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Effect of jaw-opening exercise on prevention of temporomandibular disorders pain associated with oral appliance therapy in obstructive sleep apnea patients: A randomized, double-blind, placebo-controlled trial☆

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ABSTRACT

Purpose: There are no studies on the prevention of temporomandibular joint and/or masticatory muscle pain (TMD pain) associated with oral appliance (OA) therapy in patients with obstructive sleep apnea (OSA). The aim of this study was to determine the effect of jaw-opening exercise on TMD pain associated with OA therapy in OSA patients.

Methods: Twenty-five OSA patients without pain-related TMD were consecutively enrolled into a two-arm, randomized, double-blind, placebo-controlled trial. One group performed jaw-opening exercise (JE, n=13), and the other group performed placebo exercise (PE, n=12) for 1-month, and had started 2-weeks prior to insertion of an adjustable OA. TMD sign using the Research Diagnostic Criteria for Temporomandibular Disorders and TMD pain intensity

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using a visual analog scale (VAS) in the morning and daytime were evaluated at baseline (pre-exercise) and at 2-weeks, 1-month, and 3-months after OA insertion.
Results: Pain-related TMD was not observed in the JE-group at all evaluation periods, although one subject in the PE-group was diagnosed with arthralgia at the 1-month evaluation. The JE-group showed lower morning and daytime VAS scores than the those of the PE-group at all evaluation periods, and significant group differences were found in terms of chewing pain and jaw-opening pain in the morning at the 1-month evaluation, and of jaw-opening pain during daytime at the 3-month evaluation ($P<0.05$).
Conclusions: Within the limitations of the study, jaw-opening exercise prior to OA therapy reduced the risk of TMD pain associated with OA use. Therefore, jaw-opening exercise may contribute to the prevention of TMD pain.

1. Introduction

Oral appliance (OA) therapy is a treatment option for obstructive sleep apnea (OSA). An OA dilates the upper-airway by positioning the mandible forward; this prevents upper-airway obstruction during sleep [1–3]. However, OA therapy has short-term side effects, such as excessive salivation, dry mouth, and occlusal discomfort [4,5]. In addition, it sometimes causes pain in the temporomandibular joint (TMJ) and/or masticatory muscles, which is diagnosed as temporomandibular disorders (TMD) [5–8], as OA holds the mandible in an unnatural anterior position. Pain in the TMJ and masticatory muscles associated with OA use may decrease compliance and result in treatment failure. In fact, the main reasons for dropout from OA therapy are a perceived lack of improvement and side effects [9–11]. Therefore, prevention of TMD and ensuring the oral comfort with an OA is necessary for its long-term use and successful treatment results.

TMD is commonly a self-limited disease [12]. In general, conservative treatments with noninvasive and reversible modalities are the first choice for TMD [13]. Therapeutic exercise, involving stretching of the muscle and joint, is intended to relieve pain and decrease functional impairment during the chronic phase of TMD [14]. In musculoskeletal disorders, such as bone fractures, lower back pain, and knee pain, therapeutic exercise is applied not only for treatment, but also for prevention of these diseases [15,16]. In OSA patients with TMD that includes symptomatic pain, jaw-opening exercises have been effective in reducing pain and increasing OA compliance [17]. However, it is not known whether jaw-opening exercises in OSA patients without TMD are effective for preventing TMJ and/or masticatory muscle pain (TMD pain) associated with OA use. The purpose of this study was to determine the effect of jaw-opening exercises on TMD pain associated with OA use, and OA compliance in OSA patients without pain-related TMD. The null hypothesis tested in this study was that occurrence of pain-related TMD, TMD pain intensity, OA compliance at the 3-month follow-up in patients with OSA who performed jaw-opening exercises prior to OA insertion would be no different to those in patients who performed placebo neck exercises.

