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Approaching Temporomandibular Disorders From a New Direction: A Randomized Controlled Clinical Trial of the TMDes™ Ear System

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ABSTRACT: TMDes (Registered Trademark of Ascentia Health, Inc., Rockford, Illinois), custom-fit ear inserts to aid in reducing temporomandibular disorder (TMD) pain, were evaluated in a prospective, three-month, open-label, three-arm, randomized, unblinded clinical trial, which included patients with TMD diagnoses (RDC/TMD) of myofascial pain, arthralgia, and/or disc displacement with reduction; and a screening VAS pain score of >4. The three treatment groups included: TMDes (n=60), stabilization splint (n=64), and jaw exercise regimen (n=28). The mean change in Craniomandibular Index (CMI) scores (reductions reflecting improvement) from baseline to one month were -27% (TMDes), -20% (stabilization splint), -12% (jaw exercise regimen), and from baseline to three months were -45%, -41%, -36%, reflecting statistically significant noninferiority (p=0.0096) of the TMDes to the stabilization splint (primary efficacy endpoint). The TMDes produced significant (p<0.0001) mean changes in VAS pain scores from baseline of -46% at one month and -58% at three months and demonstrated comparable efficacy and safety to the stabilization splint. (Registered at *ClinicalTrials.gov*: NCT00815776).

Dr. Alejandro Tsuchiya Tavera *received his D.D.S. degree from the School of Dentistry of the UNAM (National Autonomous University of México) in 1988, and his orthodontic degree from the Centro de Estudios e Investigacion en Ortodoncia (CEIO). He was an assistant professor of prosthodontics at the ULA Universidad Latinoamericana, and the UNAM (National Autonomous University of México), and since 2004, he has conducted clinical research at the Mexican Institute for Clinical Research (IMIC) on the study and treatment of temporomandibular joint disorders.*

Temporomandibular disorders (TMD) encompass "a group of disorders characterized by: pain in the periauricular area, in the temporomandibular joint (TMJ) or in the muscles of mastication; deviations or restriction in mandibular range of motion and TMJ noises (sounds) during mandibular function."[1] Signs and symptoms of TMD have been reported to occur at rates of 40 to 75% of the general population, primarily in women.[1-3] Pain, particularly in the masticatory musculature and/or the TMJ, is the most commonly reported symptom.[4-5]

It is widely recommended that initial therapy for TMD generally be conservative, noninvasive, and reversible.[4] Among the options currently available, the most widely used treatment is the intraoral stabilization splint.[4]

A novel, noninvasive and reversible alternative has recently been introduced that approaches the treatment of TMD using a device worn in the external auditory canal. The TMDes (Ascentia Health, Inc., Rockford, IL) is comprised of a pair of small, hollow, inconspicuous ear inserts that are custom-fit to each subject's ear canals (**Figure 1**). They are constructed from rigid, medical grade plastics that have been used in hearing devices for decades. The device is designed to rest in the outer third of the ear canal and has a small retraction post to

facilitate removal. It is designed to conform to the shape of the ear canal when the jaw is in an unoccluded position.
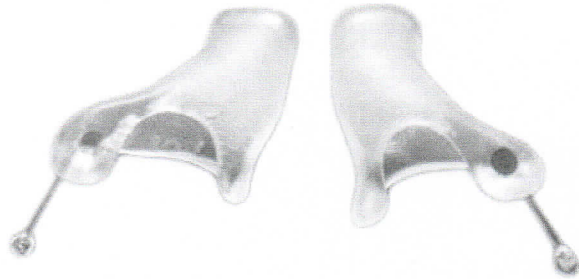

Figure 1
Photo of the patented TMD*es* device, which recently received clearance from the FDA as an aid in reducing temporomandibular disorder (TMD) pain.

A pilot study was conducted at the University of Pennsylvania School of Dental Medicine to clinically evaluate the TMD*es* during a 12-week treatment period following a 4-week pretreatment observation, providing evidence that treatment with the TMDes led to an overall reduction of the pain and dysfunction of temporomandibular disorders.[6] The pilot study incorporated the same assessment instruments as the current trial and was used to power it.

In the current study, the safety and effectiveness of the TMD*es* were evaluated, in comparison with the stabilization splint and a jaw exercise regimen, in a prospective, three-month, open-label, three-arm, randomized, unblinded clinical trial, which included patients with TMD diagnoses (RDC/TMD) of myofascial pain, arthralgia, and/or disc displacement with reduction; and a screening VAS pain score of >4.

Materials and Methods

The current study was carried out at the Mexican Institute for Clinical Research (IMIC) after being evaluated and approved by both the Clinical Investigation Bioethics Committee and the Ministry of Health, and all subjects gave written, informed consent to participate.

The study was conducted under ICH GCP principles with the ethical principles that have their origin in the Declaration of Helsinki.

