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Randomized Controlled Evaluation of Non-surgical Treatments for Temporomandibular Joint Anterior Disk Displacement without Reduction

ABSTRACT

The common methods for treating anterior disk displacement without reduction (ADDwor) are not based on randomized controlled clinical trials. Our study evaluated non-surgical treatments in 69 MRI-confirmed ADDwor subjects (m/f = 6/63). Subjects were randomly assigned to a control group and one of two treatment groups. Outcomes included maximum mouth opening, visual analogue scale of pain, and daily activity limitation. Calibrated examiners collected data at the initial interview and at 0, 2, 4, and 8 weeks of treatment. At the eight-week point, within-group improvements were present for all variables, for all groups. Between-group differences were not highly evident, with only mean daily activity limitation for the self-care/NSAID group being significantly lower than that of the occlusal appliance/jaw mobilization + self-care/NSAID group at the two- and four-week time-points. These results suggest that ADDwor subjects will improve with only minimal treatment intervention, and no significant difference was evident for the treatments tested and the control condition.

KEY WORDS: temporomandibular joint, anterior disc displacement without reduction, randomized controlled clinical trial, daily activity limitation, occlusal appliance therapy.

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INTRODUCTION

In 1996, the distinguished panel of scientists who served on the National Institutes of Health Technology Assessment Conference on Temporomandibular Disorders (TMD) evaluated all submitted evidence and testimony (James, 1997). They concluded that "randomized, controlled clinical trials are needed to determine the efficacy of TMD treatments." Unfortunately, this panel did not comment specifically about the treatment approaches for anterior disc displacement without reduction (ADDwor), except to say that "randomized controlled clinical trials to support the efficacy of individual surgical procedures have not been performed". These comments are relevant today, since there are two basic approaches used in the treatment of ADDwor (Stephan *et al.*, 1988). One approach is non-surgical and involves strictly palliative, physical-medicine approaches (Feine *et al.*, 1997; Reisner-Keller, 1997), while the other is described as "closed joint surgery", including fluid infusion and manipulation and/or arthroscopic surgery (Dimitroulis *et al.*, 1995; Fridrich *et al.*, 1996; Kurita *et al.*, 1997). Since the National Institutes of Health panel's comments were published, three relevant studies have appeared in the literature which suggest that a majority of the ADDwor signs and symptoms will resolve with time alone (Sato *et al.*, 1997a,b; Kurita *et al.*, 1998). Unfortunately, the above studies were not based on a randomized controlled clinical trial but were essentially uncontrolled case series studies. Only one randomized controlled clinical trial has been reported, and it used only visual analogue scale measures of pain as the only outcome measure (Lundh *et al.*, 1992). For these reasons, we designed a randomized controlled clinical trial to compare the efficacy of two conservative treatments with that of no-treatment control. The null hypothesis tested in this study was that the treatment groups and control group will show no difference in reducing the signs and symptoms of TMD.

SUBJECTS & METHODS

Study Population

Subjects were selected from a consecutive series of TMD patients (232 patients, male/female = 55/177) who attended the TMD clinic in the Department of Fixed Prosthodontics at Okayama University Dental School from March, 1997, to July, 1998. Eligible subjects were those with painful ADDwor, and they were selected according to the following inclusion criteria: (1) a complaint of pain with mouth opening and/or with chewing difficulty; (2) mouth opening pain in the affected temporomandibular joint region with a level of more than 10/100 mm on a visual analogue scale of pain (VAS); and (3) a positive diagnosis of ADDwor of the temporomandibular joint on the affected side by means of magnetic resonance imaging (MRI) according to the criteria for disk displacement described by Orsini *et al.* (1999). The subjects were excluded if they presented with one or more of the following conditions: (1) were unwilling or unable to participate in the experiment and attend all planned follow-up evaluations for any reason; (2) were edentulous; (3) had serious systemic disease which would potentially compromise the experiment (*e.g.*, rheumatoid

arthritis, diabetes mellitus); or (4) had previous or ongoing treatments for their TMD or tooth problems in other clinics (*e.g.*, medication, intra-oral appliance therapy, or dental restorative work).