2. Materials and methods

2.1. Subjects

Patients with OSA, diagnosed using polysomnography (PSG) according to the American Academy of Sleep Medicine guidelines in 2007 [18], were consecutively recruited from the Dental Clinic for Sleep Disorders (Apnea and Snoring) of Tokyo Medical and Dental University Dental Hospital for OA therapy. Eligibility for the study is presented in Table 1. All subjects were provided verbal and written information about the study and signed informed consent forms. The study protocol was approved by the Tokyo Medical and Dental University Dental Hospital ethics committee (No. 1037).

2.2. Study design

This study employed a two-arm, randomized, double-blind, placebo-controlled trial. The subjects were randomly allocated into a jaw-opening exercise (JE) or placebo exercise (PE) group, and performed exercises for 2-weeks before and 2-weeks after OA insertion (1-month in total). OA compliance, TMD signs, TMD pain intensity, and therapeutic outcomes were evaluated prior to starting exercise (baseline), and at 2-weeks, 1-month, and 3-months after OA insertion (Fig. 1).

Degree of TMD pain has been observed to vary with sex differences [19]. Thus, we used a block size of four, and random allocation was stratified for gender using an envelope method, which was performed by an independent study operator. A therapist (H.I) instructed the subjects in the allocated exercise. A specialist (S.I) who conducted OA treatment and a TMD examiner (A.N) were blinded to information on group allocation. Patients were told at the time of enrollment that either exercise was effective for prevention of masticatory muscle and TMJ pain; thus, they were blinded to the actual type of exercise assigned.

TMD pain with OA therapy occurs in 10–70% of cases [4–8], and the variation is large. Using the results of previous studies, we estimated the requirement of a sample size of 90 participants, with an effect size of 0.6, alpha of 0.05, power of 0.80, and allocation ratio of 1:1 between arms.

Table 1 – Eligibility criteria for subject enrolment into the study.

Inclusion criteria
Age between 20 and 70 years
Patients who had more than 20 teeth with good stability, including the residual anterior teeth
Patients diagnosed with OSA using polysomnography according to the American Academy of Sleep Medicine guidelines
Exclusion criteria
Presence of other sleep disorders
Body Mass Index > 30 kg/m^2
Patients who previously had received OSA treatment (CPAP and/or OA)
Patients who need combination treatment with OA and CPAP
Maximum mandibular advancement < 5 mm
Patients who have been taking medicine such as hypnotics, analgesics
Presence of mental illness
Patients who were diagnosed with TMD by the RDC/TMD (Research Diagnostic Criteria for TMD) except for disc displacement (group II)
Patients with cervical myofascial pain
Patients who needed dental treatment for caries and periodontal disease

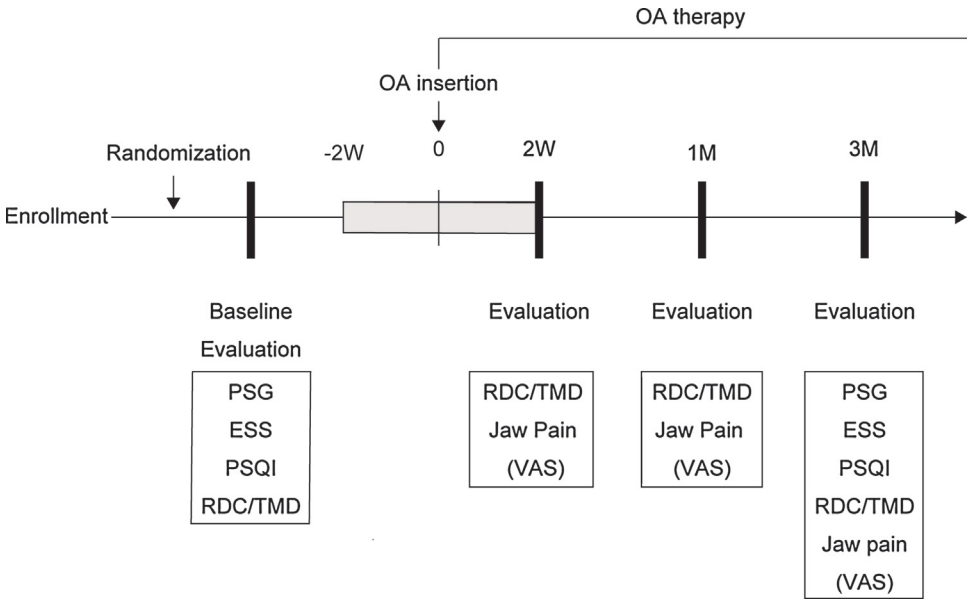

Fig. 1 – Time line in this study.