Inclusion/Exclusion Criteria

Subjects were required to meet all of the following criteria to be eligible for study participation: presented to the study site for jaw pain or dysfunction; completed informed consent process; had an RDC/TMD diagnosis that included at least one of the following: myofascial pain, arthralgia, disc displacement with reduction; had the presence of one or more of the following findings associated with pain as demonstrated with a VAS score of >4: increased (>60 mm) or decreased (<40 mm) range of interincisal jaw opening, pain upon any jaw movement, pain on digital palpation (~1 lb. pressure) of the periauricular area or external auditory meatal areas, pain on digital palpation (~1 lb. pressure) in two or more muscles of mastication, or joint sound with pain.

A subject meeting any of the following criteria was excluded from further participation in the study (some criteria were unable to be assessed until the mouth or ear impressions were taken or until an attempt was made to fit the study device): a diagnosis of rheumatoid arthritis, osteoarthritis, osteoarthrosis or another connective tissue disorder; a history of direct trauma to the jaw; use of an occlusal appliance to treat a TMD within the previous six months; prior TMJ or ear surgery; physical or behavioral disorder, which, in the opinion of the principal investigator, would interfere with the use of the device or compliance with the study protocol; unsuitable ear canal anatomy (e.g., congenital deformity) not allowing for fit of the study device; use of a narcotic pain medication in the last seven days, or aspirin or a nonsteroidal anti-inflammatory agent in the last 24 hours; a history of ear pain unrelated to TMJ; a history of ear drainage in the past two years; active ear drainage, swelling, or redness as observed on targeted physical exam; not an appropriate candidate for an intraoral splint due to missing or poor quality dentition or untreated pain of dental origin.

Assessment Instruments

Subject responses to the standardized Research Diagnostic Criteria (RDC) were evaluated according to scoring guidelines and used to diagnose and classify types of TMD among all potential study subjects. The diagnostic categories included muscle disorders (myofascial pain), arthralgia, and disc displacement with reduction. The formal assessment tool is known as the RDC/TMD, which is the most widely used diagnostic system for TMD research.[7] It is an empirically-based and operationalized system for diagnosing and classifying

RDC/TMD using a biopsychosocial model of disease as a framework.

Patients in the study were evaluated with several TMD assessment instruments, including: the Craniomandibular Index (CMI) to assess severity of TMD signs and symptoms (performed to Research Diagnostic Criteria for Temporomandibular Disorders, RDC/TMD, as described by Dworkin and LeResche)[8]; the Visual Analog Scale (VAS) to measure subject perceived pain; the modified Symptom Severity Index Questionnaire (SSI) to evaluate the degree to which subjects perceive their TMD to be a problem; and The TMJ Scale (Pain Resource Center, Hillsborough, NC) a standardized self-administered symptom inventory completed by the subject to assist in making diagnostic decisions by confirming clinical findings.

Patient Enrollment and Randomization

Subjects were recruited through advertising by the study site and were evaluated for jaw pain and dysfunction. Those diagnosed with TMD according to the criteria previously described, and who provided signed informed consent, entered the screening phase of the study. Subjects who met study inclusion criteria and did not meet study exclusion criteria were randomly assigned into one of three treatment groups: the TMDes group, the stabilization splint group, or the jaw exercise regimen group. Midway through a 4-week screening period prior to the baseline visit, subjects randomized to the TMDes or stabilization splint groups had either ear or mouth impressions taken, and the fit of the devices was assessed at the baseline visit. At baseline, and again at the 1-, 2-, and 3-month visits, subjects were assessed with the CMI, VAS, and SSI instruments. The TMJ Scale was administered at the baseline and 3-month visits.

Treatments

Subjects in the TMDes group were instructed to wear the device (previously described) as much as was tolerable, both day and night. Subjects assigned to the stabilization splint group were instructed to wear their splints every night. The stabilization splint was an intraoral flat-planed splint full coverage plastic (hard) orthotic that fits over the occlusal one-third surfaces of the dentition, similar to the stabilization appliances as described by Okeson.[5] Subjects in the jaw exercise regimen group were instructed to open their jaw as far as possible without pain and hold the jaw in that position for five seconds. Subjects would then close their jaw and rest 10 seconds. The exercise would be repeated exactly 10 times in a row, with a 10-second rest in between each stretch. Subjects were advised to apply a warm compress to the jaw area after completing their exercises for 10 minutes. (This is an exercise program supported by the American Dental Association as a standard of care treatment for TMD.) Subjects in each of the three groups were instructed to keep a daily diary to track the number of hours the device was worn (TMDes and stabilization splint groups) or the number of exercise repetitions completed.

Statistics

All statistical analyses were completed using SAS Version 9.1.3 (SAS Institute Inc., Cary, NC). The null hypothesis for primary effectiveness was that the TMDes resulted in a reduction in CMI score of less than 80% of the reduction in the score with the stabilization splint. The statistic used to test the null hypothesis of inferiority[9] was compared to the Student's t-test distribution with 2n-2 degrees of freedom, at a significance level of $\alpha = 0.05$.

Results

Study Population

A total of 152 subjects were enrolled between May and September 2008. The overall disposition of subjects is summarized in **Figure 2**.

