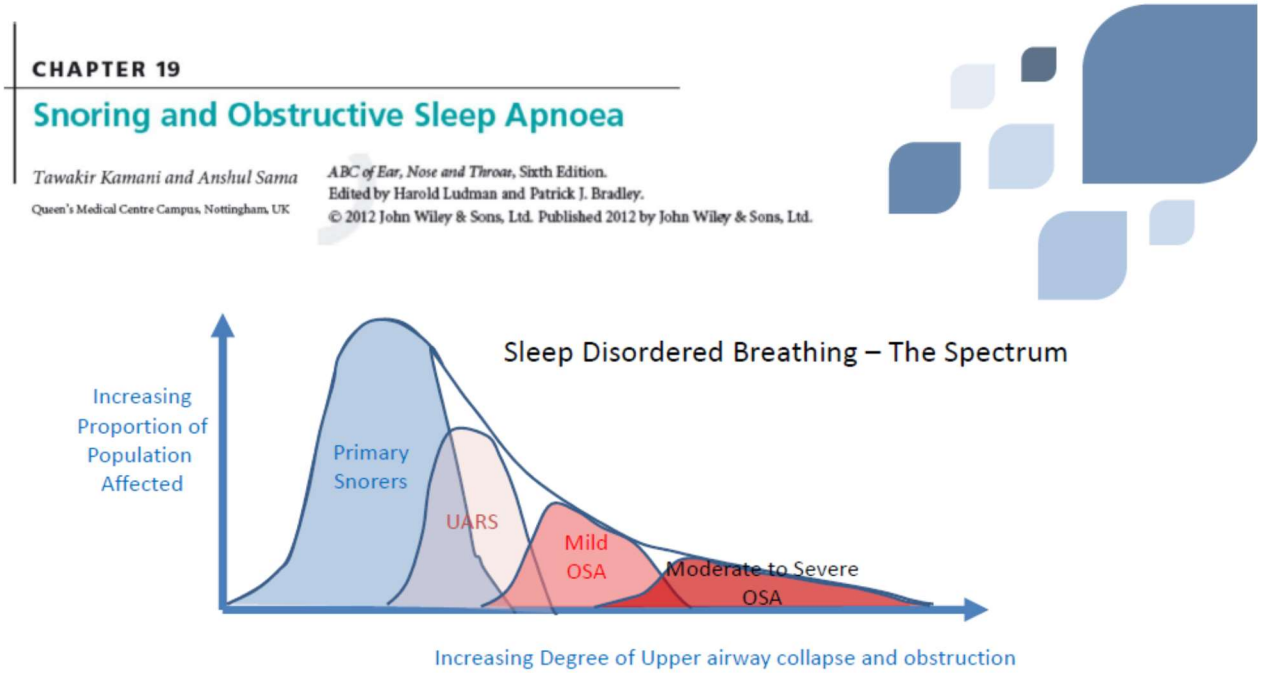
SnooZeal© White Paper

Intra-oral neuromuscular stimulation training for treatment of Snoring and Sleep Apnoea syndrome- A pilot study

Introduction

Forty five percent of the male population snore and 25% habitually (daily). Snoring is the cardinal symptom of a spectrum of Sleep-related breathing disorders (SRBD) ranging from Primary snoring at one end to Severe obstructive sleep apnoea-hypopnea syndrome (OSAHS) at the other (Fig1) [1]. The latter affects 4-6% of the population and is associated with increased incidence of hypertension, cardiac (heart attacks) and cerebral events (strokes). Although the gold standard of treatment for OSAHS is Continuous Positive Airway Pressure (CPAP), there is a significant issues with in-tolerance and compliance can range between 45 to 85% of patients due to need for continuous nocturnal use, logistics of mask fixation and high continuous pressures [2]. On the other hand, a variety of treatments are offered for simple snoring with very limited regulatory control and proven efficacy.



Although there are several lifestyle practices associated with snoring (smoking, obesity, drinking etc.), a significant proportion of individuals may snore despite not being associated with these.

