

UCUENCA

Facultad de Odontología

Especialización en Rehabilitación Oral y Prótesis Implanto-Asistida

THERAPIES FOR SLEEP BRUXISM IN DENTISTRY: A CRITICAL
EVALUATION OF SYSTEMATIC REVIEWS

Trabajo de titulación previo a la
obtención del título de
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Resumen:

El objetivo del estudio fue evaluar la calidad metodológica y el riesgo de sesgo de las revisiones sistemáticas con respecto a la literatura sobre terapias para el bruxismo del sueño (BS) en odontología, aplicando la guía cualitativa AMSTAR 2 (A MeaSurement Tool to Assess systemic Reviews), así como la efectividad de varios tipos de tratamiento de SB. Inicialmente se obtuvieron un total de 1.499 artículos de 4 bases de datos y 2 sitios web. Los artículos relevantes se obtuvieron de las bases de datos PubMed, Scopus, Cochrane y Embase, así como de Google Scholar y OpenGrey. Se incluyeron seis revisiones sistemáticas que cumplieron con el criterio de elegibilidad. La calidad metodológica de todas las revisiones sistemáticas, evaluadas con la herramienta AMSTAR 2, fue críticamente baja. En cuanto a la efectividad del tratamiento, 5 revisiones sistemáticas informaron sobre manejo farmacológico (toxina botulínica tipo A (BTX-A), clonazepam y clonidina), 2 informaron sobre aparatos orales (OA) (férulas estabilizadoras y dispositivos de avance mandibular (MAD)) y 1 estudio abordó los efectos de la biorretroalimentación (BF). Los resultados de las terapias fueron diversos y confusos. La investigación disponible no es concluyente, y no muestra una evidencia clara o un consenso por parte de los investigadores sobre el tratamiento más efectivo para el manejo de la BS. Se necesita más investigación de mejor calidad metodológica en esta área

Palabras clave: Tratamiento. Bruxismo del sueño. Rechinar de dientes. Actividad muscular masticatoria rítmica .

Abstract:

The aim of the study was to evaluate the methodological quality and the risk of bias of systematic reviews with regard to the literature on therapies for sleep bruxism (SB) in dentistry, applying the AMSTAR 2 (A MeaSurement Tool to Assess systematic Reviews) qualitative guide, as well as the effectiveness of various kinds of treatment of SB. Initially, a total of 1,499 articles were obtained from 4 databases and 2 websites. Relevant articles were obtained from the PubMed, Scopus, Cochrane, and Embase databases as well as from Google Scholar and OpenGrey. Six systematic reviews that met the eligibility criterion were included. The methodological quality of all systematic reviews, assessed with the AMSTAR 2 tool, was critically low. Regarding treatment effectiveness, 5 systematic reviews reported on pharmacological management (botulinum toxin type A (BTX-A), clonazepam and clonidine), 2 reported on oral appliances (OAs) (stabilizing splints and mandibular advancement devices (MADs)) and 1 study addressed the effects of biofeedback (BF). The results of the therapies were diverse and confusing. The available research is not conclusive, and does not show clear evidence or a consensus on the part of researchers on the most effective treatment for the management of SB. More research of better methodological quality is needed in this area.

Keywords: Treatment. Sleep bruxism. Teeth grinding. Rhythmic masticatory muscle activity.

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Introduction

For decades, the term "bruxism" has generated controversy in the academic and professional environment of dentistry due to the various definitions attributed to it and its alleged association with etiological factors that are currently considered to have no scientific relevance.