Baseline demographics and clinical characteristics of the study subjects in each of the three treatment groups are provided in **Table 1**. The average age of the subjects ranged from 36 to 38 years, and all were of Hispanic/Latino ethnicity. There were no statistically significant differences in demographic or clinical characteristics between the three groups.

The TMD history of subjects is detailed in **Table 2**. Subjects could be categorized into one or more of three diagnostic groups, including RDC/TMD Type I (muscle disorders/myofascial pain), RDC/TMD Type II-a (disc displacements with reduction), and RDC/TMD Type III-a (arthralgia). The majority of subjects in each treatment group were diagnosed as being RDC/TMD Type I, myofascial pain (97-100%), followed by Type III-a, arthralgia (55-61%), and Type II-a, disc displacement with reduction (45-48%). There was a similar distribution of diagnoses among the three groups.

Device Usage and Exercise Compliance by Study Subjects

Subjects in the TMDes group averaged 17.6 hr/day, 19.7 hr/day and 20.6 hr/day of device wear during the first, second and third months of the study, while those in the stabilization splint group averaged 7.3 hr/day, 7.8 hr/day and 8.4 hr/day of device wear for the corresponding months. Those subjects in the jaw exercise regimen group performed an average of 7.0, 6.6 and 7.0 exercise repetitions in the first, second and third months.
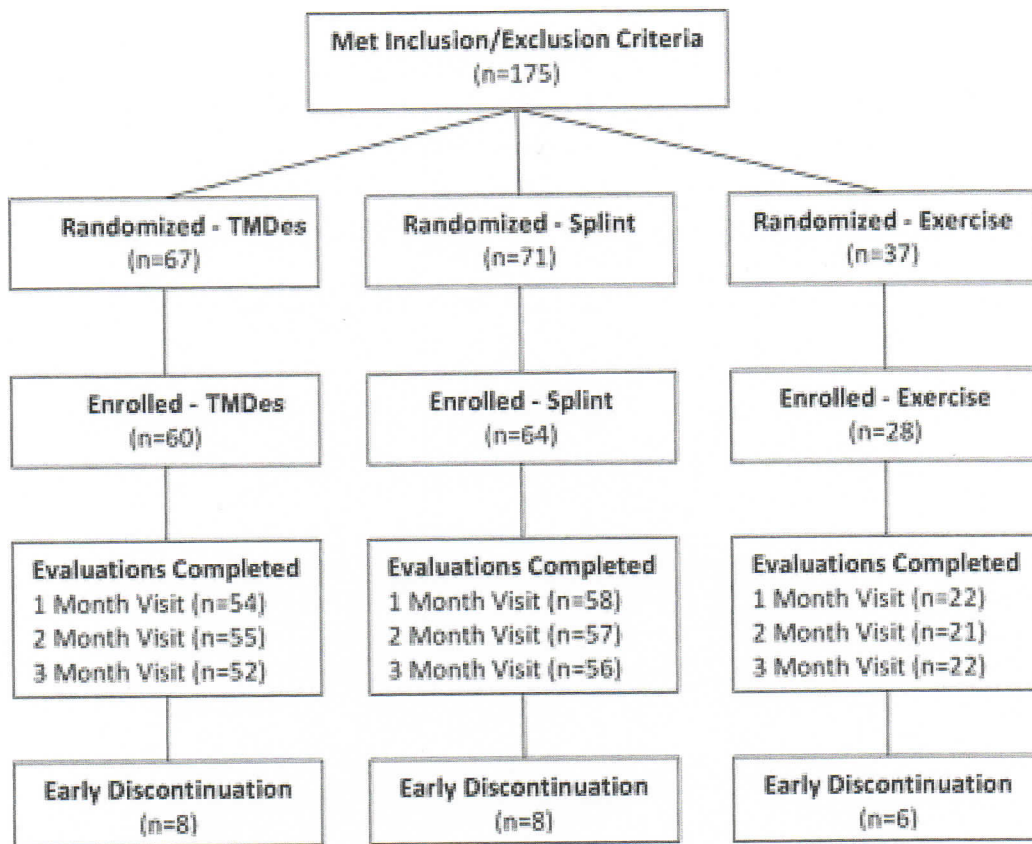
Figure 2
A total of 152 subjects were enrolled between May and September 2008. The overall disposition of subjects is summarized in the above graphic.

Craniomandibular Index (CMI)

All three treatment groups displayed reductions (i.e., improvement) in mean CMI scores from baseline to the follow-up visits at one, two and three months. The reduction was greatest for the TMD*es* group; however, the differences between treatment groups did not rise to the level of statistical significance. **Figure 3** presents the mean percentage CMI changes from baseline to one and three months.

The TMD*es* demonstrated statistically significant noninferiority (p=0.0096) to the stabilization splint, based on the change in CMI score from baseline to three months (primary efficacy endpoint). The pain reduction ratio of TMD*es* to splint, as assessed by the CMI, was 1.16.

Visual Analogue Scale for Pain (VAS)

The TMD*es* demonstrated a statistically significant reduction in pain, as assessed by the VAS, from baseline to one, two, and three months (**Figure 4**).