The most notable change that occurs in the physiology of humans during sleep is the reduction in the tone of the muscles and increased collapsibility of the throat and tongue. Notably, there is evidence to show that the collapsibility is significantly higher in patients who obstruct (OSAHS) and marginally higher in patients who

snore (Primary snorers) when compared to individuals who don't snore (Fig 2) [3]. As demonstrated in the graph below, it has been shown that when compared to "normal" individuals, the breathing passage in snorers and sleep apnoea individuals collapses at a positive rather than negative airway pressure.

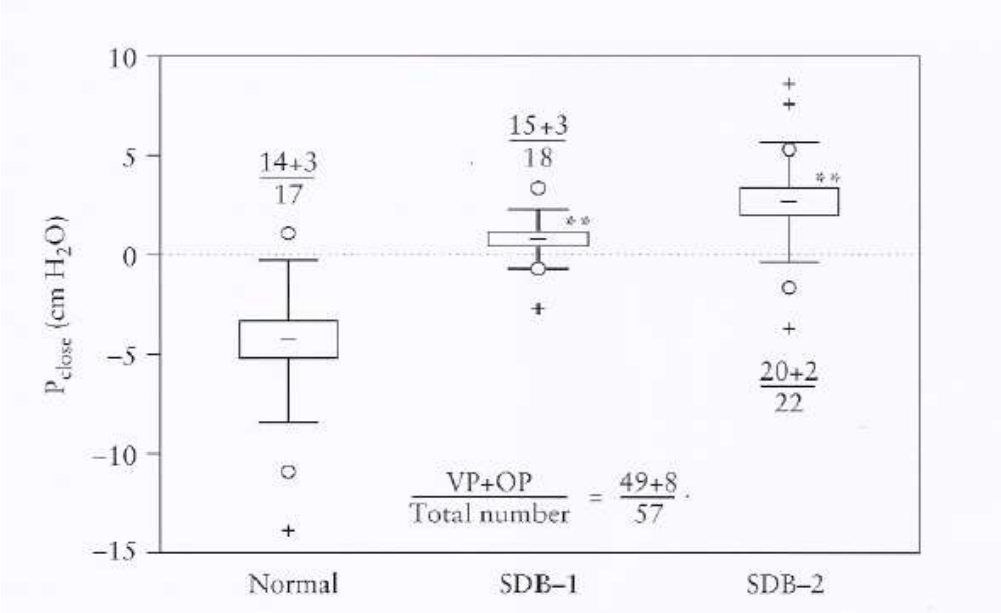


Figure 2: critical closing pressure in healthy subjects, snorers and patients with OSA (SDB-1 = snorers, SDB-2 = Sleep Apnoea), (according to Isono et al. [3])

Research has demonstrated that increasing the pharyngeal muscle activity or tone, reduces the collapsibility of the airway as demonstrated by the graphs below (figure 3). In essence, it is the reduction of throat/pharynx/tongue muscle tone that leads to this partial or complete obstruction associated with snoring and sleep apnoea syndrome [4].

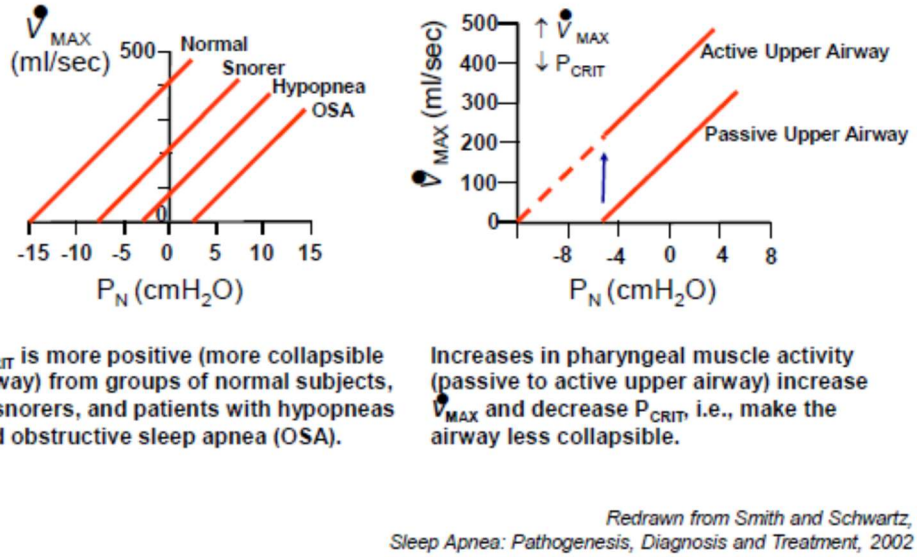


Figure 3: Upper airway collapsibility and critical closing pressure in sleeping individuals (according to Schwartz et al. [4])