Various conceptualizations have been postulated for the definition of bruxism. Lobbezoo et al. in the 2013 international consensus defines sleep bruxism (SB) as "repetitive jaw-muscle activity characterized by clenching or grinding of the teeth and/or bracing or thrusting of the mandible"¹; the International Classification of Sleep Disorders – Third Edition (ICSD-3) classifies it as a sleep-related movement disorder²; and Lobbezoo et al. in the 2018 international consensus update the above definition of bruxism with other findings: (i) suggest separate definitions for SB and awake bruxism, the same being the chewing muscle activity that occurs during sleep (characterized as rhythmic or non-rhythmic) and during wakefulness (characterized by repetitive or sustained tooth contact and/or jaw effort or thrust); (ii) stated that bruxism should not be considered as a disorder, but as a behavior that may be a risk factor (and/or a protective factor) for certain clinical consequences in healthy individuals; and (iii) grouped the techniques for the diagnosis of bruxism into non-instrumental (self-reports) and instrumental (electromyography and polysomnography)³. Regarding the etiology of bruxism, in the past, it was associated with occlusal discrepancies, but nowadays, it is no longer considered as such⁴, since several studies mention that SB is centrally regulated^{1 5}. Despite these changes, the hypothesis of occlusal discrepancies has not been completely abandoned, which has led to confusion among clinicians in terms of making an accurate diagnosis, and therefore applying effective treatment-botulinum toxin type A (BTX-A)^{6 7 8}; oral appliances (OA)⁹; biofeedback (BF)^{10 11}; physiotherapy^{12 13}; and pharmacotherapy¹⁴. Still, the efficacy of some of the abovementioned for the management of bruxism has not been scientifically proven. There should be more randomized controlled clinical studies; in some cases, the authors even suggested conducting studies with larger samples and longer treatment periods to obtain results that would be reliable for clinical application. For this reason, as researchers, we feel the need to try to establish which therapies are really valid for the management of BS.

We have not found general studies that would evaluate the methodological quality of systematic reviews on this topic; therefore, this study will surely become a reference for future research. The aim of the present study was to evaluate the methodological quality of the literature and the risk of bias in systematic reviews addressing therapies for SB by applying the AMSTAR 2 (A MeaSurement Tool to

Assess systematic Reviews) qualitative guide ¹⁵, as well as to assess the effectiveness of the therapies in terms of their clinical application. The research question was as follows: What is the methodological quality of studies analyzing the treatment of sleep bruxism and what is the effectiveness of various kinds of treatment?

Materials and methods

Protocol and Registry

This study was carried out in accordance with the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) 2020 Statement¹⁶, and a general protocol based on the INPLASY (International Platform of Registered Systematic Review and Metaanalysis Protocols) guide for the registration of systematic review protocols (2021)¹⁷ was also executed. The record is publicly available under number 2021100080 and doi: 10.37766/inplay2021.10.0080.

Eligibility criteria

The included studies were systematic reviews (SR) with or without a meta-analysis, that evaluated the different kinds of treatment used in adult patients (aged 18 years or above) diagnosed with bruxism through polysomnography, electromyography and self-reports. No time or language restrictions were applied.

The exclusion criteria embraced literature reviews, intervention studies, observational studies, in vitro laboratory research, randomized controlled clinical studies, abstracts, comments, case reports, protocols, personal opinions, expert opinions, letters and posters. If a particular article of interest was not available, the author was contacted via email; if after 3 attempts within an interval of 30 days there was no response, the study was excluded. In addition, studies in which methodology was not addressed, or studies using unspecified or non-validated diagnostic methods (self-reports) were also excluded.

Search strategy

An electronic search was conducted in February 2022 in four databases (Cochrane, Embase, PubMed, Scopus). The gray literature was also searched through Google Scholar and OpenGray. The retrieved articles were exported to a web application (Mendeley), and duplicate articles were eliminated. The search strategy used for each source of information is provided in Table 1. Study selection was carried out in 2 phases: phase 1 consisted of reading the title and the abstract, and phase 2 consisted of reading the full text. Figure 1.

The aforementioned procedures were performed by 2 reviewers independently, and in case of disagreements, a third reviewer was consulted.

Table 1. Search strategy used for each of the sources of information

Source of information	Search strategy
PubMed	("bruxism"[MeSH Terms] OR "sleep bruxism"[MeSH Terms]) AND (("systematic review"[Publication Type] OR "systematic review as topic"[MeSH Terms] OR "systematic review"[All Fields]) OR ("review"[Publication Type] OR "literature review as topic"[MeSH Terms] OR "review"[All Fields]) AND ("publications"[MeSH Terms] OR "literature"[MeSH Terms]) OR ("literature review as topic"[MeSH Terms]))
Scopus	(TITLE-ABS-KEY ("bruxism sleep") OR TITLE-ABS-KEY ("bruxism") AND TITLE-ABS-KEY ("systematic review"))
Cochrane	("systematic review" OR "systematic reviews" OR "systematic literature review" OR "systematic literature reviews" OR "meta analysis" OR "meta synthesis" OR "systematic" OR "review" OR "reviews") AND ("bruxism" OR "sleep bruxism" OR "bruxist") AND ("therapy" OR "adult" OR "treatment" OR "effectiveness") in Title Abstract Keyword
Embase	("bruxism"/exp OR 'bruxism' OR 'sleep bruxism'/exp OR 'sleep bruxism' OR 'awake bruxism') AND ('systematic review'/exp OR 'systematic review' OR 'integrative review'/exp OR 'integrative review' OR 'meta-analysis'/exp OR 'meta analysis' OR 'overview' OR 'review'/exp OR 'review' OR 'systematic literature review' OR 'rapid review'/exp OR 'rapid review')
Google Scholar	"treatment bruxism" AND "systematic review"
OpenGrey	"treatment" AND "bruxism"