2.3. OA

A custom-made, two-piece OA (SomnoDent MAS; SomnoMed Ltd., Crows Nest, Australia) was used in this study. The appliance was adjustable, and allowed mouth-opening. The absolute range of maximum mandibular advancement was measured using the George Gauge (Great Lakes Orthodontics, Ltd., Tonawanda, NY, USA) [20]. The amount of mandibular advancement in this study was set at 70% of the maximum, because approximately 50-70% of maximum has been recommended as the appropriate amount of advancement [21,22].

2.4. Exercise

In the JE-group, the subjects self-performed the exercise manually according to the following protocol (Fig. 2) [14]. All fingers, except for the thumb, on the dominant hand were placed on the edge of the mandibular incisors, and the thumb of the opposite hand was placed on the edge of the maxillary incisors. The subjects opened their mouth with finger effort until they felt masticatory muscle tightness. The opened position was held for 10s. The subjects were instructed to perform this exercise 5 times, as a single set, which was performed after each meal; a total of three sets (15 times) were performed each day.

In the PE-group, the subjects self-performed an extension exercise of the neck, according to the following protocol (Fig. 3) [17]. First, the patient rotated the head to the right side and set the right hand on the superior part of the left ear, then slowly pressed against the head with the right hand, and extended the neck until they felt the tightness of the muscles. The extended position was held for 10s. The subjects were instructed to perform this exercise three times each to the right, left, and front as a single set, which was performed after each meal; a total of three sets (nine times) were performed each day. The patients were instructed to record the number of times the exercises were performed in a diary. A therapist (H.I) checked the number of actual exercise times recorded in the diary at the

Fig. 2 – Jaw-opening exercise (JE-group): all fingers, except for the thumb, on the dominant hand were placed on the edge of the mandibular incisors, and the thumb of the opposite hand was placed on the edge of the maxillary incisors. The subjects opened their mouth with finger effort until they felt masticatory muscle tightness. The opened position was held for 10 s.

Fig. 3 – Neck exercise (placebo) (PE-group): first, the patient rotated the head to the right side and set the right hand on the superior part of the left ear, then slowly pressed against the head with the right hand, and extended the neck until they felt the tightness of the muscles. The extended position was held for 10 s.

time of OA insertion in time-line, and confirmed appropriateness of the performed exercise for each subject. If they were inappropriate, he provided instructions on the exercise methods for the patients again.

2.5. *Outcome measures*

As the primary outcome, we assessed TMD signs by clinical examination, and TMD pain intensity and OA compliance with the use of a self-administered questionnaire. As the secondary outcome, the therapeutic outcomes of the tested OA were assessed on polysomnographic parameters and on the Epworth Sleepiness Scale (ESS) [23] and the Pittsburgh Sleep Quality Index (PSQI) [24].

The expert examiner assessed TMD signs using the Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD) Axis I [25]. Examinations were standardized and performed by a calibrated examiner. If TMD was present, the examiner determined the TMD subtype: Myofascial pain (group I), disc displacement (group II), and arthralgia (group III). Groups I and/or III were referred to as pain-related TMDs (pTMD). The results of TMD signs were reported in a descriptive manner.

TMD pain intensity was measured using a 100 mm visual analog scale (VAS) with “no pain” at the left end and “intolerable pain” at the right end. The subjects were instructed to mark a vertical line on the scale at a point indicating the most severe TMD-related pain they experienced at rest, during mouth opening, and during chewing. The VAS score was defined as the distance from the left end to the vertical line. Previous studies have assessed the TMD pain related to OA therapy by different criteria [4–8,22], but no studies evaluated the diurnal variation of pain. Therefore, the pain assessments in this study were performed separately in the morning and daytime.