During the sampling period, 89 potential ADDwor subjects (male/female, 7/82; mean age, 37.1 ± 17.4; unilateral/bilateral, 68/21) were identified from the consecutive 232 TMD patients meeting the inclusion criteria. From the 89 ADDwor subjects, 69 subjects were found eligible according to the aforementioned selection criteria and subsequently enrolled (male/female, 7/62; mean age, 34.0 ± 15.4; unilateral/bilateral, 50/19). Twenty subjects were excluded for the following reasons: had no pain (n = 7) in the joint; were unavailable to attend the clinic for any reason (n = 4); were being treated in other clinics (n = 4); were edentulous (n = 2); had systemic lupus erythematosus (n = 1); had a tumor located in the temporomandibular joint region (n = 1); or declined to participate in this study (n = 1).

The experimental protocol for this study underwent review and approval by the appropriate human subjects committee in the institution. Each subject was fully informed and consent was obtained before the experiment began. The participants in this study were told the following: "The most effective therapeutic option for your problem remains unknown, and this study is being conducted to clarify which therapeutic method is most practical and effective for relieving signs and symptoms."

Random Assignment Process

The ADDwor subjects were allocated randomly by a principal investigator (H.M.) to one of three groups—Control, Self-care plus non-steroidal anti-inflammatory drugs (NSAIDs), or Occlusal appliance and jaw mobilization plus self-care/NSAIDs—by means of a computer-generated false-random-number method.

Treatment Groups

All 3 groups were shown their temporomandibular joint MRIs and provided an explanation of these findings. Moreover, the prevalence and prognosis of this disorder, with its self-limiting nature of the signs and symptoms, were also explained according to previously published information (Kurita *et al.*, 1998). All subjects were informed that 2 months of observation would be needed in this study. The control group subjects received only the above explanation and advice regarding prognosis. The self-care/NSAIDs (palliative care) group subjects were prescribed an NSAID (Diclofenac Sodium, Voltaren, CIBA-GEIGY, Tokyo, Japan) in doses of 25 mg, 3x *per* day, with an anti-gastric ulcer medication (Aldioxa, Isalon Granules, Takeda, Osaka, Japan) in doses of 300 mg, 3x *per* day. In addition, the subjects were also instructed on how to perform a self-care protocol, which included the use of cold/hot packs, a soft food diet, and gentle mouth-opening exercises. The occlusal appliance/jaw-mobilization plus self-care/NSAIDs (physical medicine) group was treated as follows: (1) A flat occlusal appliance was fabricated and inserted; (2) at each visit, 20 minutes of intermittent manual jaw mobilization therapy was performed, and (3) the previously described self-care/NSAIDs treatment was utilized. The occlusal appliances were fabricated and adjusted to have maximal contacts in the centric occlusion as well as symmetric anterior contacts in a protrusive movement of the mandible and canine guidance in lateral jaw movement. A single trained dentist performed the insertion and adjustment of all occlusal appliances. The subjects were instructed to wear the occlusal appliances while sleeping but were advised to remove them during the day. A single trained dentist also performed manual jaw mobilization therapy at every follow-up time point (0, 2, 4, 8 wks later).

Outcome Variables

The 3 classes of outcome variables were visual analogue scale (VAS) for pain at rest and during mastication, daily activity limitation associated with the subjects' TMD symptoms, and 3 measures of maximum mouth opening assessment. The VAS scale of pain involved asking the patient to mark, on a 100-mm line, his/her usual pain since the last visit. This line was anchored with the words "no pain" and "most severe pain imaginable" at each end. The daily activity limitation score was performed at every time point by means of an 18-item questionnaire asking questions on the effect of jaw pain on the subjects' various activities of daily living (Clark *et al.*, 1989). For each question item, the subject rated the effect on a 0-to-4-point scale (0 = doesn't hurt at all, 1 = hurts a little, 2 = hurts a lot, 3 = almost unbearable, 4 = unbearable pain prevents activity). These data were collected at 5 time points in the study, including the initial examination of the subject and at 0, 2, 4, and 8 wks after the start of treatment. VAS pain values were measured by a millimeter ruler and expressed in mm. All VAS measurements were performed with the examiner being blind to the patient's treatment group assignment. We calculated the total daily activity limitation score by adding the scores of the 18 items on the questionnaire; thus, a score from 0 to 72 was possible. Maximum mandibular opening measurements were done by one of three calibrated examiners. Again, these measurements were performed with the examiner blind to the subject's treatment group. Maximum mandibular opening measurements included (1) maximum comfortable range of motion, (2) active range of motion, and (3) passive range of motion. These measurements involved the values of the interincisal distances between the upper and lower right plus the vertical overlap of the incisors measured with the teeth in intercuspal position. We applied the uniform interincisal stretching force of 9.8 N to assess the passive range of motion. The force was applied by means of a pressure algometer (Pressure Algometer, Wanger Instruments, Greenwich, CT, USA).

