as massage, conventional maxillary occlusal splints or biofeedback and mandibular advancement devices, have shown a clear effectiveness by reducing the number of bruxism events and their duration, and also by alleviating the pain felt in the masticatory muscles. These treatments do not ultimately cure nocturnal bruxism, but can help improve quality of life and maximal opening of the oral cavity, and reduce myofascial pain.

Pharmacotherapy performed with oral drugs such as dopamine agonists or proton pump inhibitors has shown a low efficacy in nocturnal bruxism, failing to significantly improve the symptoms of this parafunction. As for BoNT-A drugs injected into the masseter and / or temporalis muscles, it has been observed that they cannot control the genesis of rhythmic masticatory muscle activity, but are a management option for controlling masticatory muscle intensity during nocturnal bruxism and it also protects the orofacial structures from excessive forces through localized muscle paresis.

Author Contributions:

I.M. conceived the original draft preparation. I.M., E.C., T.V., and D.M. were responsible for conception and

design of the review. M.I., T.V., and D.M. were responsible for the data acquisition. I.M, E.C., and D.M. were responsible for the collection and assembly of the articles/ published data, and their inclusion and interpretation in this review. I.M., E.C., T.V., and D.M. contributed equally to the present work. All authors contributed to the critical revision of the manuscript for valuable intellectual content. All authors have read and agreed with the final version of the manuscript.

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