Review article

Managements of sleep bruxism in adult: A systematic review

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ABSTRACT

This systematic review aimed to update the management of sleep bruxism (SB) in adults, as diagnosed using polysomnography (PSG) and/or electromyography (EMG). Management methods covered were oral appliance therapy (OAT) with stabilization splints, cognitive-behavioral therapy (CBT), biofeedback therapy (BFT), and pharmacological therapy. A comprehensive search was conducted on MEDLINE, Cochrane Library, and Web of Science up to October 1st, 2021. Reference list searches and hand searches were also performed by an external organization. Two reviewers for each therapy independently performed article selection, data extraction, and risk of bias assessment. The reviewers resolved any disagreements concerning the assortment of the articles by discussion. Finally, 11, 3, 14, and 22 articles were selected for each therapy. The results suggested that OAT tended to reduce the number of SB events, although there was no significant difference compared to other types of splints, that the potential benefits of CBT were not well supported, and that BFT, rabeprazole, clonazepam, clonidine, and botulinum toxin type A injection showed significant reductions in specific SB parameters, although several side effects were reported. It can be concluded that more methodologically rigorous randomized large-sample long-term follow-up clinical trials are needed to clarify the efficacy and safety of management for SB.

Contents

1. Introduction

An international consensus was obtained on the definition of sleep and awake bruxism (SB and AB, respectively) as masticatory muscle activities that occur during sleep (characterized as rhythmic or non-rhythmic) and wakefulness (characterized by repetitive or sustained tooth contact and/or by bracing or thrusting of the mandible), respectively. In addition, bruxism was not considered as a disorder, but instead as a behavior that can be a risk factor for certain clinical consequences [1,2]. SB may lead to excessive occlusal forces higher than the maximum clenching force under consciousness. Excessive mechanical stress is a critical risk factor for tooth fracture/chippage, periodontal disease, and masticatory muscle/temporomandibular joint disorders (TMD) [3]. Therefore, it is important to relieve this excessive mechanical stress to maintain the morphological and physiological functions of the teeth, periodontal tissue, and masticatory muscle/temporomandibular joint (TMJ).

To date, several management approaches have been applied to reduce the harmful effects of SB. A typical and widely recognized approach is oral appliance therapy (OAT), especially the maxillary stabilization appliance, which is the standard management procedure and is used in daily clinical activities. In addition, other types of oral splints, such as advanced mandibular repositioning splint that guides the mandible to the protrusive position and anterior tooth splint were also used; however, their therapeutic effects were not fully objectively compared using the polysomnography (PSG) and/or electromyography (EMG).

Furthermore, cognitive-behavioral therapy (CBT), biofeedback therapy (BFT), and pharmacological approaches have been introduced and applied. Several studies have reported that SB is related to psychosocial factors, and it has been recognized that psychological stress is one of the risk factors for SB [4–6]. This indicates that a psychological approach would be reasonable for SB in terms of risk avoidance. This psychological approach includes counseling, relaxation techniques, suggestive hypnotherapy, sleep hygiene education, and lifestyle changes [7,8]. In response, several clinical studies have evaluated the management efficacy of CBT; however, its efficacy to treat SB has not yet been examined in detail.

Currently, BFT has been introduced and has indicated a significant effect in reducing EMG activity of the SB. However, some studies reported that EMG activity returned to baseline levels after treatment [9,10], whereas a recent report indicated that it has demonstrated a long-term effect [11]. Therefore, its efficacy is still controversial.

Furthermore, several pharmacological approaches have also been applied to manage SB, such as proton pump inhibitors, anti-convulsants, anti-hypertensives, and botulinum toxin type-A (BTX-A) injections. Unfortunately, many of these pharmacological approaches have been individually examined for their SB reduction effect; however, the comparisons among various pharmacological approaches have not been sufficiently evaluated, especially by means of objective assessment.

On the other hand, several risk factors such as alcohol, tobacco intake, psychological stress, and specific medication are related to the incidence/aggravation of SB [12–16]. Therefore, these risk control or avoidance approaches would be a potential management strategy; however, a clinical study of these risk management approaches has not been obtained to our best knowledge, thus this systematic review did not cover the topic.

Several reviews have already been published for evaluating the management efficacy of these approaches; however, most reviews have not mentioned the validity level of each research result. One of the doubtful points of SB-related research is the reliability of the assessment system. Previously, several approaches have been applied to assess SB, such as the subject's self-assessment, tooth wear, report of a bed partner/family, the indentation of cheek/tongue mucosa, bone ridge, and objective assessment by EMG and/or PSG. Currently, the gold standard for SB assessment has been widely recognized as the PSG plus audio-video recording system because it can obtain the electroencephalogram, electrocardiogram, electrooculogram, and masticatory muscle EMG, consequently, scorers can accurately exclude EMG activities that are not related to SB. In addition, this physiological information is useful for obtaining the subject's sleep condition. However, PSG assessment may add a physical and psychological burden to subjects; therefore, the feasibility in clinical dental practice is not high. On the other hand, several portable-ambulatory EMG devices can be easily used to measure even in subjects' sleep environment, thus their feasibility would be high. Although a single EMG assessment tended to result in a higher false-positive rate, its validity and reliability would be relatively high compared to other subjective assessment procedures [17]. Thus, this systematic review focused on only the research results of PSG and/or EMG-based assessments that were defined in Instrumentally Base Assessment (IBA) as A5 and A7 in Axis A described in Standardized Tool for the Assessment of Bruxism (STAB) consensus [2].

The optimal endpoint would be the specific EMG parameter that relates to the risks of issues such as tooth fracture, aggravation/alleviation of periodontal disease, and change of TMD/masticatory muscle problem. However, the specific characteristics associated

with SB-related signs/symptoms have not yet been elucidated. Thus, this systematic review adopted the previously suggested criteria as surrogate endpoints [18].

This systematic review aimed to determine the appropriate management of SB among several approaches. To achieve this deeper consideration, it is necessary to consider the research quality and evidence level in addition to summarizing the research results.

2. Material and methods

2.1. Search strategy method and focused question

This systematic review was performed according to the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) statement [19]. The aim of this systematic review was to evaluate the four different management efficacies for reducing SB, therefore, the following four review questions were formulated using the PICO (participant, intervention, comparison and outcome) approach [20]: "CQ-1: Oral appliance therapy with maxillary stabilization splints was effective to reduce sleep bruxism intensity/frequency than no treatment/ other oral appliances, CQ-2: Cognitive-behavioral therapy was effective to reduce sleep bruxism intensity/frequency, CQ-3: Biofeedback therapy was effective to reduce sleep bruxism intensity/frequency, and CQ-4: Pharmacological therapy was effective to reduce sleep bruxism intensity/frequency than no treatment.

CQ-1:

- P: Healthy adult population with primary sleep bruxism
- I: Insertion and usage of oral appliance during sleep. Oral appliance was maxillary stabilization type made by acrylic resin.
- C: Insertion of other types of oral appliance
- O: Effectiveness of oral appliance (maxillary stabilization type) therapy was assessed by changes in SB events measured by PSG with audio-video recording, PSG or portable EMG.

CQ-2:

- P: Healthy adult population with primary sleep bruxism
- I: Application of cognitive-behavioral therapy
- C: No treatment or other treatment
- O: Effectiveness of cognitive-behavioral therapy was assessed by changes in SB events measured by PSG with audio-video recording, PSG or portable EMG.

CQ-3:

- P: Healthy adult population with primary sleep bruxism
- I: Application of biofeedback therapy
- C: No treatment
- O: Effectiveness of biofeedback therapy was assessed by changes in SB events measured by PSG with audio-video recording, PSG or portable EMG.

CQ-4:

- P: Healthy adult population with primary sleep bruxism
- I: Pharmacological approach to sleep bruxism. The medications of prescription were rabeprazole, tryptophan, L-dopa (levodopa), bromocriptine, amitriptyline, opipramol, clonazepam, propranolol, clonidine, gabapentin, pramipexole and botulinum toxin type A.
- C: No treatment or other treatment
- O: Effectiveness of pharmacological therapy was assessed by changes in SB events measured by PSG with audio-video recording, PSG or portable EMG.

Table 1a
Search fomula of CQ-1 maxillary stabilization splint therapy.