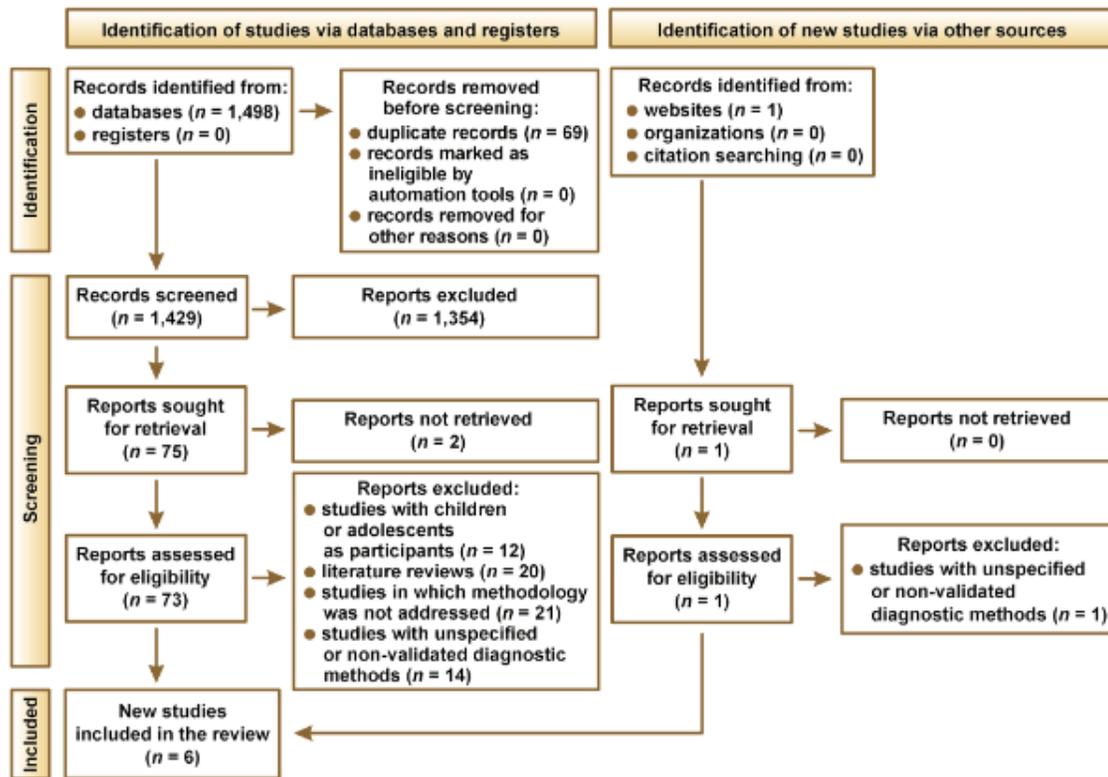


Fig. 1. Study selection flowchart

Data collection process and data elements

Once duplicate studies were eliminated, 2 reviewers independently compiled the data in a table. Any disagreement was resolved by a third reviewer. After the selection of the articles, the following information was extracted: author, year of publication, journal and impact factor; population; interventions and comparators; design of the primary studies; and diagnostic method for SB (Table 2).

Evaluation of methodological quality, quality of evidence and meta-bias

The evaluation of the methodological quality of the 6 included systematic reviews was performed by 2 reviewers independently by means of the AMSTAR 2 qualitative guide 15.

The 6 systematic reviews were evaluated according to the PRISMA 2020 Statement, which consists of 27 items.

