

compared the effectiveness of the SILENT NITE and a one-piece monoblock in management of OSAHS. A significant reduction in AHI and AI, also increased patient preference with the monoblock appliance, however, both appliances had an improvement in ESS and SS [25]. Another study was conducted by Bishop et al. [35] to determine if the design of MRA can affect the end treatment result of OSA. Despite similar outcome of both appliances, there was a significant preference of the

minimal coverage of teeth and palate MRA design [35]. According to Johal et al. [31] custom-made MRA is statistically more effective in the management of OSA and also in patients' preference and compliance. Idris et al. [32] evaluated the effectiveness of MAS to control SDB in children. Overall clinical reduction of AHI and snoring time with active MAS wearing, moreover, reported improvement of quality of life and behavior with active MAS than sham MAS [32].

Study	Study design	Observation period	Sample Size	Participants	Methods	Intervention	Comparison/control	Outcomes
Zhou [25]	A randomised titrated crossover study	6-month periods	16	Sex: (13 men and three women)	Two different types of oral appliances were tested in each patient, a one-piece Monoblock and the SILENT NITE® -Each for 3-months periods separated by a 2-week wash-out period in between	Monoblock	The SILENT NITE®	The monoblock and SILENT NITE® appliances reduced Apnoea Hypopnoea Index (AHI) from 26.38 ± 4.13 to 7.58 ± 2.28 (P < 0001) and 8.87 ± 2.88 (P < 0001), respectively.
				Age: The age range of the patients varied from 26.3 to 55.4 years (average 45.23)				The Monoblock appliance was statistically more efficient in reducing AHI and Apnoea Index (AI) than the SILENT NITE®
				Inclusion criteria				
				Diagnosed with mild to moderate OSAHS				
				More than 20 teeth present				
				Free from caries, periodontal disease, temporomandibular pain or movement limitations.				
Villa [26]	Randomized Controlled Study	6 months period	32	Sex: 20 males Age: (age range, 4 to 10 years; mean age, 7.1 ± 2.6 years)	A group of 19 subjects was randomly assigned to a 6-mo trial of an oral appliance; the remainder acted as control subjects.	19 subjects undergo a 6-mo trial of a personalized oral appliance.	13 subjects didn't undergo any therapy	Poly-somnography after the trial showed that treated subjects all had significantly lower apnea index (p 0.001) and hypopnea index values (p 0.001) than before the trial, whereas in untreated control subjects these values remained almost unchanged.
				Inclusion criteria				

				Had an apnea index (AI) of ≥ 1 event/hr of sleep during diagnostic polysomnography				
Quinnell [27]	A crossover randomised controlled trial	6 weeks of treatment with three non-adjustable MADs and 4 weeks no treatment	90	Sex: Age: above 18	6 weeks of treatment with three non-adjustable MADs: self-moulded (SleepPro 1; SP1); semi-bespoke (SleepPro 2; SP2); fully-bespoke MAD (bMAD); and 4 weeks no treatment.	62	21 no treatment	All three MADs significantly decreased the AHI against no treatment by 26% for the SP1, 33% for the SP2 and 36% for the bMAD
				Inclusion criteria		SP1:21		
				Mild to moderate OSAHS confirmed by respiratory polysomnography		SP2:21		
						bMAD:20		
Mehata [28]	A Randomized, Controlled Study		28	Sex: (22 men and six women)	Patients underwent three polysomnographies with either a control oral plate, which did not advance the mandible (A), or MAS (B), 1 wk apart, in either the ABB or BAA sequence.	Group I (sequence ABB)	Group II (BAA sequence)	Subjective improvements with the MAS were reported by the majority of patients (96%).
				Inclusion criteria				
				The presence of at least two symptoms of OSA, and evidence of OSA on polysomnography, with an apnea/hypopnea Index (AHI) > 10/h.				
Johnston [29]	a randomized clinical trial	4-6 weeks for each appliance	21	Sex: (17 males and four females)	Subjects were provided with a maxillary placebo appliance and a MAA for 4-6 weeks each, in a randomized order.	MAA	Maxillary placebo Appliance	Among the remaining 20 subjects, the MAA produced significantly lower AHI and ODI values than the placebo.
				Age: adult Inclusion criteria: Those with an hourly rate of 10 or more desaturations				
Johal [30]	A randomized crossover trial	3-month period of ready-made or custom-made MRD, with an	25	Sex: Age: adults (> 18 years)	Patients were randomly assigned to receive either a	ready-made MRD	custom-made MRD	The MRDc achieved a complete treatment