#1	"Sleep Bruxism/therapy"[MeSH]
#2	((sleep bruxism) OR (nocturnal bruxism) OR ((clenching OR grinding) AND (teeth OR tooth)) OR ((masseter muscle) AND sleep)) AND (therapy OR therapeutic OR treatment)
#3	"Occlusal Splints"[MeSH] OR ((splint* OR "oral appliance") AND "Orthodontic Appliances"[MeSH])
#4	(occlusal splint) OR ((splint* OR (oral appliance)) AND (orthodontic appliance))
#5	(#1 OR #2) AND (#3 OR #4)
#6	#5 AND (clinical trial)
#7	#5 AND (randomized controlled trial)
#8	#5 AND (case-control study)
#9	#5 AND (cohort study)
#10	#5 AND (cross-sectional study)
#11	#5 AND (multicenter study)
#12	#5 AND (observational study)
#13	#5 AND (feasibility study)
#14	#5 AND (pilot study)
#15	#5 AND (longitudinal study)
#16	#5 AND (follow-up study)
#17	#5 AND (retrospective study)
#18	#5 AND (prospective study)
#19	#5 AND (double-blind method)
#20	#5 AND (number needed to treat)
#21	#5 AND (random allocation)
#22	#5 AND (treatment outcome)
#23	#5 AND review
#24	#6 OR #7 OR #8 OR #9 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #20 OR #22 OR #23

2.2. Search methodology

An electronic search of PubMed, Cochrane Library database and Web of Science was performed to systematically identify the relevant literature. Articles published between 1990 and October 1st, 2021, were considered. The search string comprised a combination of keywords (Medical Subject Headings [MeSH]) and free-text terms. Linkage was achieved using Boolean operators (OR and AND). To ensure independence, all of these processes were linked to the Japan Medical Library Association. The search formulas used in the PubMed are listed in Tables 1a-e.

Additionally, extended search was applied to prevent the missing of the eligible article by means of the wide range of search formula and a manual search of relevant articles. Finally, the references of all selected full-text articles were also searched for relevant studies. A manual search process was applied based on the bibliographies of the selected articles. (Tables 2, 3 and 4).

2.3. Search strategy

The electronic search was completed by manual searching within the references of the selected articles. All titles revealed by this strategy were screened, followed by an abstract search to identify further relevant articles. Full-text articles were chosen based on the abstracts.

2.4. Eligibility and exclusion criteria

Two prosthodontic specialist reviewers in each clinical question (CQ-1: A.N. and K.O., CQ-2, 3: K.O. and T.I., CQ-4: Y.A. and N.T.) independently performed the article retrieval and screened the titles and abstracts to identify studies that were eligible for selection according to the following inclusion and exclusion criteria.

The following inclusion criteria were applied: published in a peer-reviewed journal, clinical studies, randomized controlled trials (RCTs), prospective and retrospective studies, publications available

Table 1b
Search fomula of CQ-2 cognitive-behavioral therapy.

#1	"Sleep Bruxism/therapy"[MeSH]
#2	((sleep bruxism) OR (nocturnal bruxism) OR ((clenching OR grinding) AND (teeth OR tooth)) OR ((masseter muscle) AND sleep)) AND (therapy OR therapeutic OR treatment)
#3	"Cognitive Therapy"[MeSH] OR ("cognitive behavior therapy" AND "Psychotherapy"[MeSH])
#4	(cognitive therapy) OR ((cognitive behavior therapy) AND psychotherapy)
#5	(#1 OR #2) AND (#3 OR #4)
#6	#5 AND (clinical trial)
#7	#5 AND (randomized controlled trial)
#8	#5 AND (case-control study)
#9	#5 AND (cohort study)
#10	#5 AND (cross-sectional study)
#11	#5 AND (multicenter study)
#12	#5 AND (observational study)
#13	#5 AND (feasibility study)
#14	#5 AND (pilot study)
#15	#5 AND (longitudinal study)
#16	#5 AND (follow-up study)
#17	#5 AND (retrospective study)
#18	#5 AND (prospective study)
#19	#5 AND (double-blind method)
#20	#5 AND (number needed to treat)
#21	#5 AND (random allocation)
#22	#5 AND (treatment outcome)
#23	#5 AND review
#24	#6 OR #7 OR #8 OR #10 OR #16 OR #22 OR #23

Table 1c
Search fomula of CQ-2 hypnotherapy.

#1	"Sleep Bruxism/therapy"[MeSH]
#2	((sleep bruxism) OR (nocturnal bruxism) OR ((clenching OR grinding) AND (teeth OR tooth)) OR ((masseter muscle) AND sleep)) AND (therapy OR therapeutic OR treatment)
#3	"Autosuggestion"[MeSH] OR "Hypnosis"[MeSH]
#4	autosuggestion OR self-suggestion*
#5	hypnotherapy OR hypnosis OR hypnosis OR mesmerism
#6	(#1 OR #2) AND (#3 OR #4 OR #5)
#7	#6 AND (clinical trial)
#8	#6 AND (randomized controlled trial)
#9	#6 AND (case-control study)
#10	#6 AND (cohort study)
#11	#6 AND (cross-sectional study)
#12	#6 AND (multicenter study)
#13	#6 AND (observational study)
#14	#6 AND (feasibility study)
#15	#6 AND (pilot study)
#16	#6 AND (longitudinal study)
#17	#6 AND (follow-up study)
#18	#6 AND (retrospective study)
#19	#6 AND (prospective study)
#20	#6 AND (double-blind method)
#21	#6 AND (number needed to treat)
#22	#6 AND (random allocation)
#23	#6 AND (treatment outcome)
#24	#6 AND review
#25	#10 OR #15 OR #16 OR #17 OR #23 OR #24

Table 1d
Search fomula of CQ-3 biofeedback therapy.

#1	"Sleep Bruxism/therapy"[MeSH]
#2	((sleep bruxism) OR (nocturnal bruxism) OR ((clenching OR grinding) AND (teeth OR tooth)) OR ((masseter muscle) AND sleep)) AND (therapy OR therapeutic OR treatment)
#3	"Biofeedback, Psychology"[MeSH]
#4	biofeedback OR (false physiological feedback) OR (bogus physiological feedback) OR neuro feedback OR (sensory feedback) OR (proprioceptive feedback) OR (visual feedback) OR (sensorimotor feedback) OR (audio feedback) OR (alpha feedback) OR (electromyography feedback) OR (EEG feedback) OR (brainwave feedback)
#5	(#1 OR #2) AND (#3 OR #4)
#6	#5 AND (clinical trial)
#7	#5 AND (randomized controlled trial)
#8	#5 AND (case-control study)
#9	#5 AND (cohort study)
#10	#5 AND (cross-sectional study)
#11	#5 AND (multicenter study)
#12	#5 AND (observational study)
#13	#5 AND (feasibility study)
#14	#5 AND (pilot study)
#15	#5 AND (longitudinal study)
#16	#5 AND (follow-up study)
#17	#5 AND (retrospective study)
#18	#5 AND (prospective study)
#19	#5 AND (double-blind method)
#20	#5 AND (number needed to treat)
#21	#5 AND (random allocation)
#22	#5 AND (treatment outcome)
#23	#5 AND review
#24	#6 OR #7 OR #8 OR #9 OR #14 OR #15 OR #16 OR #22 OR #23

Table 1e
Search fomula of CQ-4 pharmacotherapy.

#1	"Sleep Bruxism/drug therapy"[MeSH]
#2	"Bruxism/drug therapy"[MeSH] AND ("sleep bruxism" OR "nocturnal bruxism")
#3	((sleep bruxism) OR (nocturnal bruxism) OR ((clenching OR grinding) AND (teeth OR tooth)) OR ((masseter muscle) AND sleep)) AND ((drug AND (therapy OR therapeutic OR treatment)) OR chemotherapy OR pharmacotherapy)
#4	#1 OR #2 OR #3
#5	#4 AND (clinical trial)
#6	#4 AND (randomized controlled trial)
#7	#4 AND (case-control study)
#8	#4 AND (cohort study)
#9	#4 AND (cross-sectional study)
#10	#4 AND (multicenter study)
#11	#4 AND (observational study)
#12	#4 AND (feasibility study)
#13	#4 AND (pilot study)
#14	#4 AND (longitudinal study)
#15	#4 AND (follow-up study)
#16	#4 AND (retrospective study)
#17	#4 AND (prospective study)
#18	#4 AND (double-blind method)
#19	#4 AND (number needed to treat)
#20	#4 AND (random allocation)
#21	#4 AND (treatment outcome)
#22	#4 AND review
#23	#5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #13 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22

in English, and human subjects' studies. No restrictions were placed on the length of the follow-up period.

The following exclusion criteria were applied: case reports, in vitro studies, and animal studies. Duplicated and published studies that did not meet the inclusion criteria were excluded from this systematic review. Only the most recent publication was included in cases of possible duplication.

2.5. Screening procedures

Titles and abstracts were initially screened independently by two reviewers for inclusion in the review, and the selected abstracts were listed. The lists were then compared, and a definitive consensus regarding the inclusion of articles was reached by discussing each article by the assigned reviewers. The full text of all potentially relevant studies was then obtained for independent assessments by

Table 2
Summary of descriptive characteristics of splint therapy and quality assessment according to simplified GRADE checklist.