The subjects were asked by questionnaire to indicate the number of days the OA was used in the preceding week and the duration of OA usage at night to assess OA compliance. The questions (responses) were: “How many nights did you use the OA in the past week?” (1: every night, 2: 4–6 nights, 3: 1–3 nights,

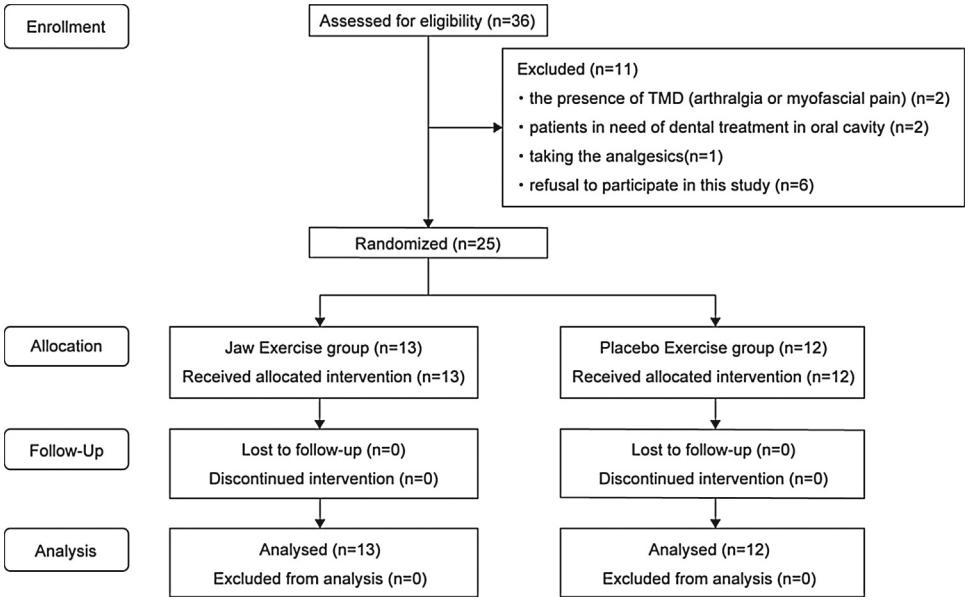

Fig. 4 – CONSORT flow diagram.

and 4: none), and "How long did you use the OA at night?" (1: all night, 2: more than half of the night, 3: half of the night, and 4: less than half of the night).

Standard overnight PSG was performed and the following polysomnographic parameters were assessed: the apnea–hypopnea index (AHI), lowest SpO2, arousal index, sleep efficiency, and the percentage of REM and NREM sleep. The ESS is subjective and is based on a questionnaire used to assess excessive daytime sleepiness. The ESS score ranges from 0 (minimum) to 24 (maximum); a higher total score represents a higher level of daytime sleepiness. The PSQI is also subjective and is based on a questionnaire used to assess the quality of sleep. The PSQI score ranges from 0 (minimum) to 21 (maximum), with a higher total score representing a decline in sleep quality.

2.6. *Statistical analyses*

The Mann–Whitney U test and chi-square test were used for comparisons between groups. The Wilcoxon signed-rank test was used for within-subject comparison of therapeutic outcomes in each group. P values for group comparisons in VAS scores were corrected using the Bonferroni method. A value of $P<0.05$ was considered statistically significant. All statistical analyses were performed using SPSS version 21.0 software (IBM, Inc., Armonk, NY, USA), and all measured values were expressed as mean with standard deviations (SD).