		intervening washout period of 2 weeks, prior to crossover.			3-month period of ready-made or custom-made MRD, with an intervening washout period of 2 weeks, prior to crossover.			response in 64% of participants, compared with 24% with the MRDr (p < 0.001).
Inclusion criteria								
Diagnosis of mild-moderate OSA								
Marklund [31]	A Randomized Clinical Trial	4-month follow-up	96	Sex: Age: aged 20 to 70 years	Study of the efficacy of an oral appliance vs an intraoral placebo	Oral appliance group	Placebo device group	An AHI lower than 5 was recorded in 49% of the patients using the oral appliance and in 11% of the patients using the placebo device (P = .001)
Inclusion criteria								
Patients With mild to moderate sleep apnea								
Idris [32]	A randomized crossover clinical trial	Each appliance was worn for three weeks and treatment periods were separated by a two-week washout.	18	Sex: Age: age range from 8 to 12 years	Each participant wore an Active and a Sham MAS appliance overnight for three weeks. Treatment periods were separated by a two-week washout period.	Active Mandibular Advancement Appliance	Sham Mandibular Advancement Appliance	Compared to the Sham MAS, the wearing of the Active MAS resulted in a significant reduction in overall AHI; p 0.002) and supine AHI; p < 0.001).
Inclusion criteria								
Parental report of loud snoring for three or more nights per week.								
Gotsopoulos [33]	A Randomized, Controlled Trial	4 weeks for treatment for each appliance with 1 week - washout period	73	Sex: 59 men and 14 women	Patients received 4 weeks of treatment MAS and a control device with an intervention 1 week -washout	Mandibular advancement splint	Inactive oral appliance	There was a highly significant reduction in both the reported frequency and intensity of snoring with the MAS compared with the control device (p 0.0001)
Age: middle - aged								
Inclusion Criteria								
Moderate and severe OSA								
Overweight								
Deane [34]	A Randomized Controlled Trial	4 weeks for each device with 1-	27	Sex: (20 males, 7 female)	The patients had an 8-week	Mandibular advancement splint	Tongue Stabilizing Device	A decrease in AHI was recorded for

		week washout period		acclimatization period (4 weeks with each device), with 1-week washout periods			91% of the patients when using MAS and 77% of the patients when using TSD.
				Age: age > 20 years			
				Inclusion criteria			
				Apnea hypopnea index (AHI) > 10 per hour.			
Bishop [35]	A randomized crossover study	24	Inclusion Criteria	Subjects in arms K and T were compared with respect to the variables measured at baseline.	The Klearway	The TAP3.	For both appliances, the Epworth Sleepiness Scale (ESS), and Sleep Apnea Quality of Life Index (SAQLI) were significantly ($p \leq 0.05$) lower than the baseline
				Diagnosed with obstructive sleep apnea by polysomnography			

DISCUSSION

As the study aims to determine the success of removable orthodontic appliances such as, MAA or MRA, Tongue Stabilizing Device. Three groups of studies were included to determine such success, the first study comparing MADs with inactive control OAs. The second study, comparing oral appliance against no treatment. The third one, comparing between two different oral appliances.

When comparing MADs with inactive control OAs, objective treatment outcome is crucial to be determined so the result can be obtained with no bias. Yet only three studies mentioned the treatment outcome clearly such as in Mehata et al. [28], Johnston et al. [29], Gotsopoulos et al. [33]. However, in Marklund et al. [31] the reduction in AHI was mentioned with indication of success or failure of such treatment. Moreover, in Mehata et al. [28] using MAS resulted in significant reduction in the mean of AHI (53%) when compared with the control. Two AHI cut-offs were measured one at 10/h which resulted in complete response in 54% and the other at 15/h which resulted in complete response in 75%. Where in Johnston et al. [29], a cut-off at 10/h or less resulted in reduction in 33% which is considered low.

Two studies comparing oral appliances against no treatment were included were both have resulted in favouring MADs against no treatment patients. However, in Villa et al. [26] the cut-off for AHI was not mentioned yet a 50% reduction in AHI was considered successful treatment. Also, in Quinnell et al. [27] AHI cut-off was not mentioned, yet the three MADs used resulted in great reduction of the AHI. Both studies have proven that MADs are clinically effective in treatment of OSA. Though, patient compliance plays a vital role in determining such success.

