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Electrical Stimulation in Obstructive Sleep Apnoea: the TESLA-home trial

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Obstructive sleep apnoea (OSA) is a highly prevalent sleep disorder, characterised by periods of apnoeas or hypopnoeas due to obstruction of the upper airway while asleep. Continuous positive airway pressure (CPAP) is the standard treatment, inflating the airway and avoiding upper airway obstruction. However, many patients experience difficulties with long-term adherence to CPAP and may not tolerate sleeping with a mask, and, currently, there are few effective alternative treatment options. Electrical stimulation (ES) has long been used to stimulate skeletal muscles. By targeting specific dilator muscles of the upper airway electrical current can treat OSA by providing neuromuscular tone and maintaining upper airway lumen patency. Electrical stimulation can be applied invasively and, more recently, non-invasively. Hypoglossal nerve stimulation (HNS), one of the invasive techniques, leads to a significant reduction in the apnoea-hypopnoea-index and the oxygen desaturation index (ODI), but due to the nature of the procedure it has several associated adverse effects and risks, and it is relatively costly. Transcutaneous electrical stimulation in OSA (TESLA) uses a non-invasive stimulation technique that is safe and convenient, but there are sparse data on its usage. Electrical stimulation may not be as effective as CPAP therapy, but it could be a suitable 2nd line treatment for patients who fail standard CPAP usage. This article summarises the state-of-the-art in electrical stimulation and introduces the first trial of domiciliary transcutaneous electrical stimulation (TESLA home), investigating efficacy and compliance in patients with OSA for a three-month period.

Obstructive sleep apnoea (OSA) is the most common form of sleep-disordered breathing (1, 2), it is caused by intermittent and repeated upper airway (UA) collapse in a sleep-stage-dependent manner which results in irregular breathing at night, loud snoring, and arousals from sleep, typically associated with excessive sleepiness while awake.

The prevalence of OSA seems to increase with obesity rates, it affects up to 10% of the 30-49 year-old men and 3% of the 30-49 year-old women (1-3). OSA is associated with significant co-morbidities including hypertension, ischaemic heart disease, stroke, congestive heart failure, obesity and metabolic syndrome, and diabetes. It has been recognized as a significant cardiovascular risk (3). The Gold standard to assess OSA is polysomnography (“sleep study”), although symptom questionnaires and scores to assess OSA risk are used both in the clinical setting and in population-based cohorts (4). Treatment is focused on controlling the upper airway patency while asleep to improve any associated symptoms, as well as the control of potential long-term outcomes, including cardiovascular risks (3).
According to current guidelines, treatment with continuous positive airway pressure (CPAP) is indicated in patients with moderate-severe OSA (5), it is typically provided via a bedside machine connected with a tube to a tight-fitting face mask, stenting the upper airway open using pressurised air (6). CPAP is an effective therapy to improve symptoms in OSA and quality of life. Other treatment options include weight loss, postural advice, reduction of alcohol and sedative medication, as well as mandibular advancement devices (MAD) that might be considered in patients with milder OSA (7, 8). In patients with anatomical abnormalities, such as enlarged tonsils or adenoids, an ENT review and surgical options might be available (7).

Although CPAP provides currently the best available treatment to control upper airway patency, adherence to this treatment is limited and dependent on symptoms and disease severity; approximately a quarter of patients develop problems with CPAP adherence within months (9), while half of the patients on CPAP have limited adherence at one-year follow up (10). It is therefore essential to develop 2nd line therapies when patients fail on CPAP therapy to achieve symptom control and avoid adverse long-term outcomes (3). Importantly, patients support the development of novel therapeutic methodologies, such as electrical stimulation (11).

**Electrical Stimulation**

Airflow limitation with sleep onset results from the loss of neuromuscular tone of upper airway dilator muscles. In healthy subjects, neuromuscular tone is sufficiently maintained during sleep to sustain a patent upper airway. In patients with OSA, the loss of the neuromuscular tone associated with sleep results in an increased collapsibility of the UA, causing snoring and high resistance, and, when airflow ceases, upper airway obstruction resulting in OSA. Targeted electrical stimulation of the upper airway dilator muscles, specifically the genioglossus muscle, provides an ongoing neuromuscular tone that maintains upper airway patency when asleep (12, 13); this is possible using an invasive approach, hypoglossal nerve stimulation (HNS) (13), as well as by non-invasive transcutaneous stimulation (TESLA) (12, 14).