Author (year) Country Journal impact factor	Population	Interventions and comparators	Primary study design	Diagnostic methods of bruxism
Ågren et al. ¹⁸ (2019) Suecia Journal of Oral Rehabilitation 3.837	Bruxism patients	BTX-A (I) Placebo (C)	RCT, prospective or retrospective studies	Instrumental approaches
Fernández-Núñez et al. ¹⁸ (2019) España Oral Medicine and Pathology 2.555	Bruxism patients	BTX-A (I) Placebo, occlusal splints, medications, or cognitive-behavioral therapy (C)	RCT	Instrumental and non-instrumental approaches
Manfredini et al. ¹⁹ (2015) Italia Journal of Oral Rehabilitation 3.837	Bruxism patients	SB diagnosis. (I) The comparison was based on the description of the control condition and features of the passive or active control group.	RCT and uncontrolled before–after studies.	Instrumental approaches
Jokubauskas et al. ²⁰ (2017) Journal of Oral Rehabilitation Lithuania 3.837	Bruxism patients	OA and MAA (I) Trigeminal nociceptive inhibitory splint, biofeedback (C)	RCT before–after crossover	Instrumental approaches
Long et al. ²¹ (2012) China International Dental Journal 2.512	Bruxism patients	BTX-A (I) Placebo or other interventional procedures (C)	RCT and non-randomized studies	Instrumental and non-instrumental approaches
Canales et al. ²² (2017) Clinical Oral Investigations 3.623	Bruxism patients	BTX-A (I) Other treatments (C)	RCT, prospective and before–after	Instrumental and non-instrumental approaches

Data synthesis

The main results of the included systematic reviews were summarized, and only the primary studies that evaluated a decrease in the electromyographic activity with the use of instrumental tools were analyzed according to each treatment applied, discarding those whose diagnostic method was non-instrumental. A visual indication system (traffic light) was used, where green represented the treatment with the best results, red indicated the treatment with the worst results, and yellow indicated that there were no differences between the compared groups. (Table 3).

Results

Review and selection of primary studies

The search in the electronic databases identified 1498 studies published between 2012 and 2022; after duplicates were eliminated, 1431 remained. In addition, 1 article was found in the gray literature. In phase 1, the title and abstract were reviewed, and 140 articles were selected; in phase 2, the text were read in full, obtaining 18, of which 6 systematic reviews were included for the qualitative synthesis. A total of 12 primary studies were identified within the systematic reviews. All systematic reviews were rated as critically low according to the AMSTAR 215 tool. More information on the evaluation of methodological quality can be found in Table 4.

Report of main findings

Of the 6 systematic reviews, 5 reported on the pharmacological management of bruxism. Four of them addressed the application of botulinum toxin type A (BTX-A), either into the temporalis or masseter muscle, unilaterally or bilaterally, with doses ranging from 8 IU to 80 IU. The information available on this topic is not conclusive, and although the results of some studies support the effectiveness of BTX-A in reducing the intensity of episodes of bruxism, there is not enough evidence to recommend this drug for the treatment of bruxism. One systematic review compared the effectiveness of clonazepam and clonidine with respect to placebo, showing a reduction in the episodes of bruxism; however, the follow-up period was limited.

Two systematic reviews reported on the effectiveness of OAs; comparison groups treated with stabilization splints and mandibular advancement devices (MADs) were included, and intermittent vs. continuous use and design were analyzed. The results of these investigations suggest that stabilization splints for intermittent use are the most recommended. Regarding MADs, both studies agree that they can significantly reduce bruxism and improve sleep quality, but can also cause muscle pain and temporomandibular disorders (TMDs).

Table 3. Results for the Effectiveness of Therapies for Sleep Fogginess Represented Graphically by Color, with Green and Red Representing the Treatments with the Best and Worst Results, Respectively, and Yellow Indicating that there are No Differences among the Compared Groups.

INSTRUMENTAL DIAGNOSTIC APPROACH						
Systematic review	Primary studies	Treatment	Intervention group	Control group	Reported results	Diagnostic method
Ågren et al. ¹⁸ , Fernández-Núñez et al. ⁸ , Canales et al. ²² , Long et al. ²¹ , Manfredini et al. ¹⁹	Lee SJ, McCall WD Jr., Kim YK, Chung SC, Chung JW. Effect of botulinum toxin injection on nocturnal bruxism: A randomized controlled trial. Am J Phys Med Rehabil. 2010;89(1):16–23. doi:10.1097/PHM.0b013e3181bc0c78	Botulinum toxin type A			p-value<.001* significant for the Botulinum toxin type A group (IG) compared with placebo (CG)	EMG
Ågren et al. ¹⁸	Ondo WG, Simmons JH, Shahid MH, Hashem V, Hunter C, Jankovic J. Onabotulinum toxin-A injections for sleep bruxism: A double-blind, placebo-controlled study. Neurology. 2018;90(7):e559–e564. doi:10.1212/WNL.0000000000004951				p-value=0.090 insignificant for both groups: Botulinum toxin type A (IG), placebo (CG)	EMG
Canales et al. ²² , Manfredini et al. ¹⁹	Shim YJ, Lee MK, Kato T, Park HU, Heo K, Kim ST.				p-value<0.01* significant	EMG