3. Results

Thirty-six patients with OSA were recruited from August 2014 to December 2015 (Fig. 4). We excluded 11 patients who did not meet the inclusion criteria of the study. Of the excluded participants, two patients had pTMD (arthralgia or myofascial pain), two patients were in need of dental treatment in the oral cavity, one patient has been taking analgesics for knee pain, and six patients refused to participate in this study because they did not have time to perform the exercises during the daytime. Thus, 25 patients (21 men and four women) were enrolled into the study, and all completed the trial; however, two patients failed to undergo PSG measurements at the 3-month evaluation. Among the cohort, the mean age was 51.4 ±9.7 years, AHI was 21.5±10.0 per hour, and BMI was 24.2 ±1.9 kg/m^2. The demographic information of the subjects in each group at baseline is shown in Table 2. Overall, the characteristics of the JE and PE groups were comparable, and there were no significant differences between the groups ($P>0.05$). The mean exercise compliance was 90.7% (13.6/15 times per day) for the JE-group and 85.6% (7.7/9 times per day) for the PE-group. There were no significant differences between groups in exercise performance ($P>0.05$).

Table 2 – Demographics of the subjects at baseline evaluation.

	JE-group (n=13)	PE-group (n=12)	P
Gender (%male)	84.6(11/13)	83.3(10/12)	0.979
Age (years)[a]	52.8(10.1)	49.9(9.5)	0.503
BMI (kg/m^2)[a]	24.5(1.6)	23.9(2.1)	0.320
Mallampati class[a]	3.4(0.7)	2.9(0.7)	0.152
MOA (mm)[a]	47.9(5.9)	49.5(7.5)	0.538
MMA (mm)[a]	11.9(1.4)	12.5(2.7)	0.973
AHI (events/h)[a]	21.3(6.0)	21.7(13.4)	0.611
Lowest SpO2 (%)[a]	83.8(5.0)	79.5(5.6)	0.077
ESS[a]	11.1(3.6)	10.0(4.8)	0.376
PSQI[a]	6.3(2.6)	5.4(2.2)	0.443

BMI: Body Mass Index, MOA: maximum opening amount, MMA: maximum mandibular advancement, AHI: Apnea Hypopnea Index, ESS: Epworth Sleepiness Scale, PSQI: Pittsburgh Sleep Quality Index.
[a] Data are presented as mean (SD).

Table 3 – Number of patients diagnosed with TMD according to the RDC/TMD.

RDC/TMD	JE-group (n=13)				PE-group (n=12)			
	Baseline	2W	1M	3M	Baseline	2W	1M	3M
Myofascial pain (group I)	0	0	0	0	0	0	0	0
Disc displacement (group II)	0	1	1	0	3	2	3	2
Arthralgia (group III)	0	0	0	0	0	0	1	0
Total TMD (%)	0 (0%)	1 (8%)	1 (8%)	0 (0%)	3 (25%)	2 (17%)	4 (33%)	2 (17%)
Pain-related TMD (%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (8%)	0 (0%)

2W: 2-weeks after OA insertion, 1M: 1-month after OA insertion, 3M: 3-months after OA insertion.