Deane et al. [34] evaluated the efficacy between MAS and TSD in the treatment of OSA. In terms of AHI reduction, both devices had a similar efficacy, yet, improvements in snoring, quality of sleep and better compliance were reported by the patients for MAS than TSD [34].

The MAS has abundance supporting literature supporting the treatment of OSP, particularly those with mild to moderate OSA [34]. Decreasing of AHI is the primary outcome of this study [34].

Additionally, the arousal index decreased significantly with MAS and TSD [34]. TSD appliance is non-adjustable; patient should squeeze the bulb and protruded the tongue into the appliance with differing force [34]. This stretching posture of the soft tissue may cause uncomfortable situation [34]. So this manner required ensuring patient safety by clinical supervision [34]. It found that MAS more comfortable and easier than the TSD, although patients achieved the same response to treatment with both MAS and TSD [34]. It has been demonstrated in other studies that quality of sleep was improved with oral appliance therapy [34]. In this study all patients reported improvement in quality of sleep with MAS, compared with 45% with TSD [34]. This could be due to the better compliance with MAS which is comparable to other studies [36-38]. There is no literature to assess compliance with TSD yet, but it can be assumed that like MAS [34]. The compliance rates are likely to decrease relative to the length of follow-up with TSD [34].

Both MAS and TSD have side effects and each appliance producing a different type and severity of problems [34]. The main concerns with MSD were jaw discomfort and dryness of mouth which were largely mild in nature [34]. With TSD appliance, the main side effects were reported

as excess salivation, dryness of mouth, and soft tissue irritation varied from mild to severe in nature [34]. Several patients described a temporary tingling sensation, minor ulceration of the lingual frenum also occurred [34]. Lingual frenum inhibited the ability to protrude the tongue into the TSD, that in turn affected compliance [34]. Swallowing was more difficult with TSD due to the vertical mouth opening [34]. The reduction of AHI in supine sleep and slight reduction in REM sleep may have been influenced by the side effects, in particular excess salivation, these side effects were severe enough to prevent nearly half of the sample continuing with the TSD which might be the cause of decreasing the compliance with follow up, however there was no statistically significant difference between MAS and TSD [34].

Another prospective crossover study compared the two different types of MAAs in the treatment for mild to moderate OSAHS concluded that, both appliances were efficient in improving AHI in patients with mild to moderate OSAHS [25]. The monoblock appliance was statistically more efficient in reducing AHI and Apnoea Index (AI) than the SILENT NITE® (GlideWell Laboratories). The scores on Epworth's Sleepiness Scale (ESS) and Snoring Scale (SS) were improved significantly by both appliances. The upper airway spaces showed significant enlargement by both mandibular advancement appliances (MAAs), while no significant differences were found between the two appliances. This result is consistent with some of the previous studies where they compare two different MAAs appliance. In another prospective study, the SILENT NITE®* and the Karwetzky activator were compared and both appliances reduced the mean Respiratory Disturbance Index (RDI) and AI. The Karwetzky activator was significantly more efficient than the SILENT NITE®*. This could be related to the vertical mandibular movement variations of the two appliances [25]. Moreover, Ghazal et al. compared the Herbst-like IST® appliance‡ with the monoblock appliance TAPTM§ in a randomised prospective study [25]. The IST® appliance‡ was assumed to be less effective than the TAPTM§ in the short-term comparison. This study revealed that the short-term acceptance of one-piece appliance is relatively higher than that of the two-piece SILENT NITE®*, where the comfort is main concern of patients when wearing appliances. The retention form has a major contribution to the comfort of patients, which is reduced in the SILENT NITE as the force transfers to the soft tissue. One of the reasons for lower preference rate is detachment of the appliance during mandible advancement. However, the monoblock appliance is retained on teeth by clasps, which translates into minimised pressure on the soft tissue and superior comfort for patients. There were no statistic differences between monoblock and SILENT NITE® appliances, most probably because of the identical vertical and horizontal advancements of both appliances, therefore eliminating the hypothesis that the reduction of the pharyngeal airway could be the reason for the efficiency differences of the appliances. The movement freedom of the two-piece appliance was considered an advantage, but it was

obvious that the structure cannot provide a solid consistent airway enlargement. This fact may constitute an explanation of the results in our study [25].