	Effects of botulinum toxin on jaw motor events during sleep in sleep bruxism patients: A polysomnographic evaluation. <i>J Clin Sleep Med.</i> 2014;10(3):291–298. doi:10.5664/jcsm.3532			t for both: Botulinum toxin type A (IG), placebo (CG)	
Manfredini et al. ¹⁹	Sato M, Iizuka T, Watanabe A, et al. Electromyogram biofeedback training for daytime clenching and its effect on sleep bruxism. <i>J Oral Rehabil.</i> 2015;42(2):83–89. doi:10.1111/joor.12233	Biofeedback		Significant p-value <0.050* for Biofeedback (IG) (p <0.05) compared with the placebo group (CG)	EMG
	Valiente López M, van Selms MK, van der Zaag J, Hamburger HL, Lobbezoo F. Do sleep hygiene measures and progressive muscle relaxation influence sleep bruxism? Report of a randomised controlled trial. <i>J Oral Rehabil.</i> 2015;42(4):259–265. doi:10.1111/joor.12252	Sleep hygiene instructions and Jacobson's relaxation techniques		p-value >0.050 insignificant for both groups: Sleep hygiene instructions and Jacobson's relaxation techniques (IG), information on the condition of SB (CG)	PSG
	Saletu A, Parapatics S, Anderer P, Matejka M, Saletu B.	Clonazepam		p-value = 0.010* significant for	PSG

	<p>Controlled clinical, polysomnographic and psychometric studies on differences between sleep bruxers and controls and acute effects of clonazepam as compared with placebo. Eur Arch Psychiatry Clin Neurosci.</p> <p>2010;260(2):163–174. doi:10.1007/s00406-009-0034-0</p>			<p>clonazepam (IG) compared with placebo (CG)</p>	
	<p>Carra MC, Macaluso GM, Rompré PH, et al. Clonidine has a paradoxical effect on cyclic arousal and sleep bruxism during NREM sleep. Sleep.</p> <p>2010;33(12):1711–1716. doi:10.1093/sleep/33.12.1711</p>	Clonidine		<p>significant p-value =0.020* for Clonidine compared with placebo (CG)</p>	PSG
	<p>Madani AS, Abdollahian E, Khiavi HA, et al. The efficacy of gabapentin versus stabilization splint in management of sleep bruxism. J Prosthodont.</p> <p>2013;22(2):126–131. doi:10.1111/j.1532-849X.2012.00914.x</p>	Hard stabilization splint		<p>p-value <0.050* significant for both groups: occlusal splint (IG), Gabapentin (CG)</p>	PSG
	<p>Matsumoto H, Tsukiyama Y, Kuwatsuru R, Koyano K.</p> <p>The effect of intermittent use of occlusal splint devices on sleep bruxism: A 4-week observation with a portable electromyographic recording device. J Oral Rehabil.</p> <p>2015;42(4):251–258. doi:10.1111/joor.12251</p>	Stabilization splint for continuous use		<p>p-value <0.050* significant for intermittent use (CG) compared with continuous use (IG)</p>	EMG

Jokubauskas y col. ²⁰	<p>Dalewski B, Chruściel-Nogalska M, Frączak B. Occlusal splint versus modified nociceptive trigeminal inhibition splint in bruxism therapy: A randomized, controlled trial using surface electromyography. Aust Dent J. 2015;60(4):445–454. doi:10.1111/adj.12259</p>	Mandibular occlusal splints			p-value > 0.050 insignificant for both groups: mandibular occlusal splints (IG) and modified nociceptive trigeminal inhibitory splint (CG)	EMG
	<p>Singh PK, Alvi HA, Singh BP, et al. Evaluation of various treatment modalities in sleep bruxism. J Prosthet Dent. 2015;114(3):426–431. doi:10.1016/j.prosdent.2015.02.025</p>	Reinforced adjustable mandibular advancement appliance			p-value > 0.050 insignificant for both groups: Reinforced adjustable mandibular advancement appliance (IG) and occlusal splints (CG)	PSG
	<p>Gu WP, Yang J, Zhang FM, Yin XM, Wei XL, Wang C.</p>	Maxillary OS +			significant p-value =0.001*	PSG

	Efficacy of biofeedback therapy via a mini Wireless device on sleep bruxism contrasted with occlusal splint: A pilot study. J Biomed Res. 2015;29(2):160–168. doi:10.7555/JBR.28.20130145	vibratory feedback			for maxillary OS and vibratory feedback (IG) compared with maxillary OS without vibration (CG)
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EMG – electromyography; PSG – polysomnography; * statistically significant.