Author:	Control splint:	Study design	Random sequence generation	Allocation concealment	Blinding (participants and personnel)	Blinding (outcome assessment)	ITT	Incomplete outcome data	Selective reporting	stopped early trial for benefits	Other sources of bias	summary	subjects	intervention	control	outcome	summary	Control Pre	Control Post	Intervention pre	Intervention post	Intervention period
Dubé C et al, 2004 [31]	Palatal coverage splint	RCT	0	-1	-1	0	0	0	0	0	0	-1	0	0	0	0	0	6.3 (3.7-10.5)	3.7 (2.8-7.9)	6.3 (3.7-10.5)	3.7 (0.2-8.2)	2 weeks
van der Zaag J et al, 2005 [32]		RCT	-1	-1	-1	0	0	0	0	0	-1	-1	0	0	0	0	0	7.41 (1.51)	10.57 (2.14)	6.22 (1.03)	11.1 (1.92)	2 weeks
Harada T et al, 2005 [33]		RCT	-1	-1	-1	0	0	0	0	0	0	-1	0	0	0	0	0	3.0 / 2.6 / 2.8		2.2 / 2.4 / 2.7		2 weeks / 4 weeks / 6 weeks
Takahashi H et al, 2013 [34]		RCT	-1	-1	-1	-1	0	0	0	0	0	-1	-1	0	0	0	-1	3.24 (0.89)	2.01 (1.18)	3.24 (0.89)	0.68 (0.65)	3 days
Gerstner G et al, 2020 [35]		RCT	0	-1	0	0	0	0	0	0	0	-1	0	0	0	0	0	9.4±6.2		13.7±7.8		4 month
Landry ML et al, 2006 [36]	Mandibular anterior repositioning splint	RCT	0	-1	-1	0	0	0	0	0	0	-1	0	0	0	0	0	7	3.8 / 1.5 / 1	7	4	2 weeks
Landry-Schönbeck A et al, 2009 [37]		RCT	0	0	-1	-1	0	0	0	0	0	-1	0	0	0	0	0	5.9(0.71)	3.6(1.0) / 3.1(0.89)	5.9(0.71)	3.9(0.89)	2 weeks
Arima T et al, 2012 [38]		RCT	-1	-1	-1	-1	0	0	0	0	0	-1	0	0	0	0	0	6.7 (1.2)	5.2 (1.1) / 5.0 (1.2)	6.7 (1.2)	4.3 (1.0)	1 weeks
Singh PK et al, 2015 [39]		RCT	0	0	-1	0	-1	0	0	0	0	-1	0	0	0	0	0	7.96(1.59)	5.11(1.19) / 1.66(0.21)	7.18(1.09)	5.0(1.1) / 3.6(0.55)	1 month / 3 months
Baad-Hansen L et al, 2007 [40]	Anterior splint	RCT/crossover	-1	-1	0	-1	0	0	0	0	0	-1	0	0	0	0	0	9.3 (6.39)	3.15 (4.41)	9.49 (7.96)	8.9 (10.59)	2 weeks
Lukic N et al, 2021 [41]		RCT/crossover	0	-1	-1	-1	0	0	0	0	0	-1	0	0	0	0	0	10.3±0.7	11±0.6	10.3±0.7	8.7±0.6	7 weeks

Table 3
Summary of descriptive characteristics of CBT and BFT and quality assessment according to simplified GRADE checklist.

Category:	Author	Intervention	Study design	Outcome	Random sequence generation	Allocation concealment	Blinding (participants and personnel)	Blinding (outcome assessment)	ITT	Incomplete outcome data	Selective reporting	stopped early trial for benefits	Other sources of bias	summary	subjects	intervention	control	outcome	summary	Control pre-intervention	Control post-intervention	Intervention pre-intervention	Intervention post-intervention	
cognitive-behavioral therapy	Clarke JH and Reynolds PJ, 1991 [20]	Hypnotherapy	Uncontrolled before-after study	EMG(RMS)	-2	-1	-2	-2	-1	-1	-1	0	0	-2	-1	-1	0	0	-2	2784.8 +/-1383.7 (pre, mean +/- SD)		1488.6 +/-743.6 (post, mean +/- SD)		p=0.001
	Ommerbom MA et al, 2007 [21]	problem-solving, progressive muscle relaxation, nocturnal biofeedback, and training of recreation and enjoyment VS occlusal splint	RCT	pixel score	-2	-1	-1	-2	-1	-1	0	0	0	-2	-1	-1	0	0	-2	7684.69 +/- 1175.21 (pre)	7223.66 +/- 1047.66 (post)	8562.00 +/- 1196.01 (pre)	6548.70 +/- 1066.21 (post)	N.S.
	López MV et al, 2015 [27]	Sleep hygiene and relaxation techniques	RCT	Episode/hour	-1	-1	-1	-1	0	0	0	0	0	-1	0	0	0	0	0	2.6 (pre)	3 (post)	3.2 (pre)	3.55 (post)	p=0.484
				burst/hour																21.8 (pre)	25.8 (post)	19.8 (pre)	33 (post)	p=0.263
Biofeedback therapy	Nishigawa K et al, 2003 [48]	noxious electrical pulses	Uncontrolled before-after study	Duration (s/event)	-2	-1	-2	-2	-1	-1	0	0	0	-1	-1	-1	0	-1	-1	10.61 +/- 2.48 (pre)		9.08 +/- 2.48 (post)		p=0.038
				Number (no./hour)																3.87 +/- 2.01 (pre)		2.42 +/- 0.78 (post)		p=0.107
	Jadidi F et al, 2008 [9]	contingent electrical stimulation	RCT/crossover	number of EMG events detected with the 10% MVC	-1	0	0	0	0	0	0	0	0	-1	0	0	0	0	0	NA		NA		P>0.045
				number of EMG events detected with the 20% MVC																NA		NA		P=0.227
	Jadidi F et al, 2011 [46]	contingent electrical stimulation	RCT/crossover	average number of EMG episodes per hour	-1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	17.7 ± 5.8	without CES	16.3 ± 4.8.	with CES	P = 0.733
	Jadidi F et al, 2013 [47]	contingent electrical stimulation	RCT	number of EMG episodes/hour	0	0	0	0	0	-1	0	0	0	0	0	0	0	0	0	no significant differences		p > 0.927	reduced (52 ± 12%)	< 0.035
	Raphael KG et al, 2013 [52]	innocuous electrical pulse	Uncontrolled before-after study	number of EMG events	-2	-2	-2	-1	-1	0	0	0	0	-1	-1	-1	0	0	-1	488.3 (21.4)		35.4		P =0.02
	Gu W et al, 2015 [50]	vibrations alert VS occlusal splint	CCT	total episodes of bruxism events	-1	-1	-1	0	0	0	0	0	0	-1	-1	-1	-1	0	-1	11.9+/-5.7 (pre)	11.4 +/- 3.7 (post 12 weeks)	10.2+/-2.8 (pre)	3.3 +/- 1.4 (post 12 week)	P =0.001
				duration of bruxism events																14.8 +/- 5.5 a (pre)	14.0 +/- 6.1 (post)	17.3 +/- 9.8 a (pre)	8.9 +/- 2.7 (post)	P > 0.05
	Conti PC et al, 2014 [51]	contingent electrical stimulation	RCT	mean number of EMG/h	0	0	0	0	0	-1	0	0	0	0	-1	-1	-1	0	0	24.8 +/- 14.8 (pre)	25.0 +/- 13.9 (post)	33.5 +/- 23.5 (pre)	20.6 +/- 16.9 (post)	P=0.003
	Sumiya M et al, 2014 [44]	electrical stimulations	Uncontrolled before-after study	mean number of SB events per night	-2	-1	-2	-2	0	0	0	0	0	-1	-1	-1	0	0	-2	NA		NA		significantly decrease
				mean number of SB events per hour																NA		NA		significantly decrease
				mean number of SB bursts per SB event																NA		NA		significantly decrease
				mean number of duration of SB events																NA		NA		significantly decrease
	Sato M et al, 2015 [49]	auditory alert	RCT	number of tonic EMG events	-1	-1	0	-1	0	0	0	0	0	-1	0	0	0	-1	-1	15.6 +/- 10.3 (pre)		18.3 +/- 10.0 (pre)	3.7 +/- 4.2 (post 3 weeks)	no significance
	Nakamura H et al, 2019 [45]	biofeedback (vibration) splint	Uncontrolled before-after study	number of bruxism episode	-2	-2	-2	-1	-1	0	0	0	0	-1	-1	-1	0	0	-1	NA		4.1 ± 2.8 (per hour)	3.0 ± 2.0 (per hour)	tended to decrease
				total bruxism duration																NA		26.0 ± 20.0 (per hour)	14.3 ± 9.5 (per hour)	P = 0.03
	Bergmann A et al, 2020 [42]	full- occlusion biofeedback (vibration) splint	RCT	total duration per hour	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0		increase 11.5 ± 28.4		increase 5.2 ± 17.5	P = 0.060
				bursts per hour																	increase 1.8 ± 11.3		increase 2.2 ± 24.9	P = 0.730
				average duration																	increase 283.7 ± 785.2		decrease 189.6 ± 278.7	P = 0.092
				maximum duration																	increase 12.01 ± 43.74		decrease 5.443 ± 10.27	P = 0.021
	Nakazato Y et al, 2020 [43]	biofeedback (vibration) splint	RCT	number of bruxism episode	-1	-1	-2	-1	0	0	0	0	-1	-1	0	0	0	0	0		5.2 (per hour)		3.9 (per hour)	P = 0.002
				total bruxism duration																	35.3 a (per hour)		15.1 a (per hour)	P = 0.002
	Ohara H et al, 2021 [46]	biofeedback (vibration) splint	RCT	number of bruxism episode	-1	-1	-2	-1	0	0	0	0	-1	-1	0	0	0	0	0	NA		NA		significantly decrease
				total bruxism duration																NA		NA		significantly decrease
	Saito-Murakami K et al, 2020 [47]	daytime bio feedback training	RCT	number of phasic burst events	-1	-1	-1	0	0	0	0	0	0	0	0	0	0	0	-1	82.0 ± 31.6		32.4 ± 19.6		significantly decrease

the same reviewers. The reviewers resolved any disagreements concerning the assortment of the articles by discussion. Any discrepancy during the screening and selection process was resolved by discussion, and a third reviewer (H.M.) was consulted as needed to reach a consensus. In cases where the desired information could not be obtained from the literature, the corresponding author was contacted. Only studies with sufficient and specific data available were included for further analysis. Discrepancies and disagreements were resolved through discussion and consensus.