Calibration of Maximum Mandibular Opening Examination

The three examiners were calibrated for the passive range of motion measurement prior to the commencement of this study. Training was performed by means of a set of 21 TMD cases from the clinic. This calibration training yielded mean interclass-correlation coefficient (ICC) values: 0.79 ± 0.05 in maximum comfortable range of motion, 0.97 ± 0.01 in active range of motion, and 0.96 ± 0.01 in passive range of motion.

Statistical Analysis

The comparison of baseline parameters among the three groups was done by a one-way factorial ANOVA to test the homogeneity in the parameters among the three groups. The mean VAS during mastication and maximum mandibular opening levels at the initial visit and 2, 4, and 8 wks after application of the interventions were compared by means of a two-way repeated-measure ANOVA to estimate the effects of group difference and time course on the outcome measures. Regarding

Table 1. Baseline Comparison of the Demographic and Standard Measures among the Three Experimental Groups

Variables	Experimental Groups[a]			*p*-value
	Physical Medicine (N = 25)	Palliative Care (N = 23)	Control (N = 21)	
Age (yrs)	32.0 (15.8)	33.3 (13.3)	36.9 (17.1)	0.547[b]
Daily Activity Limitation (scores)	6.1 (4.4)	5.6 (2.7)	6.0 (2.2)	0.995[c]
Locking duration (days)	93.7 (150.8)	84.4 (152.8)	116.6 (166.8)	0.791[b]
Pain Intensity (VAS scale)				
At rest	12.9 (21.2)	12.5 (20.9)	12.3 (11.8)	0.919[b]
During mastication	49.7 (23.8)	55.8 (25.8)	59.9 (21.7)	0.349[b]
Mouth Opening (mm)				
Maximum comfortable range	29.1 (10.2)	32.4 (10.5)	32.5 (11.1)	0.464[b]
Active range	33.6 (9.7)	36.1 (9.9)	36.7 (10.4)	0.537[b]
Passive range	37.3 (9.8)	37.8 (9.6)	39.1 (9.8)	0.812[b]

[a] Mean (standard deviation).
[b] *p*-values were calculated by one-way factorial ANOVA.
[c] *p*-value was calculated by Kruskal-Wallis test.

the daily activity limitation scores and mean VAS at rest, Kruskal-Wallis Ranks tests were used to estimate the effects of time course and group difference on the mean daily activity limitation score. Kruskal-Wallis ANOVA tests were further used as the *post hoc* multiple-comparison analysis. The cut-off level for significance was set at $\alpha = 0.05$. Outcome data were analyzed by an intent-to-treat (ITT) concept. This means that the last available measurement collected for our outcome variable on the drop-out subject was utilized for the missing data points. The magnitude of these missing data involved 9 time points out of 345 points for the subjects.

RESULTS

Group Equality and Drop-out Effect

Baseline comparison among the three experimental treatments groups were made based on age, daily activity limitation score, locking duration, and severity of the signs and symptoms. No significant differences were seen in the listed parameters (Table 1). During the two-month observation period, eight subjects failed to report and were dropped from the intended sample (one female after the two-week follow-up and five females after the four-week follow-up). Two additional female subjects were also dropped after the four-week follow-up point because they requested a rescue therapy (arthrocentesis treatment). When missing data were encountered, the data from the last time point were extended to fill the missing time points. These projected data fulfilled the principles of an intent-to-treat analysis. The intent-to-treat analysis is used so that the potential benefit to all subjects enrolled in the treatment arm of the study can be calculated, regardless of whether or not they completed the study.