Table 4. AMSTAR II: Critical appraisal tool for systematic reviews that include randomized or non-randomized studies of healthcare interventions, or both

AUTORS	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13	Q14	Q15	Q16	OVERALL CONFIANCE
(Ågren ET AL., 2019) ¹⁸	+	X	X	X	X	X	X	+	X	X	NM	NM	X	X	NM	X	Critically low
(De la Torre Canales et al., 2017) ²²	+	X	X	X	+	+	+	+	+	+	NM	NM	X	X	NM	+	Critically low
(Fernández et al., 2019) ⁸	+	X	X	X	+	+	+	+	+	X	NM	NM	+	X	NM	X	Critically low
(Jokubauskas et al., 2018) ²⁰	+	-	X	X	+	+	+	+	-	+	NM	NM	+	X	NM	+	Critically low
(Hu Long et al., 2012) ²¹	X	X	X	-	X	X	X	+	+	+	NM	NM	+	X	NM	+	Critically low
(Manfredini et al., 2015) ¹⁹	+	X	X	X	+	+	X	+	+	+	NM	NM	+	+	NM	+	Critically low

YES +
PARTIAL YES -
NO x
NO META-ANALYSIS NM

- Q1 - Did the research questions and inclusion criteria for the review include the components of PICO?
- Q2 - Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol? **
- Q3 - Did the review authors explain their selection of the study designs for inclusion in the review?
- Q4 - Did the review authors use a comprehensive literature search strategy? **
- Q5 - Did the review authors perform study selection in duplicate?
- Q6 - Did the review authors perform data extraction in duplicate?
- Q7 - Did the review authors provide a list of excluded studies and justify the exclusions? **
- Q8 - Did the review authors describe the included studies in adequate detail?

Q9 - Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review? **

Q10 - Did the review authors report on the sources of funding for the studies included in the review?

Q11- If meta-analysis was performed, did the review authors use appropriate methods for statistical combination of results?

Q12- If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?

Q13 - Did the review authors account for RoB in primary studies when interpreting/discussing the results of the review? ** 9

Q14 - Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?

Q15 - If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review? **

Q16- Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?

Rating overall confidence in the results of the review

High: No or one non-critical weakness: the systematic review provides an accurate and comprehensive summary of the results of the available studies that address the question of interest.

Moderate: More than one non-critical weakness*: the systematic review has more than one weakness but no critical flaws. It may provide an accurate summary of the results of the available studies that were included in the review

Low: One critical flaw with or without non-critical weaknesses: the review has a critical flaw and may not provide an accurate and comprehensive summary of the available studies that address the question of interest

Critically low: More than one critical flaw with or without non-critical weaknesses: the review has more than one critical flaw and should not be relied on to provide an accurate and comprehensive summary of the available studies.

*Multiple non-critical weaknesses may diminish confidence in the review and it may be appropriate to move the overall appraisal down from moderate to low confidence

Only 1 systematic review addressed the effects of BF. The findings of this study suggest a significant decrease in sleep bruxism events.

Discussion

Bruxism is a topic of interest in dentistry, so there is a need to provide scientifically proven information regarding its management. Several investigations have been carried out to confirm the safety and efficacy of various kinds of treatment aimed at solving bruxism. Systematic reviews are conducted to identify, evaluate and summarize research findings, and therefore they can provide reliable information and help guide clinical decision making. However, systematic reviews are not always carried out meticulously, and the risk of implicit bias can mislead readers and induce malpractice, as evidenced in our research, where the 6 included systematic reviews that met the eligibility criteria, when evaluated with the AMSTAR 2 tool,¹⁵ showed a low methodological quality; the critical points were not met in most of the investigations and the lack of homogeneity in terms of study design prevented us from performing any meta-analysis of the data.