2.6. Data extraction

Data extraction was performed independently by the two reviewers in each CQ team using a standardized form. A data extraction form was developed by the authors to collect general information: authors, title, year of publication, journal, study aim, study design, level of evidence, number of participants, complications, follow-up period, and outcomes.

Information on changes in frequency, intensity, and duration of SB events or episodes, as well as complications, was extracted from the included studies.

The assessment of SB was diagnosed by PSG test plus audio-video recording, PSG test alone, EMG test, or ambulatory EMG device-based assessment. SB was defined based on the description of Lavigne et al. [17], and the intensity and frequency of SB were

assessed by the number of SB events, pixel score [21], EMG value, number of SB episodes, and SB index [22–24]. Complications were characterized by objective/subjective assessments of physical and psychological problems. The two reviewers in each CQ independently extracted the data regarding SB change from each included study. After the data were checked, the consensus was reached through discussion.

2.7. Data synthesis

To evaluate all data and identify variations in study characteristics and outcomes, data were pooled into evidence tables, and a descriptive summary was generated. This enabled the detection of similarities and differences between studies, as well as the determination of the suitability of further synthesis or comparison methods.

2.8. Quality assessment

Quality and risk of bias assessments were independently performed by the two reviewers as part of the data extraction process. Discrepancies and disagreements were resolved through discussion. The quality assessment of the included RCTs, controlled clinical trials (CCTs), and observational studies was performed using the Cochrane Collaboration's tool for assessing the risk of bias [25]. This scale is
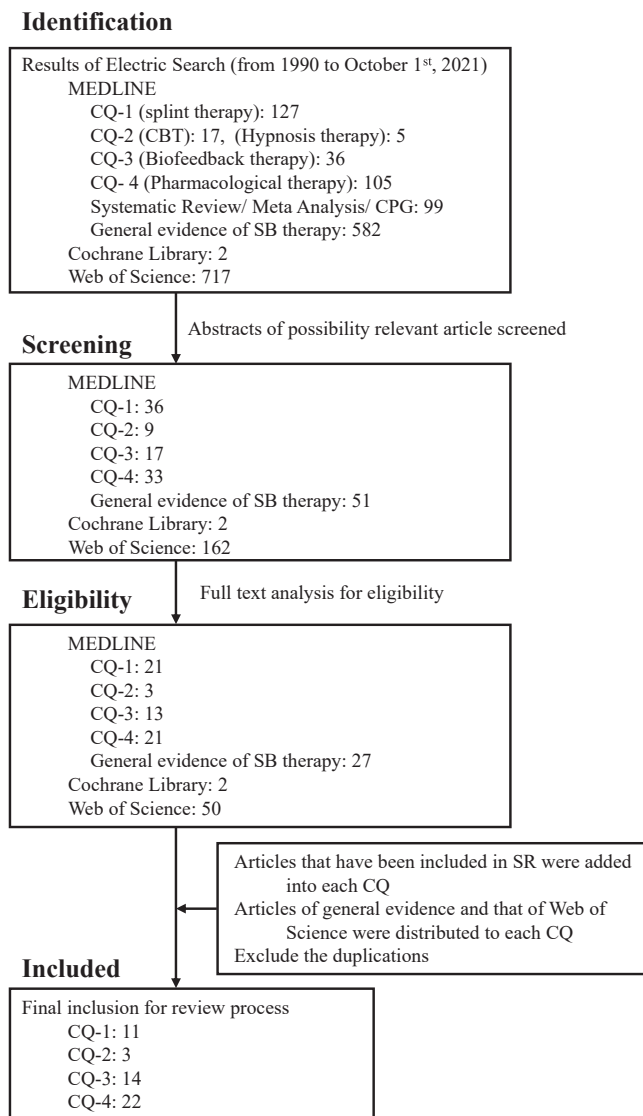
Table 4
Summary of descriptive characteristics of pharmacological approaches and quality assessment according to simplified GRADE checklist.

