Real World Data with DNA Appliance using Maxillary Expansion to Treat Obstructive Sleep Apnea

Introduction:

Study Rationale

When conducting maxillary expansion for other indications, several dentists noticed their patients also noticed significant improvements in snoring, sleep apnea, and other symptoms of sleep-disordered breathing. It is believed that treatment increases the pharyngeal space, allowing for better airflow and reduced snoring.

The origin of this study was a request by the Food and Drug Administration for additional real world data using the DNA appliance with maxillary expansion as the mechanism of action to treat obstructive sleep apnea. Upon receiving that request, the sponsor searched its data base, which is set up to allow dentists to report outcomes of all of their cases using Vivos appliances. The database was initiated in 2018.

Inclusion/Exclusion Criteria

1) Adults (18 years or older)

2) Diagnosis of OSA (AHI $\geq$ 5)

In addition, the database was filtered using the following criteria:

1) Treatment with DNA appliance

2) Must have beginning CBCT score and ending CBCT score if treatment is complete

3) Must have pre- and post-treatment AHI scores at least 5 months apart

4) Patients must be compliant with the treatment regime (i.e. wear the DNA appliance $\geq$ 10 hours per day)

Study Purpose

The purpose of this database is collect post-marketing data on a prospective basis. Doctors are allowed to update data throughout the treatment process. This study evaluates this real world data to examine the effect of an orthodontic device that expands the pharyngeal airway in reducing symptoms of obstructive sleep apnea and increase the pharyngeal airway and trans palatal width.

Each patient serves as their own control, with measurements taken before treatment and then following treatment.

Prevalence and Risk Factors

Obstructive sleep apnea (OSA) affects between 3-7% of adult men and 2-5% of adult women. Certainly populations are at significantly higher risk – for example, several studies found 14-49% of middle-aged men had clinically significant OSA. These disturbances have a negative impact on quality of life, and are linked with increased risk of diabetes, heart disease, and cancer. Obesity is one of the largest risk factors for OSA.

Cause of OSA

During sleep, the muscles in the tongue and back of the throat relax, which can cause them to sag and narrow the airway. Airflow through a narrow airway is the cause of snoring. When this narrowing of the airway is

severe, it results in Obstructive Sleep Apnea (OSA), where the airway actually closes. Upon closure, the brain detects the lack of oxygen and wakes the body to draw breath, disturbing sleep.

Maxillary Expansion as a Treatment for OSA

Palatal expansion with an orthodontic device has been shown to increase the pharyngeal space and increase the size of the airway. This would allow more air to pass through the airway and prevent the vibration of the airway that causes snoring or the closure of the airway and sleep apnea.

Methods

Device Function

The DNA appliance is a customized oral device featuring an upper tray and/or a lower tray, depending on patient need. See description in Device Design below.

Studies have shown that customized oral devices that function by increasing the patency of the airway show comparable efficacy to continuous positive airway pressure (CPAP) devices, considered the gold standard of treatment for OSA (*Oral appliance therapy in Obstructive Sleep Apnea-Hypopnea syndrome - A clinical study on therapeutic outcomes* Hoekema A PhD thesis, University Medical Centre Groningen Department of Oral and Maxillofacial Surgery. pp 110, 2007). On the basis of these studies, use of oral devices has been recommended by the American Academy of Sleep Medicine for patients with mild or moderate OSA, or for those with severe OSA who are unable to tolerate the CPAP device.

While CPAP therapy is effective, it faces several challenges. First, patient compliance with use of the device is low – one study found that almost half of patients discontinued use within the first 3 weeks after receiving the device. It can feel claustrophobic or difficult to sleep with the device attached for some patients. The underlying sleep apnea can continue to worsen, causing the pressure within the CPAP to have to rise, and contributing to dry mouth and mucosal tissues. Ultimately, while the CPAP therapy can address the symptoms of obstructive sleep apnea, it does not treat or resolve the underlying reason for sleep-disordered breathing.

Device Design

The DNA appliance consists of upper and lower customized trays. The DNA appliance is customized on models of the patient's teeth, using standard orthodontic acrylics and standard orthodontic wires for clasps and retention. The DNA appliance may be adjusted antero-posteriorly (AP), transversely (TV), as well as permitting adjustments of the vertical dimension of occlusion (VDO). At regular intervals (usually once a week, but at least once a month), the patient and/or dentist adjusts an expansion screw or loop to expand the appliance as prescribed by the dentist.

The device is used in the evenings and at night by patients. For this study, patients were required to wear the device at least 10 hours per day. Treatment usually lasts from 5 months to 36 months, as necessary.

Patient Informed Consent

Vivos provides a sample Informed Consent to all dentists using its DNA appliance. This informed consent describes the mRNA/DNA appliances and treatment regime, potential side effects and

complications of oral application therapy, potential orthodontic intervention to achieve the required cosmetic appearance, and alternative treatments.

Patient Instructions

Inserting the appliance. Place the upper plate of the DNA appliance in first. Press up with your thumbs to ensure that the plate is completely in place. It should fit securely and comfortably. Next fit the lower plate of the DNA appliance (if necessary). Press down with your index fingers to ensure that the plate is completely in place. It should fit securely and comfortably. Make sure to clean your teeth properly and floss before inserting.
Removing the appliance. In the morning, remove the DNA appliance by reversing the insertion procedure. Take the lower out first, lifting from both sides with your thumbs. Sometimes a "rocking" motion is helpful, lifting one side slightly and then the other, until it comes out. Then take the upper plate out, by pulling on both sides with your index fingers, using the same rocking motion.
Cleaning. Clean your DNA appliance daily after each use with soap and water (liquid soap is ideal), making sure to rinse the appliance well. While cleaning the DNA appliance, look for signs of damage or cracks. If the device appears damaged, discontinue use and immediately contact your dentist to arrange for repairs.
Storage. Your DNA appliance should be stored dry in the case provided.