Two of the included systematic reviews analyzed OAs, and reported diverse and confusing results, mainly due to the types of splints used, heterogeneous control groups and different observation periods. Manfredini et al. mention that almost all types of OAs for intermittent use are somehow effective in reducing the episodes of bruxism.¹⁹

However, Jokubauskas et al. indicate that although many studies support the efficacy of OA treatment for SB, the evidence is insufficient and the main role of OAs is protection against dental wear.²⁰ Therefore, both authors support the idea of

conducting future research with longer follow-up periods. Mainieri et al. reported that treatment with MADs resulted in a reduction in the activity of the chewing muscles, the signs and symptoms of SB, and occlusal strength as well as improvement in sleep quality, but 24% of their patients had to interrupt treatment due to TMDs, muscle pain and/or discomfort.²³ In contrast, Saueressig et al. reported positive effects of MADs in the therapy of SB, without any signs or symptoms of TMDs.²⁴

Another treatment for bruxism is the application of botulinum toxin, which has been referred to in a large number of studies. For example, Fernández-Núñez et al. concluded that its effectiveness was superior to any conventional treatment for SB, largely minimizing its symptoms.⁸ However, Long et al. revealed that botulinum toxin had the same efficacy as a nocturnal oral splint.²¹ De la Torre Canales et al. state that such disagreement is largely due to the lack of clinical protocols, the non-standardized dosage and different dilutions of the preparations among the different commercial brands used in each study.²² Regarding adverse effects, Lee et al.²⁵ and Zhang et al.²⁶ in their reviews reported the absence of adverse effects both at the time of treatment and after botulinum toxin injection, and if they were observed, they occurred in patients who received a dose higher than the established safe dose (≤ 100 IU) or who had a preexisting medical condition.²⁵

Studies that analyzed the effects of centrally acting drugs show very good results in the treatment of SB. It refers, among others, to clonazepam, used not only as an anticonvulsant, since its mechanism of action is also relaxation and sedation at the muscular level, mood stabilization, and relieving insomnia/anxiety.²⁷ In the study by Saletu et al., 21 patients diagnosed with BS received 1 mg of clonazepam per day, which showed efficacy in the polysomnographic study, with a statistically significant reduction of BS as compared to placebo.¹⁴ However, several authors mention that it is necessary to be cautious with this type of medication, since after a period of use of 2–4 weeks, it could cause dependence.^{28 29} Clonidine has an antihypertensive effect by acting as a selective agonist of the α_2 receptor, which influences the sympathetic–parasympathetic balance as well as the sleep structure and motor activities during sleep.³⁰ It is also used to treat migraine, chronic pain, psychiatric disorders, and SB.²⁷ Polysomnographic records have shown that clonidine is effective in reducing SB significantly.³¹

Recently, a group of researchers have evaluated the effect of 100 mg opi Pramol (a single dose), which shows positive effects in reducing SB. This information could be useful for researchers who delve into this topic of great interest, taking into consideration a larger population with a control group and long-term follow-up periods.³²

It has also been suggested that bruxism is a risk factor for developing TMDs, since an increase in the activity of the masticatory muscles could cause joint overload and myofascial pain. However, almost all studies that point to such an association used non-validated methods to diagnose bruxism, which indicates a possible diagnostic bias that could have increased the level of significance of the discussed association.^{33 34 35} Studies such as those by Smardz et al.³⁶ and Wieckiewicz et al.³⁷ showed through their results that the relationship between SB and TMDs was not statistically significant, clearly indicating that SB is not related to TMDs, nor does it increase the risk of the appearance of any specific diagnosis of TMDs. These studies support the importance of using scientifically proven methods for making an accurate diagnosis, and thus choosing the optimal treatment.

Regarding BF, it is a subject that is still under debate, as there are studies, such as those by Lobbezoo et al.¹ and Jokubauskas et al.,¹¹ which show positive effects, i.e., a reduction in the episodes of bruxism in the short term; however, the authors suggest more well-designed longitudinal studies with larger samples.