Moreover, a study conducted by Bishop et al. [35] aimed to determine if the design of mandibular repositioning appliance (MRA) can affect the end treatment result of OSA [35]. No statistically significant difference was found between the two appliances of different designs. Clear majority of subjects preferred an appliance that is less bulky and covers fewer surfaces of the mouth. So, when selecting or designing an appliance, bulk of the appliance should be minimized, allow treatable protrusion and should provide some increase in the vertical space between the maxillary and mandibular teeth [35].

According to Johal et al, [30] MRD could lower the baseline AHI and ODI values, whilst there was a significant difference in their relative effectiveness in its different designs. Custom-made MRA is more effective in the management of OSA and also in patients' preference and compliance than ready-made [30]. Both designs of MRD achieved a reduction in reported daytime sleepiness, which was similar in magnitude to previous reports [39,40]. Excessive daytime sleepiness persisted less in custom-made than ready-made MRDs. Quinnett et al. [40] and Johal et al. [30] reported that, custom-made MRD achieved greatest improvement in terms of both generic (SF-36) and specific (FOSQ) measures, which in term improve the quality of life. The potential benefits of a custom-made MRD, with incremental advancement, permitting better adaptation to the device may explain the more favourable results [30]. MRD therapy is an entirely patient-dependent treatment and its success has to be patient comfort and consequent use. In Vanderveken et al. [39] and Johal et al [30] studies, patients expressing preference more favour to MRDc as compared to MRDr. In contrast, in the Quinnett et al. study [40], 96% of patients reported minor adverse events, which related predominantly to discomfort. However, this may reflect the short duration of the study, that lead to insufficient time for adaptation [31,40,41]. In spite of that, Patients found the ready-made MRD difficult to tolerate too [30]. Ready-made MRDs unfortunately are limited in their design, by the very fact that the manufacturer is attempting to cater to the needs of a very diverse population, with inherent differences in the size of their jaws and ability to protrude their mandible [30]. Nevertheless, Patients and sleep physicians are recommending or purchasing the ready-made MRD devices, not least because they are easily available from multiple sources and relatively cheap. Thus, clinical use and patients were instructed to "follow the manufacturer's instructions" with regards to the ready-made MRD and provided a custom-made MRD by a dental professional, in order to highlight both the clinical and patient centered aspects of their use [30].

Idris et al. [32] evaluated the effectiveness of MAS to control SDB in children with an Active or a Sham MAS. This randomized crossover trial concludes that wearing of the Active MAS resulted in a significant reduction in overall AHI, supine AHI and improved the ratings of

quality of life [33]. In addition, mean snoring time per night was shorter with the Active MAS than with the Sham MAS. In fact, the AHI showed a tendency to increase after treatment when using the Sham MAS. This may be due to the inevitable bite opening of 0.5–1mm with the Sham MAS (upper and lower Hawley retainers), that caused by retention clasps on posterior teeth. Acrylic base plates that cover the palate and the lingual side of the mandibular dental arch and may occupy some of the tongue space and push the tongue to a slightly backward position could be a possible cause. Moreover, some participant's suffered from the common cold during at the end of one treatment period, it might cause increase in the evaluated AHI compared to base records [33]. Positive behavioural changes after adenotonsillectomy, a resolution of obstruction in the upper airway, which in agreement with positive behavioural changes when using MAS in this study [41].

CONCLUSION

The last decade has been a breakthrough with pioneer studies resulting in an overall improvement of patient care and underlining the importance of multidisciplinary management of OSAS. Considering the limited number of included studies "12 published studies were selected for this systematic review", the presented orthodontic treatments is found to be effective in managing snoring and OSAS. Thus, the respective results suggested that the correction of craniofacial structure disharmony to the optimal conditions; which in turns led to diminish snoring and OSAS. Other important health outcomes related to OSAS, such as quality of life, Neuro-cognitive function and cardiovascular health have not yet been systematically addressed and no conclusion on orthodontic treatments should be taken in this regard. The challenge to educate healthcare practitioners, and health organizations to investigate the impact of integrating dentistry and medicine at educational and operational levels on determining the medical necessity of the conditions at the time of treatment.

Orthodontic treatment of OSAS guidelines cannot be extrapolated and generalized from this systematic review and meta-analysis. In the future, more studies should be conducted with larger sample size and with specific inclusion and exclusion criteria.

CONFLICTS OF INTEREST

The authors do not have any conflicts of interest to disclose.

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