Several studies have shown that implanting electrical nerve stimulators (for the tongue and limited numbers for diaphragm) are effective in treatment of OSA. However, this involves an operation and implantation of devices [5,6,7,8]. Furthermore, studies involving apnoea-triggered nocturnal stimulation reportedly disturbing the patient sleep by arousals due to the electrical stimulation [8]. Also, similar to implanted pacemakers, there are multiple maintenance and logistic complications (battery replacement, unable to be in electromagnetic fields, cannot have other external electrical circuits attached, detected by external detection devices like airport security etc. etc.).

There is a considerable body of knowledge, literature and evidence to state that use of transcutaneous electrical stimulation in paralysed or inactive limbs (muscles with low or absent muscle tone) significantly improves muscle power and tone recovery [9]. Considering the muscles of the throat, pharynx and tongue are of the same muscle type as of the limbs (skeletal muscle), the hypothesis is electrical stimulation of the pharyngeal and tongue muscles would lead to a similar effect of increased resting muscle tone and muscle tone during sleep.

Studies show that training the upper airway muscles either by playing a wind instrument (didgeridoo) [10] or oropharyngeal exercises [11,12,13] can ameliorate moderate OSA and snoring. A recent meta-analysis demonstrated that oropharyngeal exercises provide a reduction in apnea-hypopnea index (AHI) of 50% in adults and decreases snoring [14]. Oropharyngeal exercises are, therefore, a viable option to treat patients suffering from snoring and OSA. The presumption is that these changes are due to improvement in pharyngeal muscle tone.

In a placebo controlled prospective randomised study of tongue stimulation for OSA, although the OSA index did not significantly improve, there was a significant reduction in the snoring.[15] The number of snoring epochs decreased in the training group (baseline 63.9 ± 23.1 epochs per hour versus 47.5 ± 31.2; $P < .05$).

In a further study using external day time neck stimulators to stimulate the tongue for average of 4 weeks noted a significant drop in Apnoea-Hypopnea index (AHI) from 29.2 to 21.2 and in the partners witnessed snoring scale from 7.0 to 3.4 on a visual analogue scale of 1 to10 (10 = Unbearable snoring) [16].

Unlike the above-mentioned studies, our study uses an entirely intra-oral stimulation device (SnooZeal©). The muscle stimulator will be used twice a day for 25 minutes each time during the 6 week training period. The mouth piece will be placed with two electrodes below and two above the tongue for muscle stimulation.

The aim of this preliminary study will be to assess the efficacy of transoral neuromuscular stimulation training during wakefulness on snoring and OSA.

Patients and Methodology

This is a preliminary report of an ongoing cohort prospective observational pilot study of snoring and sleep apnoea patients. To date twenty volunteers have completed the trial. All subjects are between the ages of 20 and 65 years, of both

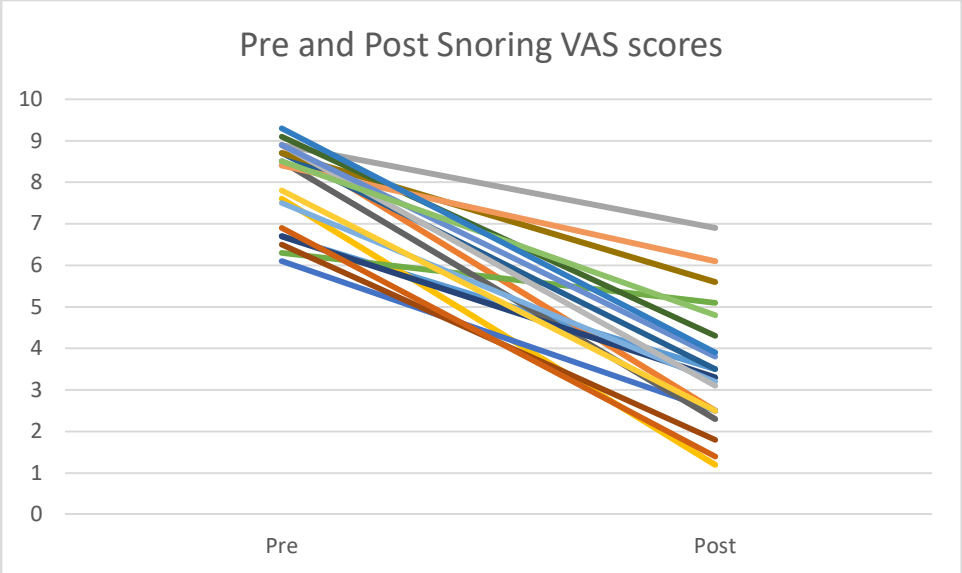
genders with a history of habitual (daily) snoring for more than six months. Volunteers without a live in partner to rate the snoring, with history of significant nasal symptoms, previous oral or throat surgery for snoring, any oral piercing or history of pacemaker or implanted electrical devices were excluded.