All three treatment groups displayed reductions, indicating improvement, in mean VAS scores from baseline to the follow-up visits at one, two and three months. The reduction was greatest for the TMD*es* group; however, the differences between treatment groups did not rise to the level of statistical significance. **Figure 5** presents the mean percentage VAS changes from baseline to one and three months.

A jitter plot of absolute change in VAS scores from baseline to three months for individual subjects suggests a greater magnitude of pain reduction among responders in the TMD*es* group (**Figure 6**).

The TMD*es* also demonstrated statistically significant noninferiority (p<0.0001) to the stabilization splint based on the change in VAS score from baseline to three months, with a pain reduction ratio of TMD*es* to splint of 1.56.

Table 1

Baseline Demographics and Clinical Characteristics of the Study Subjects

	Treatment Group		
	TMD*es*	Splint	Exercise
Age (yrs.)	37.3±10.6	38.0±11.0	36.3±13.0
Number	(60)	(64)	(28)
Gender	%	%	%
Male	20.0	17.2	10.7
Female	80.0	82.8	89.3
Weight (lb)	149±27	153±33	142±28
BMI (kg/m²)	26.8±4.5	26.8±5.2	25.9±5.0
Medical history	%	%	%
Cancer	1.7	0	0
Diabetes	0	6.3	3.6
Sleep disorders	11.7	15.6	17.9
Neurological disorders	0	1.6	0
Depression	6.7	15.6	7.1
Anxiety	10.0	7.8	7.1

Numbers are mean ± SD (N) for continuous measures, and percent (count/N) for categorical measures.

Modified Symptom Severity Index (SSI)

All three treatment groups displayed reductions, reflecting improvement, in mean SSI scores from baseline to the follow-up visits at one, two and three months. The reduction again was greatest for the TMD*es* group; however, the differences between treatment groups did not rise to the level of statistical significance. **Figure 7** presents the mean percentage SSI changes from baseline to one and three months.

The TMD*es* demonstrated statistically significant non-inferiority ($p<0.0001$) to the stabilization splint based on the change in SSI score from baseline to three months, with a pain reduction ratio of TMD*es* to splint of 1.70.

TMJ Scale

Improvement from baseline to three months was observed in all three treatment groups for all TMJ Scale categories, though the differences between study groups were not statistically significant.

Patient Global Satisfaction

A high level of patient satisfaction was observed, with 100% of subjects in TMD*es* group indicating excellent (71%) or good (29%) overall satisfaction with the device, while 96% of subjects in the stabilization splint group indicated excellent (62%) or good (34%) overall satisfaction.

Safety

There were no unanticipated adverse device effects or serious adverse events reported during the study. No study patients were found to have ear drainage, allergic reactions, swelling or changes to the mouth, ear or jaw at any of the follow-up visits. There were no reports of diminished hearing acuity in patients treated with the TMD*es*. **Table 3** lists the treatment-related adverse events observed among the three groups.

The most frequently reported treatment-related adverse event in all three groups was discomfort or pain. The TMD*es* group, stabilization splint group, and exercise group had incidence rates of discomfort or pain of 6.7%, 9.4% and 7.1%, respectively. The second most frequently reported treatment-related adverse event was headache, which was reported in 5.0% of TMD*es* subjects, 4.7% of stabilization splint group subjects and 3.6% of exercise group subjects. The TMD*es* was shown to have a safety profile that was not statistically significantly different from the stabilization splint ($p=0.688$).

Discussion

An ever-expanding consensus recommends that conservative measures be pursued as initial therapy for TMD. The National Institute of Dental and Craniofacial Research (NIDCR)[4] noted that "experts strongly recom-

Table 2
TMD History of Subjects

	Treatment Group		
	TMD*es* (n=60) %	Splint (n=64) %	Exercise (n=28) %
Jaw disorder history			
Pain in face/jaw/temple/ear within 1 mo.	96.7	100.0	100.0
Jaw locking or catching	60.0	60.9	60.7
If yes, jaw locking interfered with eating	50.0	56.4	47.1
Systemic arthritic disease	1.7	0	0
Family history of jaw disorders	23.3	10.9	10.7
Other swollen or painful joints	18.3	18.8	21.4
If yes, pain in other joints for $\geq$ 1 yr.	81.8	66.7	50.0
Recent injury to face or jaw	0	1.6	0
If yes, jaw pain before injury	0	100.0	0
RDC/TMD diagnosis			
I: Myofascial pain	96.7	100.0	100.0
II-a: Disc displacement with reduction	45.0	48.4	46.4
III-a: Arthralgia	55.0	54.7	60.7
Multiple relevant RDC/TMD diagnoses			
I only	38.3	42.2	39.3
II-a only	3.3	0	0
III-a only	0	0	0
I and II-a	3.3	3.1	0
I and III-a	16.7	9.4	14.3
II-a and III-a	0	0	0
I, II-a, and III-a	38.3	45.3	46.4