**Hypoglossal nerve stimulation (HNS)**

HNS is an invasive stimulation method using an implanted stimulator device, targeting the genioglossus muscle via the hypoglossal nerve unilaterally. It leads to a significant reduction in the apnoea-hypopnoea-index (AHI) and the oxygen desaturation index (ODI) in patients with OSA (15). However, HNS remains an invasive and costly procedure with associated risks. Following the publication of the STAR-trial (13) this method has been approved in the US, and the National Institute for Health and Care Excellence (NICE) have published a public consultation on this method in 2017 (16).

**Transcutaneous electrical stimulation in OSA (TESLA)**

TESLA is currently an experimental method to treat patients with OSA who have failed on CPAP therapy. It uses a non-invasive stimulation method with transcutaneous patches applied to the skin in the submental area; it is safe and convenient (14), and a well-tolerated method by patients which is titrated to levels of comfort
while awake (11). TESLA stimulates the upper airway dilator muscles, particularly the genioglossus, to maintain a patent upper airway while asleep (12) (Figure 1). The specifications of electrical current for both HNS and TESLA are the focus of ongoing research trials (13, 14).

**Figure 1**: contraction of the genioglossus muscle resulting in an increase in pharyngeal space.

A physiological feasibility study using TESLA was published by our group in 2011 (12). Patients with OSA were monitored during nocturnal apnoeas and hypopnoeas and TESLA was applied for 10-minute periods (12). It reduced the AHI and the ODI by about 2/3, improved oxygenation and reduced snoring. Moreover, a randomised, sham-controlled double-blinded crossover trial was performed identifying groups of responders and non-responders to this method (14). Responders to TESLA are characterised by less severe disease (AHI <35/h), lower body-mass-index (BMI <32) and a slimmer neck circumference; although the numbers were small, all women included in this trial were responders.

Our patient-and-public involvement published data of 162 patients with OSA established on CPAP who were asked about their preference for different treatments, including existing (CPAP, mandibular advancement devices) and emerging treatments (HNS, TESLA). It confirmed that more than 9-out-of-10 patients were interested in trying emerging technologies (11). However, despite the above evidence additional data on longer term efficacy, compliance, safety and feasibility of TESLA in the domiciliary setting are required to advance this methodology.

**TESLA-home Trial (NCT03160456)**

The TESLA-home trial is the 1st randomised controlled trial of domiciliary transcutaneous electrical stimulation in OSA, testing the feasibility of transcutaneous electrical stimulation compared to ongoing usual care (Figure 2).

**Figure 2**: Frontal view of the placement of the stimulation patches on the neck.

Patients with OSA (AHI <35/h) will be randomised into a prospective, interventional, controlled, two parallel arms trial for a three-months period, using either TESLA or remaining on their previous treatment (CPAP). This NIHR portfolio study started in July 2018 at Guy’s &
St Thomas’ NHS Foundation Trust, London, with additional recruitment sites from King’s College Hospital NHS Foundation Trust and the Royal Brompton & Harefield NHS Foundation Trust; the trial is supported by a grant of the British Lung Foundation (BLF). The primary outcome will be to assess the efficacy of transcutaneous electrical stimulation in patients with obstructive sleep apnoea in the community compared to usual care (CPAP), and follow up for 3 months. Secondary outcomes are to assess feasibility and compliance with the method, assess symptom control and improvement in quality of life. The sample size calculation based on the data from the previous crossover trial indicated that a total number of 68 participants are required, 34 randomised into each arm (14). The main in- and exclusion criteria are patients with obstructive sleep apnoea (AHI <35/h) who have failed CPAP (adherence < 4 hours/night). Patients with severe obesity are excluded as an increased load and a large neck circumference have been shown to adversely impact on the effective delivery of TESLA.

Participants are assessed at baseline, 6-weeks, and three months, including polysomnography assessments at the beginning and the end of the trial. Weekly follow up phone calls record adherence and symptoms scores. Additional measurements are directed at muscle contraction and the visualisation of diameters of the upper airway.

Conclusion

In summary, electrical stimulation is an emerging treatment for patients with OSA when 1st line therapy has failed. NICE has published a public consultation on HNS which could soon become available in selected centres in the UK under audit conditions. TESLA-home is the 1st non-commercial trial using transcutaneous electrical stimulation in the domiciliary setting which has recently started recruitment. Due to the safe nature of TESLA and its low costs, the results of this trial may help to support the case to establish this novel method in routine clinical practice.

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