Author:	Outcome:	Intervention:	Dose:	Study design	Random sequence generation	Allocation concealment	Blinding (participants and personnel)	Blinding (outcome assessment)	ITT	Incomplete outcome data	Selective reporting	Stopped early for benefits	Other sources of bias	Summary	Subjects	Intervention	Control	Outcome	Summary	Control mean	Control s.d.	Intervention mean	Intervention s.d.	Standard mean difference (Hedges' g)
					Selection bias		Performance bias	Detection bias		Attrition bias		Other sources of bias				Indirectness				Standard mean difference (Hedges' g)				
Miyawaki S et al, 2003	RMMA index	Rabeprazole	Rabeprazole (10 mg)	CCT	-1		0	-1	0	0	-1		-1							6.0	2.2	3.7	1.9	-1.07
	mean episode duration																			10.2	4.4	9.2	4.4	-0.22
Ohmure H et al, 2016	RMMA index	Rabeprazole	Rabeprazole (10 mg)	RCTcrossover	0	0	0	-1	0	0	0		0	0	0	0	0	0	59.7	33.1	46.0	21.7	-0.47
	num. of episode w/ noise																			6.1	3.3	4.8	2.3	-0.44
Etzel KR et al, 1991	masseter muscle activities	L-Tryptophan	L-Tryptophan (50 mg/ weight kg)	RCTcrossover	-1	-1	0	-1	0	0	-1		-1		0	0	0	0	9108.0	6382.0	9640.0	6680.0	0.08
Lobbezoo F et al, 1997	root mean square	Levodopa	Levodopa (100 mg) and benserazide (25 mg)	Uncontrolled before-after study	-1	-1	0	-1	0	0	-1		0		0	0	0	0	NA	NA	NA	NA	NA
	num. of episode/h																			7.0	3.0	9.4	2.4	0.86
	mean episode duration																			NA	NA	NA	NA	NA
Lobbezoo F et al, 1997	num. of burst/episode	Bromocriptine	Bromocriptine (7.5 mg)	Uncontrolled before-after study	-1	-1	0	-1	-2	-2	-1		0	-2					12.5	1.1	9.5	0.1	-2.17
	num. of episode/h																			10.1	5.8	9.7	5.7	-0.04
Lavigne GJ et al, 2001	num. of burst/episode	Bromocriptine	Bromocriptine (1.25mg to 7.5 mg) and domperidone (20 mg)	RCTcrossover	0	-1	0	-1	0	0	-1		0	0	0	0	0	0	9.0	1.0	9.6	1.5	0.44
	root mean square																			6.9	0.8	7.4	0.9	0.55
	root mean square																			48.2	15.5	46.9	12.7	-0.09
Lobbezoo F et al, 1997	num. of burst/episode	Bromocriptine	Bromocriptine (7.5 mg)	CCTcrossover	-1	-1	0	-1	-2	-2	-1		0	-2					27.9	10.8	30.3	8.1	0.24
	masseter muscle activities																			29.9	3.7	22.8	2.7	-1.24
Mohamed SE et al, 1997	masseter muscle activities	Amitriptyline	Amitriptyline (25 mg)	RCTcrossover	-1	-1	0	-1	0	-1	-1		-1		0	0	0	0	1125.5	2367.3	755.6	1119.0	-0.19
Raigrodski AJ et al, 2001	masseter muscle activities	Amitriptyline		CCTcrossover	0	-1	0	-1	0	-1	-1		-1		0	0	0	0	372.0	522.4	206.7	264.2	-0.38
Wieckiewicz M et al, 2021	num. of episode/h	Opipramol	Opipramol (100 mg)	Uncontrolled before-after study	-2	-1	-2	-2	-1	0	-1		0	-2					6.6	1.8	4.3	2.2	-1.16
	num. of episode/h																			6.7	3.8	5.5	3.9	-0.32
Saletu A et al, 2005	num. of episode/h	Clonazepam	Clonazepam (1 mg)	Uncontrolled before-after study	-2	-1	-2	-2	0	-1	-1		0	-2					9.3	6.5	6.3	3.4	-0.55
Saletu A et al, 2010	num. of episode/h	Clonazepam	Clonazepam (1 mg)	Uncontrolled before-after study	-2	-1	-2	-1	-3	-1	0		-1	-3					7.2	4.9	4.2	2.6	-0.74
Sakai T et al, 2017	RMMA index	Propranolol	Propranolol (120 mg)	RCTcrossover	0	0	0	-2	-2	0	0		0	-1	0	0	0	0	2.0	1.1	2.6	1.9	0.38
Huynh N et al, 2006	num. of burst/h	Propranolol	Propranolol (120 mg)	RCTcrossover	-1	-1	0	-1	0	0	0		0	-1					9.4	NA	9.1	NA	NA
	num. of burst/h																			6.5	NA	5.8	NA	NA
Huynh N et al, 2006	num. of burst/h	Clonidine	Clonidine (0.3 mg)	RCTcrossover	-1	-1	0	-1	0	0	0		0	-1					5.4	NA	2.1	NA	NA
Sakai T et al, 2017	RMMA index	Clonidine	Clonidine (0.15 mg)	RCTcrossover	0	0	0	-2	-2	0	0		0	-1	0	0	0	0	34.0	NA	9.1	NA	NA
	num. of burst/h																			2.0	1.1	0.9	1.1	-0.98
	num. of burst/h																			3.4	1.5	1.7	0.8	-1.35
Madani AS et al, 2013	masseter muscle activities	Gabapentin	Gabapentin (100 to 300 mg), Oral splint	RCT	-2	-2	-2	-1	-2	-2	-1		0	-2	0	0	-1	-1	189.0	40.3	139.7	33.2	-1.28
Cahlin BJ et al, 2017	num. of burst/h	Pramipexole	Pramipexole (0.09 to 0.54 mg)	RCTcrossover	-1	-1	-2	0	-2	-1	-1		0	-2	0	0	-1	-1	9.8	5.2	12.7	8.5	0.40
	num. of episode/h																			32.1	18.1	43.6	29.1	0.46
Lee SJ et al, 2010	num. of episode/h	BoNT-A	80 U/ saline, masseter injection (4 weeks follow-up)	RCT	-1	-1	0	0	0	0	0		0		0	0	0	0	2.2	1.1	0.2	0.3	-2.48
	num. of episode/h		80 U/ saline, masseter injection (8 weeks follow-up)																	4.1	1.3	0.6	0.6	-3.23
	num. of episode/h																			2.5	1.4	0.3	0.4	-2.07
	num. of episode/h		80 U/ saline, masseter injection (12 weeks follow-up)																	4.1	0.9	1.3	1.1	-2.57
	num. of episode/h																			2.7	1.4	0.3	0.2	-2.15
	num. of episode/h																			4.4	1.5	1.7	0.9	-1.99
Shim YJ et al, 2014	RMMA index	BoNT-A	25 U each, masseter injection (4 weeks follow-up)	RCT	-1	0	-2	0	-2	-2	-1		0	-2	0	0	-1	-1	3.3	1.4	2.8	2.5	-0.21
	masseter muscle activities																			280.5	NA	72.4	NA	NA
	temporalis muscle activities																			277.0	NA	194.0	NA	NA
	num. of burst/h																			4.1	1.1	4.7	2.8	0.28
	num. of episode/h																			10.1	NA	6.8	NA	NA
	num. of episode w/ noise																			0.0	NA	0.0	NA	NA
	mean episode duration																			5.7	1.2	6.0	3.0	0.13
	RMMA index		25 U each, masseter/temporalis injection (4 weeks follow-up)																	2.1	1.4	2.9	2.6	0.03
	masseter muscle activities																			215.7	NA	72.3	NA	NA
	temporalis muscle activities																			306.4	NA	83.0	NA	NA
	num. of burst/h																			5.0	1.8	4.7	3.1	-0.12
	num. of episode/h																			12.0	NA	12.5	NA	NA
	num. of episode w/ noise																			0.0	NA	NA	NA	NA
	mean episode duration																			6.8	1.4	5.8	3.3	-0.39
Ondo WG et al, 2018	num. of episode/h	BoNT-A	60 U for bilateral masseter, 40 U for bilateral temporalis injection (4 to 8 weeks follow-up)	RCT	-1	-1	0	-1	-1	-1	0		0	-1	0	0	0	0	10.7	9.6	7.0	7.0	-0.44
Shim YJ et al, 2020	RMMA index	BoNT-A	25 U each, masseter injection (4 weeks follow-up)	RCT	-1	-1	0	-1	-1	0	0		0	-1	0	0	0	0	4.6	3.5	4.8	2.9	0.05
	num. of burst/episode																			25.3	24.2	31.9	38.4	0.19
	mean episode duration																			5.4	2.9	5.6	3.0	0.41
	num. of episode w/ noise																			9.3	17.4	8.5	18.2	-0.05
	RMMA index		25 U each, masseter injection (12 weeks follow-up)			-1	-1	0	-1	-1	0	0		0	-1	0	0	0	0	2.5	5.2	5.1	0.85	
	num. of burst/episode																			12.0	14.6	45.8	73.2	0.58
	mean episode duration																			4.6	1.3	6.2	4.1	0.49
	num. of episode w/ noise																			5.2	1.7	6.2	3.9	0.30
	num. of episode w/ noise																			4.3	12.2	18.2	26.0	0.63

based on four specific components that define the quality of the studies and assess the risk of bias. These components consisted of risk of bias [26], indirectness [27], imprecision [28], inconsistency [29], and publication bias [30].

The two prosthodontic specialist reviewers in each CQ evaluated all selected studies. After the evaluation process, the study considered a score of six or greater out of a total of nine to have a high risk of bias. Based on the systematic review objectives, inferential statistical analysis was not performed. The selected studies did not provide all of the necessary general information, and in some studies, the information was only provided narratively. Performing a complete meta-analysis was impossible because of the lack of information and heterogeneity of the selected studies.

3. Results and discussion

3.1. General outcomes

The final electronic search of the databases provided the 1690 articles. Based on a review of the titles and abstracts, 310 articles were selected for the second evaluation. In the second phase, 60 full-text articles were screened and evaluated thoroughly. A total of 173 publications were excluded at this stage because they did not fulfill the inclusion criteria. Finally, 137 articles were selected for systematic review. Details of the search strategy are shown in Fig. 1. Duplicate articles were excluded, and the articles that were included in the systematic review article but had not been selected were added to this database. In response, all of the selected articles were 37 RCTs, 4 CCTs, and 10 uncontrolled before-after studies, thus finally 11, 3, 14, and 22 articles were included in OAT, CBT, BFT, and pharmacological approaches, respectively.

3.2. Oral appliance therapy

Finally, 11 RCT articles were identified as eligible for this study. In this study, several types of splints were used as controls, and five articles applied the only palatal coverage splint. Four articles applied a mandibular anterior repositioning splint, and the other two applied the anterior splint. Combining the results of four studies that used the only palatal coverage splint as a control, the stabilization appliance showed a higher tendency to reduce the SB number during the short-term period; however, there was no difference after 2–6 weeks follow-up [31–35]. The total sample size of intervention/control was 89/89 subjects, and intervention periods were 3 days to 4 months.

Four studies verified the efficacy of SB reduction compared to the mandibular anterior repositioning splint. In response, both the stabilization appliance and mandibular anterior repositioning splint indicated a small reduction in the number of SB events; however, the effect showed a tendency that the effect of stabilization splint was lower than that of the mandibular anterior repositioning splint [36–39]. The total sample size of intervention/control was 50/50 subjects, and the intervention periods of these studies ranged from 1 week to 3 months, and anterior alignment was described as 25–75% of the maximum protrusive value.

Another two studies indicated that the anterior splint showed a significant reduction in the number of SB events, whereas the stabilization splint did not show a significant reduction in the number of SB events. The number of SB in this research was counted the EMG event (episode) exceeding 20% of the maximum voluntary clenching, and the total sample size of the intervention/control group was 20 subjects each. These were 2-week and 7-week randomized crossover studies [40,41].