mend using the most conservative, reversible treatments possible" for treating TMD. A recent review in the New England Journal of Medicine[3] noted that approximately 85-90% of TMD can be treated with noninvasive, non-surgical and reversible interventions. The 2010 revision to the American Association of Dental Research's science information statement on TMD similarly noted that, "it is strongly recommended that, unless there are specific and justifiable indications to the contrary, treatment of TMD patients initially should be based on the use of conservative, reversible and evidence-based therapeutic modalities."[10] Such conservative approaches have included physical therapy, behavioral therapy, medication therapy and intraoral splint therapy.[11,12] Studies reviewing each of these treatment modalities have shown some degree of efficacy for each,[12-15] though there appears to be a consensus that more research is needed to better characterize their individual effectiveness. The most widely used current treatment option is intraoral stabilization splints.[4] Potential patient compliance issues with

stabilization splints, however, may include aesthetics, comfort, and interference with speech and eating, which may limit their use in some patients to nighttime wear only. There have also been reports of clinically significant, irreversible occlusal alterations in association with the use of stabilization splints.[16]

The recently introduced TMD*es* device evaluated in this clinical study provides an alternative noninvasive and reversible option that involves approaching the treatment of TMD from a new direction (literally), with the device worn in the patients' external auditory canals. Though it may not be widely appreciated outside the community of TMD specialists, the ear canal is in immediate anatomical proximity to the temporomandibular joint (TMJ). The position of the condyle and disc within the TMJ, relative to the ear canal, differs depending on whether the jaw is in an opened or closed position. Olveira[17] demonstrated using MRI that the configuration of the ear canal is slightly altered when the jaw is in a closed versus open position. As a result, the TMD*es*
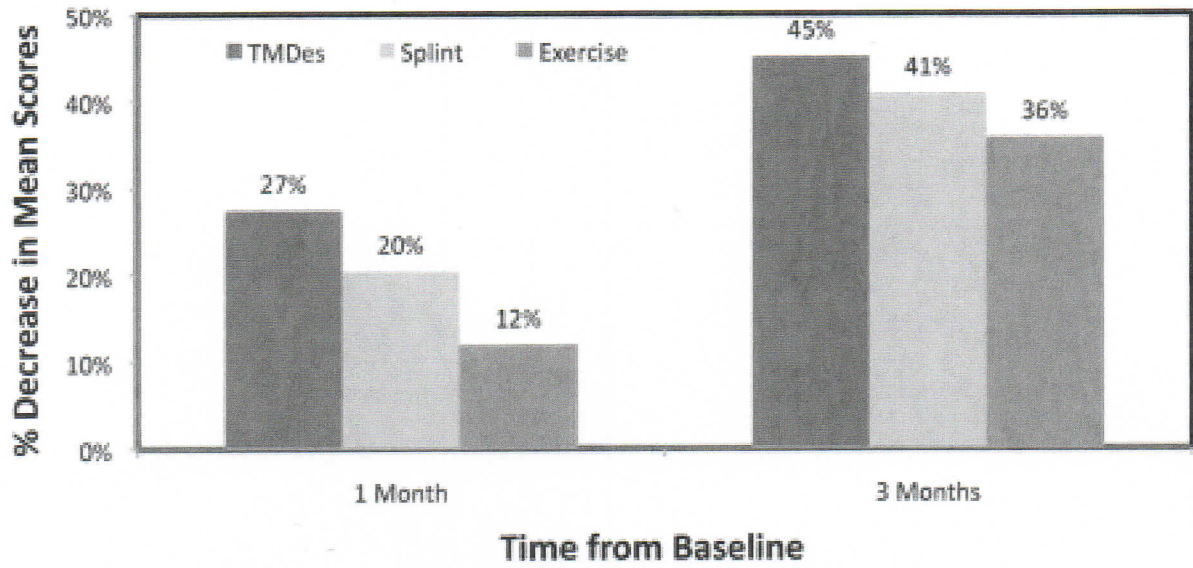
Figure 3
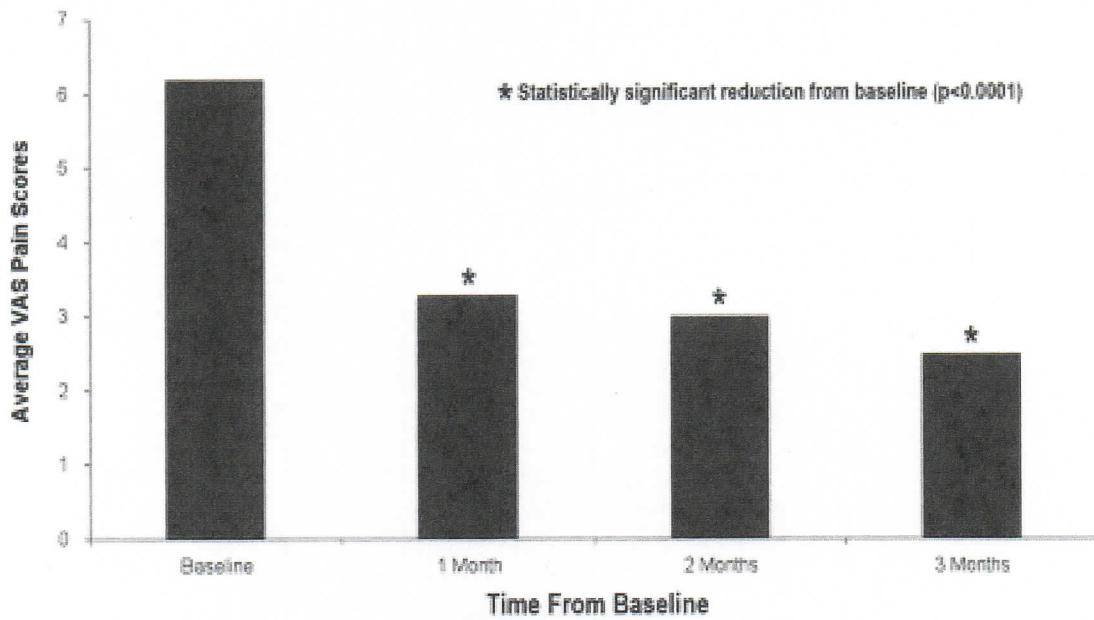Graph presents the mean percentage CMI changes from baseline to one and three months.