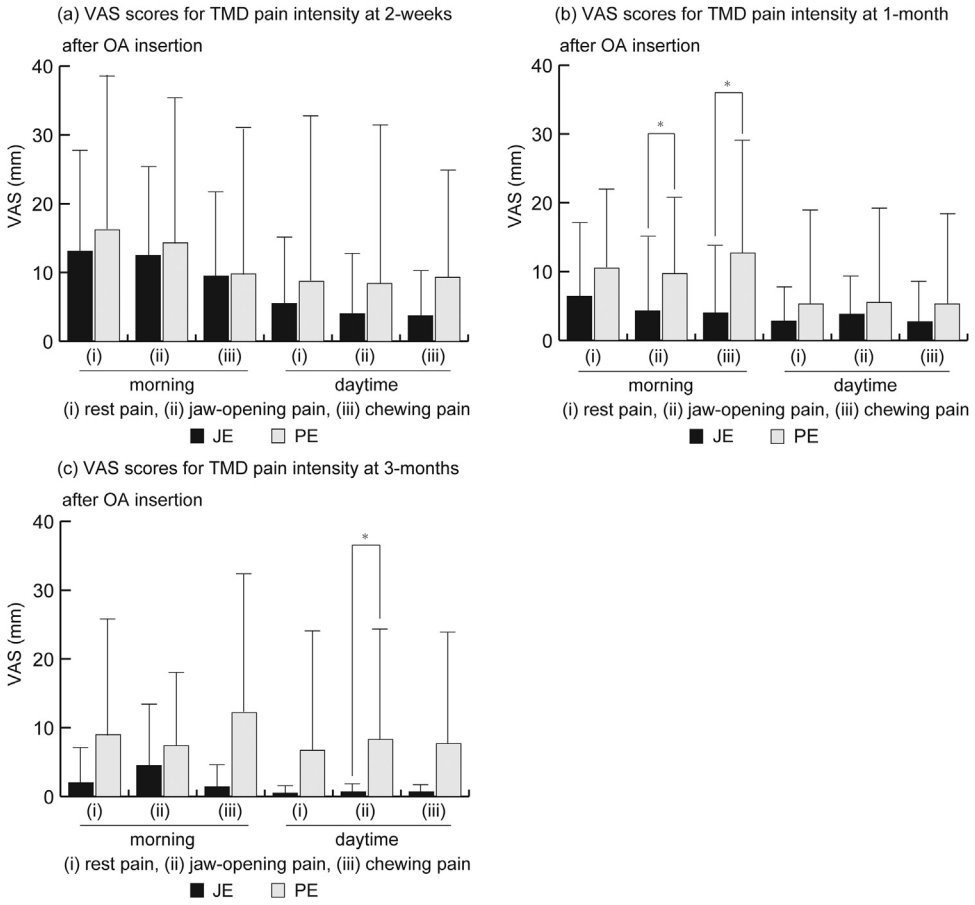

Fig. 5 – VAS scores for TMD pain intensity at (a) 2-weeks and (b) 1-month and (c) 3-months after OA insertion (*P < 0.05).

TMD signs using the RDC/TMD are summarized in Table 3. None of the subjects in either group had myofascial pain (TMD group I) at any evaluation interval, and only one subject in the PE-group developed arthralgia (TMD group III) at the 1-month evaluation. Disc displacement (TMD group II) developed in one subject in the JE-group at the 2-week and 1-month evaluations, and in two or three subjects in the PE-group across evaluation periods. In the JE-group, no subjects developed pTMD at any evaluation period. In the PE-group, one subject developed pTMD at the 1-month evaluation.

TMD pain intensity in the morning and daytime are shown in Fig. 5. In both groups, the VAS score in the morning and daytime gradually decreased with time. The JE-group showed lower morning and daytime VAS scores than the PE-group at all evaluation periods, but group differences were only statistically significant for chewing pain and jaw-opening pain in the morning at the 1-month evaluation and for jaw-opening pain in the daytime at the 3-months evaluation ($P < 0.05$).

The percentage of subjects using the OA every day is shown in Fig. 6a, and the percentage of subjects wearing the OA for the full time asleep is shown in Fig. 6b. The JE-group showed higher percentages than the PE-group at all evaluation periods in both questionnaires, but the differences were not significant ($P > 0.05$).

The therapeutic outcomes at the baseline and 3-month evaluations are shown in Table 4. Overall, the therapeutic outcomes of the JE and PE groups were similar at both evaluation periods and no statistically significant differences were found between groups ($P > 0.05$). With respect to within-