Overall, combining the results, the use of stabilization splints tended to reduce the number of SB events; however, there was no

Identification

Results of Electric Search (from 1990 to October 1st, 2021)
　MEDLINE
　　CQ-1 (splint therapy): 127
　　CQ-2 (CBT): 17, (Hypnosis therapy): 5
　　CQ-3 (Biofeedback therapy): 36
　　CQ- 4 (Pharmacological therapy): 105
　　Systematic Review/ Meta Analysis/ CPG: 99
　　General evidence of SB therapy: 582
　Cochrane Library: 2
　Web of Science: 717

Abstracts of possibility relevant article screened

Screening

MEDLINE
　　CQ-1: 36
　　CQ-2: 9
　　CQ-3: 17
　　CQ-4: 33
　　General evidence of SB therapy: 51
　Cochrane Library: 2
　Web of Science: 162

Full text analysis for eligibility

Eligibility

MEDLINE
　　CQ-1: 21
　　CQ-2: 3
　　CQ-3: 13
　　CQ-4: 21
　　General evidence of SB therapy: 27
　Cochrane Library: 2
　Web of Science: 50

Articles that have been included in SR were added into each CQ
Articles of general evidence and that of Web of Science were distributed to each CQ
Exclude the duplications

Included

Final inclusion for review process
　　CQ-1: 11
　　CQ-2: 3
　　CQ-3: 14
　　CQ-4: 22

Fig. 1. Flow diagram for literature screening and selection.

significant difference compared to other types of oral appliances (OAs). A meta-analysis based on the five studies that obtained the raw data of mean and standard deviation indicated that the stabilization appliance did not show a significant reduction in the number of SB events compared to other types of OAs.

On the other hand, the detailed method of randomization was not described; it was impossible to apply the completely masking method for the treatment procedures to the examiner. All the interventions and control therapy used intraoral splints, and the indirectness was assessed as low; however, there were several types of splints and these adjustment settings were not normalized and there were variations. Regarding the characteristics of the subjects, the age of the sample population was 20–40 years, so the effect for the older age generation was unclear. Regarding the bias risk, it should be assessed as moderate to high since there were dropout subjects for whom detailed information was unclear. In addition, the effects of selection bias, performance bias, and detection bias were assessed as moderate; thus, bias risk was assessed as high. Regarding the inconsistency, two studies showed that the stabilization splint significantly reduced the number of SB events after the intervention compared to the control splint [42,43]. However, Baad-Hansen et al. and Lukic et al. reported that the stabilization splint did not show a

significant reduction [40,41]. This controversy would be one of the factors in reducing inconsistency. Furthermore, there was a wide variety of SB severity before intervention (minimum 2.1 times/hour, maximum 15.9 times/hour) and duration of splint usage (from 8 days to 13 weeks). These effects could not be ignored, and the strength of the evidence level was determined to be low or extremely low.

3.3. Cognitive-behavioral therapy

Regarding CBT, four research articles and two review articles were selected, of which two research articles studied stress management [21] and hypnotherapy [44], and a review article focused on the effect of physical therapy (muscle relaxation) and relaxation techniques [45,46]. To increase the evidence source, selected review articles were also added to the review process of this CBT.

Ommerborn et al. compared the management effects of CBT with an occlusal splint. In response, the CBT group showed a significant reduction in EMG-based SB activity after 6 months. The reduction in SB activity in the occlusal splint group during the treatment was lower than that in the CBT group; however, no statistical significance was observed [21]. Clarke et al. evaluated the effectiveness of hypnotherapy with eight subjects for a 7-night series of EMG recordings. The post-treatment SB activity was lower for every subject, and this effect was significant [44].

Amorim et al. focused on 24 articles in their systematic review, of which 23 articles were omitted because they consisted of biofeedback (n = 11), no EMG assessment (n = 6), no sleep study (n = 4), no English literature (n = 1), and already included (n = 1) [45]. Finally, one article was included in the review. López et al. reported in their RCT research that evaluated the effects of sleep hygiene measures combined with muscle relaxation techniques to reduce SB. The results indicated that the number of bruxism episodes per hour, the number of bursts per hour, and the bruxism time index showed no significant differences between before and after the 4 weeks [47].

At this point, the evidence level of the management effect of CBT would be assessed as extremely low since only a small number of well-designed research were available and the number of subjects was small. Thus, it cannot be concluded that CBT has a clear positive management effect, and further research is needed to evaluate the SB management efficacy of CBT with well-designed clinical research and a large number of subjects.

3.4. Biofeedback therapy

Finally, 11 articles were selected as review papers, of which seven focused on electric stimulation [48–54], and five on vibration [55–59] and two on sound [60,61] stimulation. In addition, two review articles (one systematic review [62] and one meta-analysis [63]) were included in the review process.

For electric stimulation, four out of seven studies used an identical small-in-one device; one was that of the prototype. A study used the manufactured intraoral device that obtains the signals from the occlusal force using a sensor and the switch triggers a stimulator, which delivers slightly noxious electrical pulses to the subject's lip [55]. The other five devices delivered a nonpainful electrical stimulus (contingent electrical stimulation (CES)) to the skin overlying the temporalis muscle when the subject's temporalis muscle EMG activity exceeds the amplitude determined during nightly bio calibration. These reports consisted of four RCTs and one cross-over study and demonstrated the positive results that the number of EMG episodes/hour of sleep was significantly reduced during the biofeedback sessions (54 ± 14%; 55 ± 17%, P < 0.001) compared with baseline EMG activity and the session without biofeedback. In the session without biofeedback [49], the number of EMG episodes per hour of sleep was significantly reduced (52 ± 12%) in the CES group

during the sessions with CES (ANOVA: p = 0.021) compared to baseline [51]; patients in the active group had 35% lower EMG/hour with/without CES application period and 38.4% lower EMG/hour in the non-biofeedback follow-up period compared with baseline [53]. On the other hand, Jadidi et al. also reported that the number of EMG episodes per hour of sleep during the nights with and without CES was not significantly different (16.3 ± 4.8, 17.7 ± 5.8; respectively, p = 0.733). Thus, the present study showed that CES was not associated with any significant perturbation of PSG on sleep and sleep quality [50]. Raphael et al. reported a reliable reduction in EMG events for 6 weeks CES periods and 2 weeks observation period after the end of CES; however, the frequency of EMG events returned to baseline levels after that of the observation period (linear term, p = 0.002; quadratic term, p = 0.001) [52].

In a crossover trial, Nishigawa et al. [48] reported that electric lip stimulation significantly reduced only the duration of individual bruxism events (p = 0.038) [48]. Sumiya et al. [54] applied an electrocardiogram signal monitoring EMG device that delivered electrical stimulations to the masseter muscle immediately after the heart rate exceeded 110%. This crossover study indicated that the number of SB events, the number of EMG bursts per SB event, and the duration of SB events decreased significantly compared with the baseline [54].

Gu et al. [55] developed the vibration alteration system was a manufactured device that consisted of a pressure sensor and wireless wristwatch-type vibrator. The pressure sensor was inserted into the fabricated intraoral splint, and it sends the signal to a wristwatch-style vibrator when excessive force was detected. This cohort study indicated that both SB episodes and duration were significantly reduced in the vibration group (n = 12); however, no significant differences were observed in the control group (n = 12) at 6 and 12 weeks after starting the intervention [55]. Three studies applied vibratory stimulus to OA. Nakamura et al. investigated the effect of contingent vibratory feedback stimuli using an occlusal splint for inhibition of SB [56]. Although their results demonstrated that the number of SB episodes was tended to decrease with the vibration stimuli, and the decrease in the total SB duration was statistically significant (p = 0.03), their experimental design did not include a control group. On the other hand, Nakazato et al. also investigated the effects of vibratory stimulation on SB in the case of diminished effects of the OA after adaptation using the same device as Nakamura et al. [58]. Their results suggested that contingent vibratory stimulus via an OA may be effective for the management of SB even after adaptation to OA. In addition, Bergmann et al. and Ohara et al. also demonstrated that vibratory stimulus through OA could reduce the several SB parameters [57,59].

The auditory alert system consisted of surface EMGs and an auditory biofeedback unit including a data logger, and a small auditory alert that sends a signal when EMG activity exceeded the threshold. The subjects wore this auditory alert system throughout the day; however, the alert system was activated only during the daytime. This RCT reported that tonic EMG events during daytime and sleeping time in the auditory alert group showed a significant reduction compared to pre-intervention. However, the control group did not show any significant alterations throughout the experimental period [60]. In addition, Saito-Murakami et al. investigated the effect of daytime clenching control by an auditory biofeedback system for the phasic component of SB, suggesting that EMG biofeedback during the daytime can reduce phasic EMG events during sleep [61].

The SB inhibitory effect of BFT showed a highly significant reduction of SB-related EMG data. Furthermore, there were no weak points regarding the research design and the accuracy and reliability of the SB measuring system. Meanwhile, indirectness was also assessed to be low because many reports indicated identical results. From this point of view, the strength of the evidence level of BFT was considered high. From the collected evidence and evidence strength, it can be concluded that BFT, mainly electric stimulation, would certainly have a reduction effect on SB-related EMG activities. On the other hand, there have not been deeply elucidated the learning effect, long-term effect, and adverse event for the sleep quality, teeth, and orofacial muscle. In the future, further research is expected to examine the negative components of BFT in addition to the SB inhibitory effect in a well-designed study.