Figure 4
Graph presenting that TMD*es* demonstrated a statistically significant reduction in pain, as assessed by the VAS, from baseline to one, two and three months.
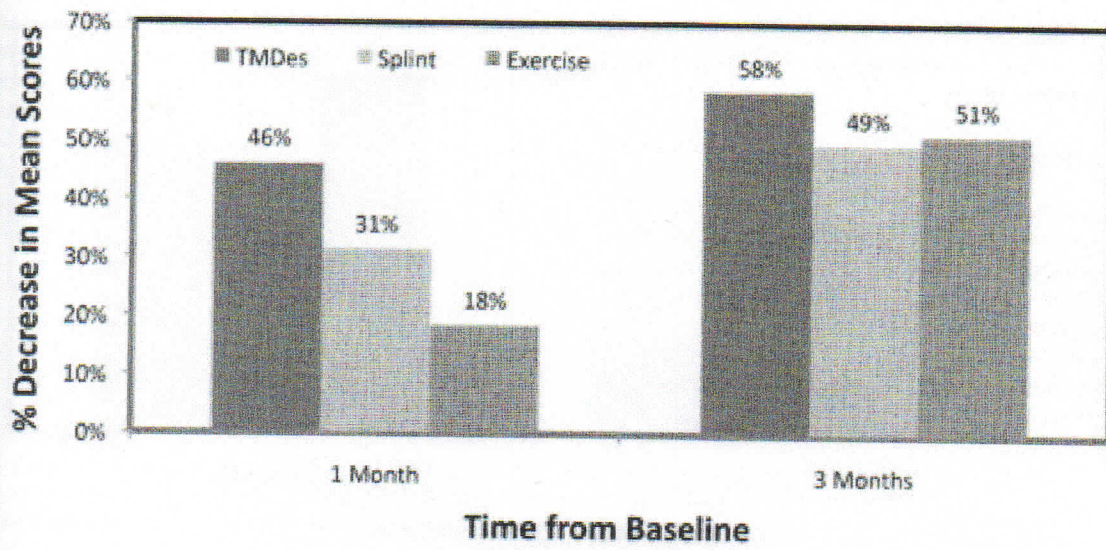
Figure 5
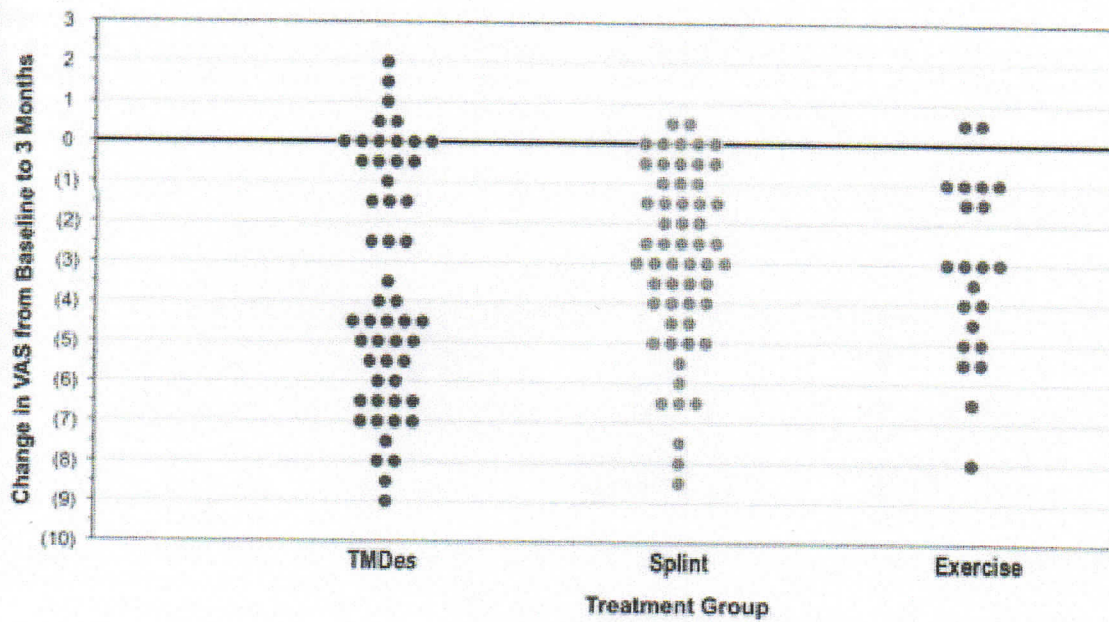Graph presents the mean percentage VAS changes from baseline to one and three months.