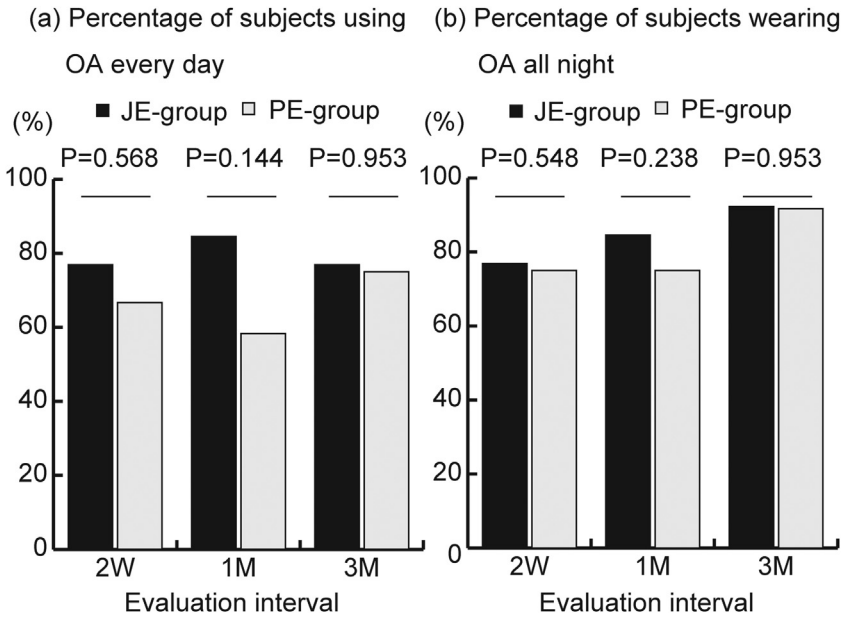

Fig. 6 – Percentage of subjects using OA every day (%) (a) and percentage of subjects wearing OA all night (%) (b) at 2-weeks (2W), 1-month (1M) and 3-months (3M) after OA insertion.

Table 4 – Therapeutic outcomes at baseline and 3-month (3M) evaluations.

	JE-group (n=12)			PE-group (n=11)		
	Baseline	3M	P##	Baseline	3M	P##
AHI (events/h)#	21.1(6.2)	8.1(5.8)	0.003	22.6(13.7)	10.7(6.9)	0.009
Lowest SpO_2 (%)#	84.4(4.8)	88.5(3.2)	0.034	79.4(5.9)	83.4(5.9)	0.028
Arousal index (events/h)#	21.2(7.7)	16.2(6.8)	0.041	28.2(15.0)	22.3(7.0)	0.139
Sleep efficiency (%)#	81.2(9.1)	85.7(8.3)	0.374	82.1(9.5)	82.2(9.0)	0.959
REM sleep (%)#	17.7(5.0)	22.7(3.8)	0.012	17.6(5.5)	19.8(5.7)	0.241
NREM sleep (%)#	82.3(5.0)	78.2(4.6)	0.071	82.4(5.6)	80.2(5.7)	0.241
ESS#	11.1(3.6)	6.4(3.8)	0.029	10.0(4.9)	7.6(4.0)	0.159
PSQI#	6.3(2.6)	3.8(1.8)	0.027	5.2(2.1)	4.6(1.7)	0.287

Data are presented as mean (SD). AHI: Apnea Hypopnea Index, ESS: Epworth Sleepiness Scale, PSQI: Pittsburgh Sleep Quality Index.
Not significant between groups (P>0.05).
Within-subjects comparison in each group.

subject comparisons, both JE and PE groups showed a significant decrease in the AHI and a significant increase in lowest SpO_2 with the OA ($P<0.05$). In terms of sleep architecture, the arousal index showed a significant decrease and REM sleep showed a significant increase in the JE-group ($P<0.05$), but these changes were absent in the PE-group. ESS and PSQI scores decreased at the 3-month evaluation, but this was only statistically significant in the JE-group ($P<0.05$).

4. Discussion

To our knowledge, this is the first study to determine the effect of jaw-opening exercise on OA-related TMD pain in OSA patients who had no pain-related TMD. It has been reported that TMD pain during OA therapy is commonly experienced in the early phase and tends to decrease in later phases [22]. Moreover, a long-term period may make the patients' compliance to continue the exercise more difficult over time. Therefore, we focused on preventing TMD pain during the early phase of OA therapy in this study and instructed the patients to perform the exercise only 1 month. We found little difference between groups in terms of the occurrence of TMD, and only one subject in the PE-group developed pTMD (arthralgia) at the 1-month evaluation. However, this disappeared at the 3-months evaluation, and no pTMD was observed in the PE-group. Therefore, the results suggested that the preventative effect of a jaw-opening exercise on the occurrence of pain-related TMD was small.