3.5. Pharmacological therapy

Finally, the selected pharmacological agents were rabeprazole (proton pump inhibitor), L-tryptophan (α-amino acid), levodopa (L-dopa), bromocriptine (dopaminergic agonist), amitriptyline and opipramol (tricyclic antidepressant), clonazepam (anticonvulsant), propranolol (non-selective adrenergic β receptor-blocking agent), clonidine (selective α2 receptor agonist), gabapentin (anticonvulsant), pramipexole (dopaminergic agonist), and BTX-A (botulinum toxin type A).

Indicators of SB were the number of episodes per hour, rhythmic masticatory muscle activity (RMMA) index, masseter or temporalis muscle activity, number of bursts per episode, number of bursts per hour, number of episodes with noise, root mean square of EMG of SB event, and mean episode duration. There have been only a few studies on each pharmacological therapy; therefore, the strength of the evidence was considered weak. Of these pharmacological therapies, the following report indicated a significant reduction in SB-related parameters.

Two clinical trials indicated that the application of rabeprazole (10 mg/night) reduced the RMMA index significantly; however, there was no significant reduction in the number of episodes with noise and mean episode duration [64,65]. The effect of bromocriptine (7.5 mg/night) application was assessed by three clinical trials, and they showed similar results, such as a significant reduction in the root mean square of masseter EMG during SB; however, there was no tendency to reduce the number of episodes per hour, the number of bursts per episodes, number of bursts per hour, and number of episodes with noise [66,67]. The effect of opipramol (100 mg/night) administration was evaluated in one clinical trial, which showed a significant reduction in the number of episodes per hour, but not in the number of bursts per hour [68]. The effect of clonazepam (1 mg/night) application was assessed in three clinical trials with four parameters. The number of episodes per hour and bruxism index indicated a significant reduction [22,24,69]; otherwise, there was no tendency to reduce the RMMA index and number of bursts per hour [22,69]. The effect of clonidine administration (0.15 mg or 0.3 mg/night) was determined by the two RCTs with the following parameters: the number of episodes per hour, RMMA index, and the number of bursts per hour. In response, these parameters were significantly reduced after clonidine administration [23,69].

One RCT reported that gabapentin (100–300 mg/night) significantly reduced SB-related parameters such as the number of episodes per hour, mean masseter EMG activities, and mean episode duration. No adverse events have been reported [70]. Four RCT were reviewed regarding BTX-A injections into bilateral masseter or temporalis (50–100 units overall). They showed the efficacy of BTX-A in reducing the number of SB events [71], peak amplitude of EMG burst [72,73], number/duration of SB episodes [74]; however, other SB-related parameters did not indicate a clear reduction.

Tryptophan (50 mg/weight kg) [75], levodopa (200 mg/night) [76], amitriptyline (25 mg/night) [77,78], propranolol (120 mg/night) [23], and pramipexole (0.09–0.54 mg/night) [79] were assessed for their management efficacy using one, one, two, one, and one clinical trial, respectively. However, no significant changes or reductions were observed in SB-related EMG parameters such as mean muscle activities [75], number of episodes, root mean square, mean episode

duration [76], mean muscle activity during sleep [77,78], number of episodes, number of bursts [23], number of bruxism episodes, phasic, tonic, and mixed episodes per hour [79].

Overall, the certainty of the evidence body would be determined as low since the sample size of most research was relatively small (approximately 10 subjects), and the majority of these studies were not parallel RCTs but crossover trials.

3.6. Adverse event

Among the articles included in this systematic review, none reported the adverse effects of the stabilization splint. Whereas anterior open bite was reported in the anterior splint group [40]. Additionally, one subject reported increased salivation, and seven subjects reported lower comfort while wearing the anterior splint, whereas no occlusal changes occurred in any patient [41].

Regarding the results of manual search, several studies reported the adverse events of stabilization splints such as change of occlusion and difficulty in jaw-closing, including open bite [80,81]. Fujii et al. reported that occlusal change was observed in half of the subjects with 10.5 weeks usage of 5 mm thickness splint. The difficulty of jaw-closing, including open bite after 1–3 years of splint usage has also been reported [80]. Todd et al. reported the anterior open bite as a complication of long-term usage (> 3 years) of splint [81].

No adverse event was reported in all of the CBT-related research. Regarding the 14 biofeedback-related articles, 10 articles investigated the aspect of the adverse events. Of which, one adverse effect was reported: two subjects in the intervention group and one subject in the control group reported some interference with sleep, and the Pittsburgh Sleep Quality Index was higher than five (5−10) whereas no awake event occurred during sleep [55]. Nonetheless, other nine reports indicated no significant differences in the total sleep hours, mean sleep efficiency, and REM sleep duration [50], no influence on perceived pain [53], no significant difference on the degree of maxillofacial fatigue or sleep quality [54], no statistical significance on McGill Pain Questionnaire scores, depression scores, Oral Health Impact Profile scores and Sleep/Tiredness/Snoring questionnaire score [51], no subject who woke up due to vibratory stimulation [57], no sleep interruption [61], no substantial change of the micro-arousal index [56], no significant differences in any sleep variables [59] and slight but non-significant self-reported discomfort [58].

Regarding the pharmacotherapy approaches, the following adverse events were reported: severe gastrointestinal symptoms (nausea, constipation, abdominal pain, and diarrhea) (n = 1/6) and drug reactions (n = 3/6) in bromocriptine [66]. Reduction of sleep quality, dry mouth, and dizziness were reported by Sakai et al.; however, there was no mention of the distinction between clonazepam and clonidine [69]. Symptomatological hypotension (n = 3/16), reduction of systolic blood pressure, and thirst in clonidine [23], nausea (n = 3/13), drowsiness (n = 3/13), poor sleep (n = 1/13), and blurred vision (n = 1/13) were reported with pramipexole [79]. An increase of Apnea-Hypopnea Index and Oxygen Desaturation Index in male participants was reported with opipramol administration and facial changes due to masseter intramuscular injection were reported in BTX-A [68,74].

3.7. Confidence in cumulative evidence

The overall quality of evidence identified using the GRADE evidence profile was assessed as low to moderate (Tables 5–7). RCT studies presented a moderate quality of evidence, showing a serious imprecision due to lack of description of concealment, detail of dropout, sampling procedure, small sample size, and the small number of included studies. Low quality of evidence was found for

non-RCT studies, also due to imprecision and inconsistency between studies.

3.8. Discussion

Bruxism, specifically SB and its management, is a globally discussed topic among academics and clinicians [82]. Therefore, updates and rigorous critical appraisals of existing evidence are necessary to send information to healthcare providers adequately. Thus, in this overview, we evaluated the most appropriate strategies to manage bruxism in a clinical setting based on the results of systematic reviews.

Overall, the risk of bias for the primary studies included was elevated because of the lack of randomization and allocation concealment description as well as blinding of participants and outcome assessors. These drawbacks limit the confidence in clinical recommendations based on these findings. Taking the results of all included systematic reviews together, combining the main findings, adverse effects, and evidence level, it was concluded that stabilization splint and BFT may be considered as the standard management strategies.

The nature of the oral splint has been previously evaluated, and biological safety and SB management ability against both invasive excessive mechanical force and reducing muscle hyperactivity have been well-known. In these systematic reviews, the oral stabilization splint type was considered the standard approach because of the SB suppression effect equivalent to other splints and low incidence of adverse events. The GRADE system assessed the SB reduction effects in these systematic reviews, and it was concluded to have a low degree of certainty.

Stimulation during sleep would be either intended to disrupt sleep continuity or provide a non-waking stimulus to reduce SB through the sensory feedback system [49]. SB episodes frequently occurred secondary to sleep micro-arousals associated with cerebral and cardiac activity [83]. Studies have shown that micro-arousals are triggered by sensory stimulation [84–86], and a short-term reduction in SB activity is achieved through sensory feedback [87,88]. Thus, it would be reasonable to stimulate the sensory system to reduce nocturnal EMG activity. Five studies investigated whether biofeedback stimulation interfered with normal sleep. In response, ECG-based CES (one article) [54], EMG-based CES (three articles) [50,51,53], and occlusal force-based vibratory feedback (five articles) [55–59] reduced the SB without substantial interference in sleep, as evidenced by questionnaire-based assessment and the EMG/PSG study. These results may indicate that CES at non-painful intensities did not cause major arousal responses in sleep parameters or interfered with self-reported sleep quality. Further research is needed to determine how new BFT affects sleep structure by full PSG investigations [54–58].