Figure 6
Jitter plot graph of absolute change in VAS scores from baseline to three months for individual subjects, suggesting a greater magnitude of pain reduction among respondents in the TMDes group.
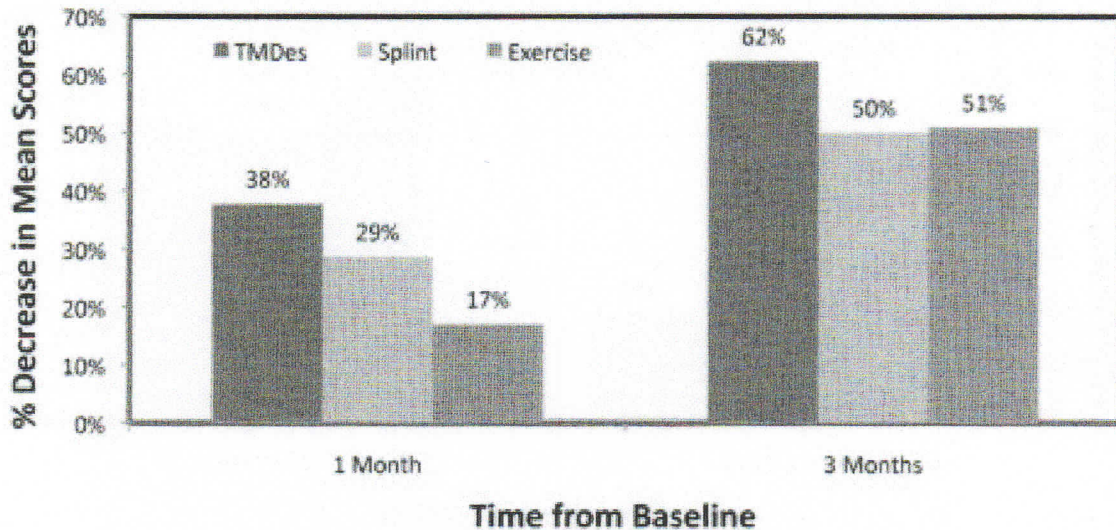
Figure 7
Graph presents the mean percentage SSI changes from baseline to one and three months.

represents a more *near-field* approach in addressing issues related to the temporomandibular joint, as compared to the more *far-field* approach of flat-plane occlusal stabilization splints.

In the current prospective, randomized clinical trial, the safety and effectiveness of the TMD*es* was demonstrated to be comparable (i.e., statistically significantly noninferior) to that of the stabilization splint in a well-characterized population of TMD patients. The majority of patients in this clinical trial presented with more than one diagnosis, consistent with findings of a recently published study of prevalence of clinical diagnostic groups in patients with TMD.[1]

The jaw exercise regimen, though demonstrating a consistent trend toward a lower percentage of improvement for essentially all of the assessment instruments

Table 3
Treatment-Related Adverse Events Observed Among the Three Groups

	Treatment Group		
	TMD*es* (N=60)	Stabilization Splint (N=64)	Exercise regimen (N=28)
Discomfort or pain	6.7% (4/60)	9.4% (6/64)	7.1% (2/28)
Increased TMD symptoms	1.7% (1/60)	0% (0/64)	0% (0/28)
Diminished hearing acuity	0% (0/60)	1.6% (1/64)	0% (0/28)
Headache	5.0% (3/60)	4.7% (3/64)	3.6% (1/28)
Dizziness or nausea	1.7% (1/60)	3.1% (2/64)	3.6% (1/28)
Other	3.3% (2/60)	3.1% (2/64)	0% (0/28)

"Other" events in the TMD*es* group include a single report each of "sensation in the ear" (starting on day 8, lasting 11 days) and "ringing in both ears" (starting and ending on day 4); and in the stabilization splint group, a single report each of "musculature contracture" (starting on day 47, lasting 33 days) and "inflammation of the gums" (starting on day 33, lasting 1 day).

employed (particularly from baseline to one month), was not found to be statistically significantly inferior to either the stabilization splint or TMD*es* treatment. Although larger sample sizes may have been capable of demonstrating such a significant difference, as is the case for a range of medical conditions, the existence of effective exercise regimens does not obviate the need for effective alternative surgical, pharmaceutical or device interventions. Adherence to exercise regimens in the general population is often of quite limited duration.