These volunteer's partners rated their snoring levels on a visual analogue scale (VAS) from 1 to 10 (10=unbearable snoring) which was recorded for the 14days days prior to start of the trial. The volunteers then used the SnooZeal device twice daily for a 6 week period. The volunteer's partners made further recordings of their partner's snoring on the VAS for the final 14 days of the trial. The Pre-treatment VAS scores were compared with the last two week's treatment VAS scores. Any side effects or feedback was recorded.

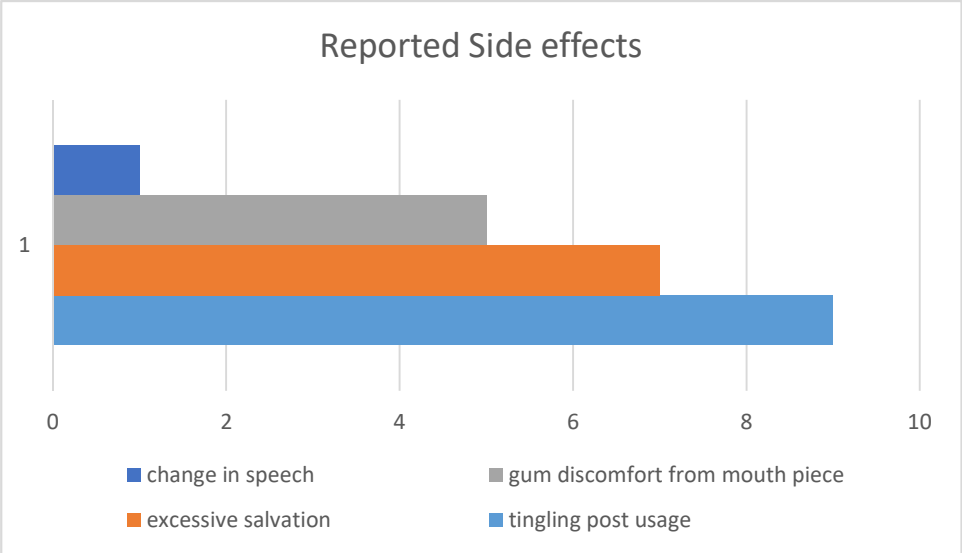
In a parallel case study, three patients with Moderate to severe Obstructive sleep apnoea established on CPAP for more than six months were recruited for a trial of SnooZeal at the same time as continuing the CPAP treatment. The intension was to investigate the impact of intra-oral electrical stimulation on the pressures required by CPAP machines. The average pressures required to maintain airway patency were monitored for the month prior to and in the last 2 weeks of a 6 week treatment period.

Results

In the snoring group the age ranged from 27 years to 63 years (average 45.6 years) with 16 men and 4 women. The BMI ranged from 21 to 35 (average 30.8) with 4 volunteers with BMI greater than 33. The pre-treatment snoring VAS ranged from 6.1 to 9.3 (Average 7.95). In the snoring group, the average snoring score fell from 7.95 to 3.57 on the visual analogue scale. In the two patients who had pre and post treatment sleep studies, the AHI reduced from 14.2 to 5.5 and 12.5 to 9.1 respectively. The latter was a patient with a BMI of 35, in whom the snoring score showed a minimal change from 8.9 to 6.9 on the VAS.