Outcome Variable Results

The means and standard deviations for the 3 maximum mandibular opening variables across the experimental period for the three subject groups are seen in Table 2. The means and standard deviations for the daily activity limitation

Table 2. The Changes of Mean Maximum Mandibular Opening Levels among the Three Experimental Groups

Variables	Experimental Groups	Maximum Mandibular Opening Levels (mm)[a]					*p*-value[c]		
		Initial Visit	0 week[b]	2 weeks[b]	4 weeks[b]	8 weeks[b]	Group Difference	Time Course	Interaction
Maximum Comfortable	Physical medicine (N = 25)	29.1 (10.2)	29.2 (7.69)	34.4 (9.87)	37.5 (9.91)	39.8 (10.1)	0.700	< 0.001	0.034
	Palliative care (N = 23)	32.4 (10.5)	32.4 (10.4)	35.4 (9.56)	37.0 (10.5)	38.1 (10.5)			
	Control (N = 21)	32.5 (11.1)	35.2 (10.9)	37.1 (8.94)	37.9 (9.84)	38.5 (9.68)			
Active	Physical medicine (N = 25)	33.6 (9.68)	34.3 (8.17)	37.4 (9.84)	40.4 (10.1)	42.4 (10.1)	0.733	< 0.001	0.012
	Palliative care (N = 23)	36.1 (9.98)	36.5 (10.4)	37.5 (9.05)	39.1 (9.53)	39.6 (10.2)			
	Control (N = 21)	36.7 (10.36)	39.5 (9.94)	39.6 (8.48)	40.6 (8.64)	41.0 (8.39)			
Passive	Physical medicine (N = 25)	37.3 (9.82)	37.6 (9.14)	39.4 (9.66)	41.8 (9.60)	43.5 (9.53)	0.776	< 0.001	0.088
	Palliative care (N = 23)	37.8 (9.62)	38.6 (9.99)	39.0 (9.12)	40.3 (9.57)	40.8 (10.4)			
	Control (N = 21)	39.1 (9.81)	41.6 (9.09)	40.9 (8.38)	41.6 (8.43)	42.5 (8.09)			

[a] Mean (standerd deviation).
[b] Follow-up time points after starting treatments.
[c] *p*-values for the main effects and interaction were calculated by two-way repeated-measures ANOVA tests.

variable across the experimental period for the three subject groups are seen in Table 3. The means and standard deviations for the 2 VAS-pain variables across the experimental period for the three subject groups are seen in Table 4. In these tables, all statistically significant main effects and any important interactions are indicated.

Table 3. The Changes of Mean DAL Levels among the Three Experimental Groups

Experimental Groups	DAL Levels[a]					p-value[c] for Time Course
	Initial Visit	0 week[b]	2 weeks[b]	4 weeks[b]	8 weeks[b]	
Physical medicine (N = 25)	6.1 (4.4)	6.2 (3.9)	6.2 (4.5)	5.7 (3.8)	5.1 (3.9)	0.754
Palliative care (N = 23)	5.6 (2.7)	4.0 (2.0)	3.8 (2.3)	3.0 (1.9)	3.3 (2.9)	**0.001**
Control (N = 21)	6.0 (4.2)	5.6 (4.7)	4.7 (2.9)	4.7 (4.4)	3.8 (3.7)	0.166
p-value[d] for Group Difference	0.995	0.100	0.153	**0.029**	0.175	

[a] Mean (standard deviation).
[b] Follow-up time points after starting treatments.
[c] p-values for the main effect of time course in each treatment group were calculated by Kruskal-Wallis tests.
[d] p-values for the main effects of group differences in each observation time point were calculated by Kruskal-Wallis ANOVA tests.