Study Limitations

The current study was a prospective, three-month, open-label, three-arm, randomized, but unblinded clinical trial. Blinding was not an option for this study design, as subjects either wore the TMD*es* device, a stabilization splint, or performed jaw exercises. Although a blinded study design for a pharmaceutical product may include a sugar pill or an active ingredient pill that for all other purposes appears the same to the subject or the blinded investigator, for this study the three possible treatments of TMD*es*, stabilization splint, or jaw exercises included different device-fitting procedures, completely different (and quickly identifiable) treatments, different subject instructions, and risk profiles that prevented blinding from being utilized as a study control in the present study.

Ear canal or oral impressions had to be taken by trained investigators for the TMD*es* or stabilization splint, respectively. Each of the three investigators was trained on the processes of making ear impressions and mouth impressions, in order to maintain consistent quality control. These same three investigators performed device-fitting procedures and later assessed subjects for treatment-specific adverse events based on their specific group assignment (TMD*es*, stabilization splint, or jaw exercises). Follow-up schedules and procedures were not identical for all three randomization options. For example, subjects assigned to either the TMD*es* or stabilization splint had device-specific impressions taken approximately two weeks after screening, whereas subjects assigned to jaw exercises did not have a "device-fitting" visit. Questionnaires included treatment-specific data collection, including "number of hours device was worn per day" for both the TMD*es* and the stabilization splint, whereas the exercise group documented the number of exercises completed each day.

Conclusion

The TMD*es*, an inconspicuous device worn in the external auditory canals, provides a novel, noninvasive, nonsurgical and reversible treatment for TMD. Subjects treated with the TMD*es* device experienced significantly reduced TMD pain. This prospective, randomized clinical trial demonstrated comparable efficacy and safety for the TMD*es* and the stabilization splint, the most widely used current treatment for TMD.

References

1. Machado LP, Nery CdeG, Leles CR, Nery MB, Okeson JP: The prevalence of clinical diagnostic groups in patients with temporomandibular disorders. *J Craniomandib Pract* 2009; 27(3):194-199.
2. Dworkin SF, Huggins KH, LeResche L, Von Korff M, Howard J, Truelove E, Sommers E: Epidemiology of signs and symptoms in temporomandibular disorders: clinical signs in cases and controls. *J Am Dent Assoc* 1990; 120:273-281.
3. Scrivani SJ, Keith DA, Kaban LB: Temporomandibular disorders. *N Engl J Med* 2008; 359(25):2693-2705.
4. National Institute of Dental and Craniofacial Research (NIDCR): *TMJ Disorders. NIH Publication No. 06-3487*. Bethesda: National Institutes of Health, 2006.
5. Okeson JP: *Management of temporomandibular disorders and occlusion*, 6th ed. St. Louis: Mosby, 2008.
6. Sollecito TP, Clayton LG, DeRossi SS, Laster L, Greenberg MS: The Clayton intraaural device for temporomandibular disorders. *Oral Surg Oral Med Oral Pathol* 2004; 97(4):455.
7. Janal MN, Raphael KG, Nayak S, Klausner J: Prevalence of myofascial temporomandibular disorder in US community women. *J Oral Rehabil* 2008; 35:801-809.
8. Dworkin SF, LeResche L: Research diagnostic criteria for temporomandibular disorders: Review, criteria, examinations and specifications, critique. *J Craniomandib Disord* 1992; 6(4):301-355.
9. Laster LL, Johnson MF: Non-inferiority trials: The 'at least as good as' criterion. *Statistics in Medicine* 2003; 22:187-200.
10. Greene CS, Klasser GD, Epstein JB: Revision of the American Association of Dental Research's science information statement about temporomandibular disorders. *J Can Dent Assoc* 2010; 76:a115.
11. Fricton JR, Schiffman EL: The craniomandibular index validity. *J Prosthet Dent* 1987; 58:222-228.
12. Hanian P, Sollecito TP, Silverton SF, Greenberg MS: Outcome of treatment of moderate myofascial pain: a gender specific retrospective study. *Oral Surg Oral Med Oral Pathol Endod* 1998; 85(4):418.-419.
13. Bell WE: *Temporomandibular disorders classification, diagnosis and management*. Chicago: YearBook Medical, 1989.
14. Fricton JR, Dubner R: *Orofacial pain and temporomandibular disorders: advances in pain research and therapy*, Volume 21. New York: Raven Press,1995.
15. List T, Dworkin SF: Comparing TMD Diagnoses and clinical findings at Swedish and US TMD centers using research diagnostic criteria for temporomandibular disorders. *J Orofac Pain* 1996; 10(3):240-253.
16. Magdaleno F, Ginestal: Side effects of stabilization occlusal splints: A report of three cases and literature review. *J Craniomandib Pract* 2010; 28(2):128-135.
17. Oliveira RJ: The active earcanal. *J Am Acad Audiol* 1997; 8(6):401-410.

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