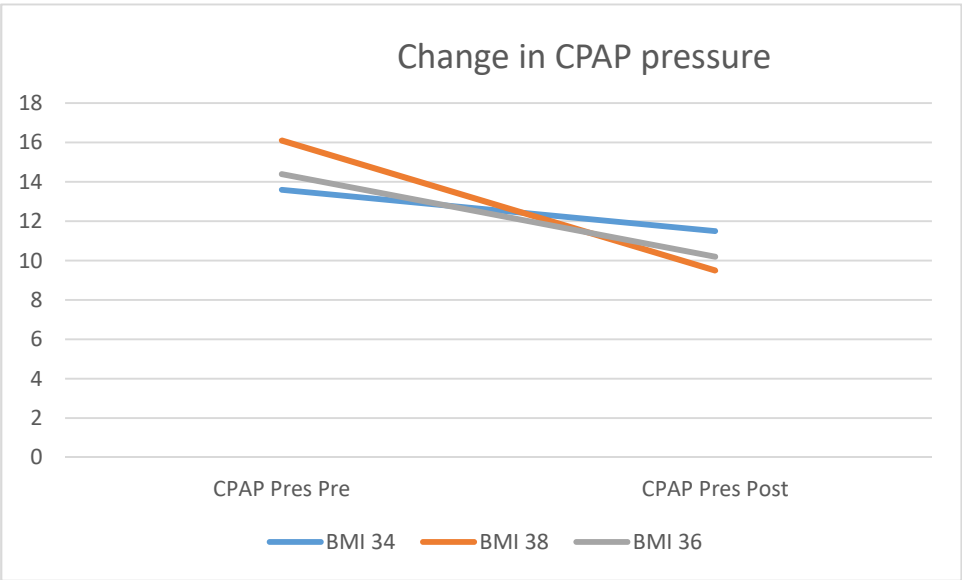


All the side effects and feedback are presented below.



Temporary tingling sensation of the tongue and excessive saliva were the commonest side effects described in the early part of the trial. However, by the end of the trial period, only one person respectively still declared that these symptoms had persisted or were troublesome.

Three patients using CPAP for moderate to severe sleep apnoea were recruited. There were both men with BMI index of 34, 36 and 38 respectively and pre-treatment AHI of 25.5, 26.5 and 34.3 respectively. The change in the CPAP pressures for the 4 weeks before and the last 2 of the 6 week usage changed from 13.6 to 11.5, 14.4 to 10.2 and 16.1 to 9.5 respectively and are displayed below.



Discussion

The primary cause of snoring and sleep apnoea is the loss of muscle tone in throat and tongue muscle resulting in collapsibility even at positive airway pressures [3,4]. The technique of using electrical stimulation of the tongue during the day to improve throat and tongue muscle tone and reduce collapsibility offers an entirely novel approach to the management of the Sleep disordered breathing.

Although previous studies have shown benefits with such an approach, these have been conducted through a transcutaneous route. This pilot study is aimed at establishing the efficacy of an entirely intraoral targeted therapy.

In our 20 volunteer snoring cohort, the snoring VAS dropped from 7.95 to 3.57, effective equating to an overall reduction of 55% for the group. This is substantially greater that the published data to date confirming our impression that a more targeted intra-oral route of electrical stimulation will yield better outcomes than the transcutaneous methods used in the past. Furthermore, in this cohort 5 patients were poor responders with snoring reduction of less than 50%. Due to the size of the cohort, it is not possible to consider a sub-analysis to identify indicators for poorer outcomes. Conversely, in the remaining good responders (75%), the average reduction in snoring was 63%. Similar results are evident in the raw data analysis from Verse et al paper [16]. In their prospective trial of 15 patients, 4 (26%) showed no change or worsening of their AHI post treatment. A subanalysis of the 11 responders in their trail reveals a drop in AHI of 11.5, substantially greater than the drop of AHI of 8 evident for their overall cohort.

These results are extremely promising revealing a notable response rate in 75% of the cohort undertaking this treatment. This is a surprisingly high responder rate considering the multilevel and often multifactorial nature of the diverse group of patients that belong to the diagnosis of Sleep Disordered breathing. This data also emphasises the need for larger cohort studies with wider demographic and epidemiological data collection to establish the characteristics that better identify the responders and non-responders.