Finally, three articles investigating the effect of CES on pain-related outcomes in probable bruxers with myofascial masticatory muscle pain are not supportive of its effectiveness [51–53]. Raphael et al. reported a significant reduction in palpated pain and spontaneous pain intensity [52]. In addition, Jadidi et al. and Conti et al. reported that EMG-triggered CES during sleep significantly reduced EMG events in the temporalis muscle; however, this was not associated with a reduction in symptoms or signs of TMD problems [51] and masticatory muscle pressure pain threshold in patients with masticatory myofascial pain and probable SB [53]. In contrast, a partial posterior interocclusal biofeedback device reduced both AB and masticatory myofascial pain, TMJ, and neck pain [89]. At this point, whether the reduction in EMG activity through CES could also alleviate the pain variables, thus revealing a link between oromotor activity and pain, remains to be addressed. The results of these systematic reviews indicated that changes in pain could not be entirely attributed to changes in nocturnal EMG events. A recent study

Table 5
GRADE evidence profile: effect of stabilization splint therapy on sleep bruxism reduction.

management	Research design/ number of study	Risk of bias	inconsistency	imprecision	indirectness	other bias (publication bias)	certainty of evidence
overall	RCT/ 12	-1	-1	-1	-1	-1	Very low (D)
Control: palatal coverage splint	RCT/ 6	-1	0	-1	-1	-1	Low (C)
Control: mandibular anterior repositioning splint	RCT/ 4	-1	0	0	-1	-1	Low (C)
Control: anterior splint	RCT/ 2	-1	-1	-1	-1	-1	Very low (D)

Table 6
GRADE evidence profile: effect of CBT and BFT on sleep bruxism reduction.

outcome	Researcg design/ number of study	Risk of bias	inconsistency	imprecision	indirectness	other bias (publication bias)	certainty of evidence
cognitive-behavioral therapy	RCT/ 2, Uncontrolled before-after study/ 1	-2	-2	-2	-2	0	Very low (D)
Biofeedback therapy	RCT/ 9, CCT/1, Uncontrolled before-after study/ 4	-1	0	-1	0	0	Moderate (B)

Table 7
GRADE evidence profile: effect of pharmacological approaches on sleep bruxism reduction.

Medication	Dose	Outcome	Research design/number of study	Risk of bias	Inconsistency	Imprecision	Indirectness	Other bias (publication bias)	Certainty of evidence
Rabeprazole	10mg/night p.o.	RMMA index	RCT/1, CCT/1	-1	-1	-1	0	0	Moderate (B)
		Num. of burst/h	RCT/1	0		-1	0	0	Low (C)
		Num. of episode w/ noise	RCT/1	0		-1	0	0	Low (C)
		mean episode duration	CCT/1	-1		-1	0	0	Low (C)
L-Tryptophan	50 mg/weight kg p.o., 8 days	masseter muscle activities	RCT/1	-1		-1	0	0	Very Low (D)
Levodopa	200 mg/night p.o.	Num. of episode/h	Uncontrolled before-after study/1	-1		-1	0	0	Low (C)
		root mean square	Uncontrolled before-after study/1	-1		-1	0	0	Very Low (D)
		mean episode duration	Uncontrolled before-after study/1	-1		-1	0	0	Very Low (D)
		Num. of burst/episode	Uncontrolled before-after study/1	-1		-1	0	0	Very Low (D)
Bromocriptine	maximum 7.5 mg/night p.o., 2 weeks	Num. of episode/h	RCT/1, Uncontrolled before-after study/1	-1	-1	-1	0	0	Low (C)
		Num. of burst/episode	RCT/1, Uncontrolled before-after study/1	-1	-1	-1	0	0	Low (C)
		Num. of burst/h	RCT/1	-1		-1	0	0	Low (C)
		Num. of episode w/ noise	RCT/1	-1		-1	0	0	Low (C)
		root mean square	RCT/1, CCT/1	-1	-1	-1	0	0	Low (C)
Amitriptyline	25 mg/night p.o., 1 to 4 weeks	masseter muscle activities	RCT/1, CCT/1	-1	-1	-1	0	0	Low (C)
Opipramol	100 mg/night p.o., 8 weeks	Num. of episode/h	Uncontrolled before-after study/1	-2		-1	0	0	Very Low (D)
		Num. of burst/h	Uncontrolled before-after study/1	-2		-1	0	0	Very Low (D)
Clonazepam	1 mg/night p.o.	Num. of episode/h	Uncontrolled before-after study/2	-2	0	-1	-1	0	Low (C)
		RMMA index	RCT/1	-1		-1	0	0	Low (C)
		Num. of burst/h	RCT/1	-1		-1	0	0	Very Low (D)
Propranolol	120 mg/night p.o.	Num. of episode/h	RCT/1	-1		-1	0	0	Very Low (D)
		Num. of burst/h	RCT/1	-1		-1	0	0	Very Low (D)
Clonidine	0.15 or 0.3 mg/night p.o.	Num. of episode/h	RCT/1	-1		-1	0	0	Low (C)
		RMMA index	RCT/1	-1		-1	0	0	Moderate (B)
		Num. of burst/h	RCT/2	-1		-1	0	0	Low (C)
Gabapentin	100 to 300 mg/night, 8 weeks	Num. of episode/h	RCT/1	-2		-1	-1	0	Moderate (B)
		masster muscle activities	RCT/1	-2		-1	-1	0	Moderate (B)
		mean episode duration	RCT/1	-2		-1	-1	0	Low (C)
Pramipexole	0.09 to 0.54 mg/night, 3 weeks	Num. of episode/h	RCT/1	-2		-1	-1	0	Low (C)
		Num. of burst/h	RCT/1	-2		-1	-1	0	Low (C)
BTX-A injection	50 to 100 U overall masticatory muscle injection, 4 to 12 weeks follow-up	Num. of episode/h	RCT/2	-1		-1	0	-1	Moderate (B)
		RMMA index	RCT/2	-2		-1	-1	-1	Low (C)
		masseter muscle activities	RCT/1	-2		-1	-1	-1	Low (C)
		temporalis muscle activities	RCT/1	-2		-1	-1	-1	Low (C)
		Num. of burst/episode	RCT/2	-2		-1	-1	-1	Low (C)
		Num. of burst/h	RCT/2	-2		-1	-1	-1	Low (C)
		Num. of episode w/ noise	RCT/2	-2		-1	-1	-1	Low (C)
		mean episode duration	RCT/2	-2		-1	-1	-1	Low (C)

also failed to support an association between myofascial TMD pain and increased SB episodes or decreased time between SB events [90]. When EMG activities of the current criteria were applied to the alternative outcome, it could be concluded that BFT obtained clear evidence to reduce these outcomes; however, the validity of these criteria for EMG activities is still unclear, and the clinical effectiveness of BFT has not been evaluated yet. Thus, elucidation of the highly validated EMG criteria as alternative outcomes and evaluation with the clinical signs, symptoms, and consequences are necessary to assess the efficacy of the BFT.

On the other hand, rabeprazole also showed management efficacy and low side effects. Generally, proton pump inhibitors have a

very good safety profile for short-term administration; however, several neurological adverse events due to long-term use have also been reported, such as dementia, including psychotic symptoms and affectivity disorders [91]. Thus, it may be better to use the minimum dose as needed. Conversely, the results of rabeprazole-related studies have indicated the possibility of gastroesophageal reflux disease; therefore, the management efficacy for normal subjects remains unclear. It is necessary to consider potential risks in the case of usage fully.

Lavigne et al. [18] suggested that the diagnostic criteria for PSG assessment included total episodes, episodes per unit time, bursts per episode, bursts per unit time, and the number of SB sound episodes [18]. Therefore, it was desirable to apply the above-mentioned parameters to determine treatment efficacy because it was possible to compare the research results directly. However, many SB-related studies obtained heterogeneous outcome measurements; thus, it was difficult to compare quantitatively among each research result. In this systematic review, especially in the biofeedback and pharmacology approaches, portable EMG indicated the specific outcome parameter instead of PSG, which was difficult to use because of the long-term observation period. Thus, it would be necessary to (1) elucidate clinically relevant and reliable EMG parameters and (2) develop and establish devices that can record reliable and valid parameters. In response, it would be possible to perform a qualitative comparison among several clinical research results.

Considering this issue, future studies should include a large sample size, a variety of sample populations, appropriate random allocation methods, clinically relevant outcomes and follow-up periods, and well-designed parallel RCTs.

4. Conclusion

Based on the currently available literature, the posed question in this review of the clinical efficacy and effectiveness of several types of management methods cannot be answered in a scientifically compelling manner. The accrued knowledge is based on scientifically weak evidence: no large sample of RCTs was available, short-term and long-term evaluations were mixed, non-standardized SB-related parameters were used, randomization and concealment process in the study design was unclear, and properties of the subject's population were biased toward young and young adult subjects. Nonetheless, a preliminary evaluation of the literature suggests that stabilization splints represent a safe and relatively effective management approach to reduce EMG-based SB frequency and intensity. This systematic review included a GRADE assessment of the evidence. It concluded with a moderate degree of certainty that the biofeedback modalities, especially CES, significantly reduced the SB-related EMG episodes after a short-term period. Thus, BFT also can be recognized as an effective management procedure with further research supporting its use. Evidence of long-term positive/adverse effects is lacking; thus, more scientifically robust, well-designed, longitudinal studies with larger samples are needed to acknowledge the clinical application of biofeedback management. For the practical application of pharmacological therapy, further consideration is necessary to evaluate the positive and adverse effects and the properties of the target subjects.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Scientifc field of dental science

Prosthodontics and Neuroscience.

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