In general, with our study, we were able to demonstrate that, due to the lack of scientific evidence of Good methodological quality, there is still controversy and confusion about SB. A lot of misinformation has been provided about its pathophysiology in countless articles; dentists commonly relate it to peripheral factors – dental, occlusal and skeletal, believing that occlusal corrections decrease or stop this sleep activity.^{38 39} Yet, Manfredini et al. in their research questioned occlusal disharmony or premature contacts as an etiological factor, concluding that the contribution of occlusion was not statistically significant in patients with and without bruxism.⁴ Similarly, in a study by Ommerborn et al., a review of the functional and occlusal role was made, and no relationship was found with regard to the occlusal parameters, or skeletal or orofacial anatomy, that could explain bruxism events; on the contrary, the authors found that the role of psychology, neurotransmitters and microarousals as central factors prevailed. Obviously, as in any pathology, whether an associated disorder occurs or not depends on the adaptive capacity of the person, e.g., coping with pain or stress, and genetic predisposition.⁴⁰ Therefore, SB is no longer considered to be simply related to dental occlusion factors, but it is known to have a central origin, which involves biological factors (e.g., neurochemical factors, such as dopamine and other neurotransmitters, genetics and sleep disorders), physiological factors (e.g., brain activity, muscle activity, and cardiac and respiratory functions, etc.) and psychological factors (e.g., stress sensitivity, personality traits and anxiety).^{5 41 42 43 44 45 46} This has resulted in a major transformation in our understanding of BS.

Therefore, it is important to know how SB is generated and to be aware of the different stages of sleep that a person normally goes through. Sleep ideally should

last 7–8 h, starting with wakefulness, continuing with non-REM (rapid eye movement) sleep (N1, N2, N3) until the depth of sleep or REM sleep increases, and this cycle is repeated several times during the night. However, there are moments in which the individual goes to wakefulness, and these brief periods are known as micro-arousals. The term ‘micro-arousal’ refers to a response or a sudden change in sleep during which the individual reaches a lighter sleep, and then there is an interruption of sleep for at least 3 s, characterized by an increase in brain, autonomic, cardiac, and muscular activity, without a complete return to consciousness.⁴⁷ Taking micro-arousals as a reference, associated pathologies can be identified, such as obstructive sleep apnea (OSA), which consists in the interruption of sleep due to the lack of air in an attempt to breathe again.^{48 49} Several studies have considered the possible association between SB and OSA, as SB may be a motor reflex of the central nervous system in response to a sleep arousal and OSA leads to sleep arousals.^{50 51 52} Another pathology associated with bruxism is gastroesophageal reflux (GER), which occurs when gastric acid passes from the stomach into the esophagus, and once it exceeds the adaptive capacity of the epithelium, it generates symptoms or histological damage.⁵³ Li et al. showed a strong association between bruxism and symptomatic GER, and recommended that the GER status be taken into consideration as a fundamental part of the diagnosis of bruxism.⁵⁴

Previous studies identified that also hypoxia,⁵⁵ increased body mass index (BMI),⁵⁶ hypertension,^{1 56 57} excessive daytime sleepiness⁵⁸ and snoring⁵⁹ acted as independent risk factors for SB; in this study we did not investigate these issues, and another type of study could be conducted in the future to clarify them. Taking into account all the background described above, researchers saw the need to update information about SB, and it is in the 2018 consensus where SB is defined as the activity of the masticatory muscles during sleep (characterized as rhythmic or non-rhythmic) and where it is considered as a behavior.³ According to its clinical consequences, it was classified as: (i) a risk factor if it presents one or more negative consequences for oral health, such as severe masticatory muscle pain or joint pain, increasing the likelihood of developing a disease, without necessarily inducing it; (ii) a protective factor if it provides one or more positive health outcomes, as in the case of OSA, where the upper airway can be prevented from collapsing or its patency can be restored during sleep, or in the case of GER, where increased salivation reduces the risk of harmful chemical tooth wear; or (iii) it is neither a risk factor or a protective factor, i.e., it is only considered a motor activity of multifactorial etiology, with no consequences at the level of oral health; it is extremely important not to overdiagnose it as a pathology, since its intensity or frequency does not mean pathogenicity.^{60 61 62 63}

Conclusions

Taking the limitations of the present study into consideration, the following conclusions can be drawn: the methodological quality of the studies included in this research, after being analyzed with AMSTAR 2, proved critically low; the authors recommend future research studies of better methodological quality so that the results can be applied in clinical practice. The use of centrally acting drugs, such as clonazepam and clonidine, demonstrated efficacy in reducing the episodes of SB; however, caution is recommended in their administration because of adverse effects. Treatment with botulinum toxin, OAs and BF did not demonstrate short-term efficacy; therefore, prospective studies with a longer duration are recommended.

The difficulty involved in treating SB is that it does not always need to be controlled, as in most cases, it should not be considered a pathology according to the current literature. It can be a risk factor or a protective factor; therefore, treatment should not be focused on SB as such, but on investigating the pathologies, comorbidities or associated factors that lead to its onset.

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