It has been reported that the TMD pain causes a decrease in quality of life [26], and it is important to assess the intensity and pattern of pain. Morning pain after removal of the OA and daytime pain were evaluated separately in this study. In both groups, the pain was stronger in the morning. We presume that this can be attributed to the insertion of the OA; thus, it is essential to control morning pain in order to increase the compliance with OA therapy. Collins et al. reported that a patient with a VAS score exceeding 30mm would be

experiencing at least moderate pain, and that a VAS score exceeding 54 mm would indicate severe pain [27]. The VAS scores of both groups in this study were less than 30 mm at any evaluation period, indicating that the patients experienced mild pain. However, the jaw-opening exercise was able to reduce chewing pain and jaw-opening pain intensity more in the morning at the 1-month evaluation, and jaw-opening pain in the daytime at the 3-month evaluation. Therefore, the jaw-opening exercise may be effective in reducing TMD pain associated with OA use.

In both groups, the AHI showed a significant reduction with OA use, and the therapeutic effects were notable. A relationship between side effects and compliance has been reported [9]. In order to obtain a therapeutic effect, it is important to increase compliance. No statistically significant differences in OA compliance were found between groups. However, OA compliance in the JE-group exceeded 75% at all evaluation intervals, and seemed to show a higher tendency than in previous studies [28]. Therefore, jaw-opening exercise may increase OA compliance, but analysis of a larger sample size is needed.

Shrivastava et al. reported that tensile stresses in the posterosuperior aspect of the mandibular condyle and on the posterior aspect of the mandibular fossa were caused during mandibular protraction, based on finite element models [29]. Masticatory muscle fatigue was reportedly caused by OA use [4,5]. Therefore, we believe that these strains were the result of an excessive load on the intra-articular and masticatory muscle caused by OA insertion. We assumed that poor blood circulation and cumulative fatigue are induced by strain, and TMD develops as a result of these factors. Poor blood circulation reportedly leads to a failure of oxygen supply to the peripheral tissues and induces pain-producing substances in the blood. An increase in flexibility has been reported to reduce the risk of injury, as well as pain [30]. Therefore, it is necessary to increase the flexibility of the joints and muscles in order to prevent pain. We believe that performing jaw-opening exercise for a certain period of time prior to OA therapy can improve flexibility and increase the range of motion and muscle extensibility [31]. Furthermore, we presume that there are motor learning effects, such as improvement of adaptability, which are induced by placing a load on the joint before treatment.

Our study has some potential limitations. First, the occurrence of pain in the absence of exercise was not evaluated. Moreover, we presume that placebo exercise may also influence the pain, as inferred from the results of this study. The instruction to the patients in terms of exercise performance introduced a bias in the study results. Patients who do not perform these exercises can be conveniently recruited and should be evaluated as a non-exercise group, but it is impossible to blind such patients; further, comparison of groups with and without exercise is difficult. However, it is necessary to evaluate the effects of placebo exercise. Second, the sample size of this study was small. The number of patients who met the eligibility criteria was small. In particular, there were many patients who were diagnosed with OSA by the out of center sleep testing only without polysomnography. The time in duration was limited for this study, and we strictly set the eligibility criteria in order to prevent subject selection biases. Therefore, the number of subjects in this study was less than the sample size that we had originally calculated. We believe that analysis of a larger sample size is needed. Third, the patients were instructed to perform exercises in the daytime, but we could not verify that the exercises were actually performed. However, we confirmed whether the patients performed exercise as directed at the time of OA insertion. In fact, it was confirmed in all the subjects of this study that the required tasks were thoroughly conducted, in terms of the exercise times and the methods. Finally, although OA compliance was evaluated based on patient reports, this may differ from actual usage. If a device for measuring objective compliance could be developed, more reliable data could be obtained [32].

5. Conclusion

In conclusion, within the limitations of the study, the jaw-opening exercise, performed prior to OA therapy in OSA patients without pain-related TMD, resulted in reduced TMD pain associated with OA use. Therefore, jaw-opening exercise may reduce the risk of TMD pain. However, the effect of exercise on the occurrence of pain-related TMD and OA compliance seems to be limited. Further studies with a larger sample size are required to estimate the extent of the effect of exercise on TMD pain.

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