Results

As of June 2021, seventy-four patients met the inclusion/exclusion and database filtering criteria.

Patient Characteristics

	Average	Range
Age	48	19-84
BMI	26.1	16.7-37.8
Length of Treatment	14 months	5-35 months

Gender Breakdown

Male	Female
31	43

Results of Expansion

Airway Volume

Airway Volume Pre-Treatment	Airway Volume Post-Treatment	Airway Change	Percent Increase	p-value
20786	23950	3345	15%	$p < 0.00001$

Transpalatal Width

Transpalatal Width Pre-Treatment	Transpalatal Width Post-Treatment	Transpalatal Width Change	Percent Increase	p-value
32.9	35.2	2.1	7.0%	$p < 0.00001$

Fifty-three of 61 patients with pre- and post-treatment scores showed improvement in airway volume (87%). (When patient treatment is completed final CBCT scores will be input for all patients.) The improvement in both transpalatal width and airway volume is statistically significant with a p level less than 0.00001.

Sleep Study Results

AHI Changes

AHI Pre-Treatment	AHI Post-Treatment	Percent Decrease	p-value
23.5	12.7	46%	$p < 0.00001$

Prior to treatment, 20 patients had severe OSA, which has improved (post-treatment) or is improving (mid-treatment) by 53%. Of these 20 patients, none worsened, while 3 patients still have severe OSA, 12 have moderate OSA, 4 have mild OSA and 1 has no OSA.

If the 18 patients that began the study with moderate OSA, the average percent improvement is 53%. One patient's AHI score worsened by 1 category (10.4), while another slightly increase by 2.1. The balance of the patients improved by 64%. After treatment or mid-treatment, 2 patients remained moderate, 10 have mild symptoms and 5 have resolved their OSA symptoms.

Thirty-six patients had mild symptoms pre-treatment. Of these, 1 now has severe symptoms, 4 have moderate symptoms, 16 still have mild symptoms and 15 have no OSA.

Number of Patients by OSA Classification

	Pre-treatment	Post-Treatment No OSA	Post-Treatment Mild	Post-Treatment Moderate	Post-Treatment Severe
Mild	36	15	16	4	1
Moderate	18	5	10	2	1
Severe	20	1	4	12	3

Eighty-one percent of the patients showed some improvement in AHI score, while 10% worsened and 9% showed no change (i.e. <4.6 increase is within variability for events/hour on AHI sleep testing, Anitua, E. et. al. "Predicting night-to-night variability in the severity of OSA, Sleep Science 2019). Sixty-five percent of these patients improved by at least 1 classification, for example from severe to moderate or moderate to mild. Finally 27% of these patients had their OSA symptoms completely resolve (AHI<5).

Safety Results

Dentists reported 4 patients (5%) with open bite, three caused by the appliance and 1 caused by tongue thrusting. All of the open bites caused by the DNA appliance were treated successfully with aligners and the patient was satisfied with the outcome. The Informed Consent discloses to the patients that secondary orthodontia may be required. One patient (1%) had mild gum regression either caused by medication or the device. No treatment was required. One patient suffered secondary traumatic occlusion, which the dentist believes will be completely resolved with post-treatment aligner therapy, which is just beginning. None of these complications have affected the patient's satisfaction with the outcome and none have caused serious health or dental issues.

It is concerning that 7 patients had more AHI episodes, although these measurements are taken without the device in the mouth (MAD measurements are usually taken with the device in the mouth). With the device in the mouth, the airway is held open and AHI numbers would be lower. There were also 7 patients that

rounded within the variability of the sleep test. Of the 7 patients that worsened, 3 of them were the 1st or 2nd patient treated and entered by a dentist so they may be part of a learning curve. Four other patients came from one dentist. All of these patients use the CPAP in addition to the DNA, but these readings were taken without the CPAP or the DNA. These patients will use the CPAP device, until they can make enough progress with the DNA device in expanding their airway. In Vivos experience, all patients will either improve or stay the same once the treatment is completed. If a dentist becomes concerned about the progress a patient is making or until they have made enough progress, the beauty of the DNA appliance is that we can add the fins that connect the trays making it into a mRNA appliance that has two mechanisms of action – MAD and expansion or use the DNA in conjunction with CPAP.

Conclusion

This real world data with a 46% decrease in AHI ($p<0.00001$) compares to a summary of all published data with a 52% decrease in AHI. This data is marred by a few patients from 1 dentist and the first patients reported by other dentists. This is a potential consequence of using real world data. If we exclude those patients (but leave in patients with AHI increases or no changes from experienced dentists, i.e. exclude training issues), the AHI is 54%. By treating the root cause of the problem instead of continuous positive air pressure or mandibular advancement, 27% of these patients had their symptoms completely resolved. These measurements are taken without the DNA appliance in the mouth (MAD measurements are taken with the appliance in place). It is possible or even probable that these changes may be sustained over time. A few patients with data out more than 5 years have shown that this is possible, but further studies must be done to confirm that these changes are permanent in a larger clinical trial. Expansion data confirms that the device does increase airway volume and transpalatal width ($p<0.00001$).