DISCUSSION

Unique to our study *vs.* prior treatment outcome studies on ADDwor was that we used calibrated examiners, designed and implemented bias-controlled measures (examiner blinding wherever possible), and established a standard method for measuring passive-stretch mouth opening. In addition, we elected to use 3 types of outcomes (VAS-pain, maximum mandibular opening, and daily activity limitation) to assess our treatment effects. We believe that such a multidimensional assessment of outcomes is essential. While VAS-pain and maximum mandibular opening outcomes are standard tools, a daily activity limitation score is not as common. However, this questionnaire captures the patient's subjective disability in a way that the other two uni-dimensional variables do not. The results in this study showed that, with time, all three experimental groups had a significant improvement for most of the outcome variables studied. The only group effect seen was with the daily activity limitation variable, and it showed that the self-care/NSAIDs treatment protocol had a stronger effect (*i.e.*, more improvement) than the other two interventions. However, this difference was present only for two post-treatment time points, and with the last time point (8 wks), there were no significant group differences. Based on the data presented, we are unable to reject the null hypothesis that there was no difference in the TMD signs and symptoms among our three experimental groups.

Our RCT data are in full agreement with the previously

Table 4. The Changes of Mean VAS Pain Levels among the Three Experimental Groups

Variables	Experimental Groups	VAS Levels (mm)[a]					p-value[c]		
		Initial Visit	0 week[b]	2 weeks[b]	4 weeks[b]	8 weeks[b]			
At rest	Physical medicine (N = 25)	12.4 (20.9)	13.2 (19.4)	6.5 (7.5)	5.4 (6.4)	3.8 (5.0)	0.621		
	Palliative care (N = 23)	11.4 (19.3)	6.1 (8.9)	6.9 (16.5)	5.7 (15.4)	6.4 (17.7)	0.490		
	Control (N = 21)	10.8 (10.9)	10.1 (15.7)	5.2 (6.8)	10.9 (14.3)	7.3 (9.6)	0.566		
p-value[d] for Group Difference	0.385	0.535	0.529	0.217	0.486				
		Initial Visit	0 week[b]	2 weeks[b]	4 weeks[b]	8 weeks[b]	Group Difference[e]	Time Course[e]	Interaction[e]
During Mastication	Physical medicine (N = 25)	47.7 (25.2)	47.0 (21.4)	34.9 (18.8)	29.7 (18.8)	26.2 (19.5)			
	Palliative care (N = 23)	55.8 (25.8)	40.7 (28.9)	32.8 (25.6)	26.2 (24.1)	24.6 (25.7)	0.849	< 0.001	0.286
	Control (N = 21)	59.0 (24.0)	44.3 (30.0)	30.5 (25.3)	34.0 (25.2)	29.0 (25.5)			

[a] Mean (standard deviation).
[b] Follow-up time points after starting treatments.
[c] p-values for the main effect of time course in each treatment group were calculated by Kruskal-Wallis tests.
[d] p-values for the main effects of group differences in each observation time point were calculated by Kruskal-Wallis ANOVA tests.
[e] p-values for the main effects and interaction were calculated by two-way repeated-measures ANOVA tests.

published longer-term follow-up case series studies on ADDwor subjects (Yatani *et al.*, 1997; Kurita *et al.*, 1998). Specifically, Kurita *et al.* (1998) showed that time alone is a powerful treatment modality for the management of ADDwor subjects. Kurita and his colleagues reported that 42.5% of the ADDwor subjects became asymptomatic and 32.5% had improved spontaneously without treatment after 2.5 years. In the other comparable RCT-based study on ADDwor subjects (Lundh *et al.*, 1992), these investigators compared the effects of a stabilization occlusal appliance against a no-treatment group of subjects with ADDwor. Unfortunately, this study used only a VAS-pain score as the outcome measure and did not provide a physical examination of the cases in the follow-up. In full agreement with our data, they reported no significant differences between the groups at follow-up. Overall, these studies establish the magnitude of the regression-to-the-mean trend for subjects with a new diagnosis of ADDwor. Such information is extremely valuable, since it sets the standard that other therapeutic interventions will have to surpass to show efficacy. The next challenge to researchers is to assess non-surgical therapy vs. closed-joint surgical manipulation interventions in a larger sample size.

In summary, consecutive ADDwor subjects in our TMD clinic were randomly allocated to the three experimental treatment groups, including "no treatment". All groups showed a significant change (improvement) in their signs and symptoms with time. However, there were no significant differences among the three experimental groups during the two-month period. Analysis of these data suggests that the gradual reduction of signs and symptoms of ADDwor was non-specific and was related not to the type of treatment, but more to the passage of time.

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