Although the reduction is snoring and AHI of up to 11.5 are very encouraging as stand-alone treatments for Snoring and Mild to Moderate sleep apnoea, we explored the possibility of considering such a modality of treatment as an adjuvant to CPAP for the more severe OSA patients. In the three patients recruited, notable drops in the pressures required for the CPAP were noted. Any drop in the CPAP pressures required will significantly improve compliance with CPAP. On the basis of these positive findings, larger studies should be undertaken to establish the role and place of SnooZeal in the management of Moderate to Severe OSA as an adjuvant treatment modality.

References

1. Bradley EP, Ludman H. Snoring and Sleep Disordered Breathing Children and Adults, British Medical Journal - ABC of Otolaryngology. Blackwell Publishing LTD. March 2011

2. Kirk J, Kotecha, B. When Continous Positve airway pressure (CPAP) fails. J Thorac Dis 2016;8(10): E1112-E1121

3. Isono S, Remmers JE, Tanaka A et al. Anatomy of pharynx in patients with Obstructive sleep apnoea and in normal subjects. J Appl Physiology 1997;82(4):1319-1326

4. Schwartz AR, Smith PL, Wise RA, et al. Induction of upper airway occlusion in sleeping individuals with subatmospheric nasal pressure. J Appl Physiol 1988;64:532-542

5. Smith PL, Eisele DW, Podszus T, et al. Electrical stimulation of upper airway musculature. Sleep 1996;19:S284-7.

6. Mann EA, Burnett T, Cornell S, Ludlow CL. The effect of neuromuscular stimulation of the genioglossus on the hypopharyngeal airway. Laryngoscope 2002;112:351-6.

7. Schwartz AR, Bennett ML, Smith PL, et al. Therapeutic electrical stimulation of the hypoglossus nerve in obstructive sleep apnea. Arch Otolaryngol Head Neck Surg 2001;127:1216-23.

8. Guilleminault C, Powell N, Bowman B, Stoohs R. The Effect of Electrical Stimulation on Obstructive Sleep Apnea Syndrome. Chest 1995;107:67-73.

9. Sillen MJ1, Franssen FM, Gosker HR, Wouters EF, Spruit MA. Metabolic and structural changes in lower-limb skeletal muscle following neuromuscular electrical stimulation: a systematic review. PLoS One. 2013 Sep 3;8(9):e69391

10. Puhan MA , Suarez A , Lo Cascio C , Zahn A , Heitz M , Braendli O . Didgeridoo playing as alternative treatment for obstructive sleep apnoea syndrome: randomised controlled trial. BMJ 2006; 332 (7536):266-270

11. Guimares KC , Drager LF , Genta PR , Marcondes BF , Lorenzi-Filho G . Effects of oropharyngeal exercises on patients with moderate obstructive sleep apnea syndrome. Am J Respir Crit Care Med. 2009; 179 (10): 962 – 966

12. Ieto V, Kayamori F, Montes MI, Hirata RP, Gregório MG, Alencar AM, Drager LF, Genta PR, Lorenzi-Filho G. Effects of Oropharyngeal Exercises on Snoring. A Randomized Trial. Chest 2015;148(3):683-691

13. Physiotherapy in obstructive sleep apnea syndrome: preliminary results T. Lequeux Æ G. Chantrain Æ M. Bonnand A. J. Chelle Æ M. P. Thill Eur Arch Otorhinolaryngol 2005,262: 501–503

14. Camacho M, Certal V , Abdullatif J , et al . Myofunctional therapy to treat obstructive sleep apnea: a systematic review and meta-analysis. Sleep. 2015; 38: 669 - 675

15. Randerath WJ, Galetke W, Domanski U, Weitkunat R, Ruhle KH. Tongue-muscle training by intraoral electrical neurostimulation in patients with obstructive sleep apnea. Sleep. 2004;27(2):254-9

16. Submental transcutaneous electrical stimulation for obstructive sleep apnea. Verse T, Schwalb J, Hörmann K, Stuck BA, Maurer JT. HNO. 2003;51(12):966-70