

## Clinical trials in obstructive sleep apnoea

S1

**TOMADO: A CROSSOVER RANDOMISED CONTROLLED TRIAL OF ORAL MANDIBULAR ADVANCEMENT DEVICES FOR OBSTRUCTIVE SLEEP APNOEA-HYPOPNOEA**

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**Introduction** Obstructive sleep apnoea-hypopnoea (OSAH) causes excessive daytime sleepiness (EDS), impairs quality of life (QoL), and increases cardiovascular disease and road traffic accident risks. Continuous positive airway pressure therapy is effective but undermined by intolerance and cost effectiveness is borderline in milder cases. Mandibular Advancement Devices (MADs) are another treatment option but evidence is lacking regarding their effectiveness compared to no treatment in milder disease. This study compared clinical and cost effectiveness of a range of MADs and no treatment in these patients.

**Methods** This 4-period, randomised, controlled, crossover trial was undertaken at a UK sleep centre. Adults with mild to moderate OSAH and EDS (Apnoea-Hypopnoea Index (AHI) 5-30/hour; Epworth Sleepiness Scale score (ESS)  $\geq 9$ ) underwent 6 weeks of treatment with three non-adjustable MADs: self-moulded (SP1); semi-bespoke (SP2); fully-bespoke (bMAD); and 4 weeks no treatment. Primary outcome was AHI scored by a polysomnographer blinded to treatment and analysed by intention to treat. Secondary outcomes included ESS and QoL. Cost effectiveness was evaluated using validated tools, treatment costs and healthcare usage.

**Results** Ninety patients were recruited. Sixteen withdrew before trial end. Seven did not complete any treatment and were excluded from analyses. All devices reduced AHI against no treatment, by 26% (95%CI 11%, 38%,  $p = 0.001$ ) for SP1 to 36% (95%CI 24%, 45%,  $p < 0.001$ ) for bMAD. ESS was 1.51 (SP1) to 2.37 (bMAD) lower versus no treatment ( $p < 0.001$  for all). Compliance was lower for SP1 which was unpopular at trial exit. All devices were cost-effective compared with no treatment at a willingness to pay (WTP) of £20,000/quality-adjusted life year (QALY), based on mean costs and QALYs. SP2 was most cost-effective up to a WTP of £39,800/QALY after which, bMAD superseded it. Serious adverse events occurred in four patients (4%).

**Conclusions** Mandibular Advancement Devices achieve clinically important improvements in mild to moderate OSAH syndrome and are cost effective. A semi-bespoke non-adjustable MAD would appear to be the appropriate first choice in most patients. Future work should explore whether adjustable MADs give additional clinical and cost benefits in this patient group.

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S2

**THE IMPACT OF CONTINUOUS POSITIVE AIRWAY PRESSURE (CPAP) THERAPY ON COGNITIVE FUNCTION IN OLDER PEOPLE WITH SLEEP DISORDERED BREATHING (SDB) AND CO MORBIDITY**

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The impact of SDB on cognitive function is debatable, with sleepiness and intermittent hypoxia being implicated as potential mechanisms. The purpose of this study was to investigate the relationship between cognitive function and brain structure in older patients with SDB, who may be more vulnerable to cognitive decline, and in whom SDB is more common. A randomised controlled trial was carried out to determine if CPAP therapy could reverse any changes in cognitive function and brain structure.

**Methods** Older patients  $\geq 65$  years, with SDB [ $\geq 4\%$  Oxygenation Desaturation Index (ODI)  $> 7.5$  events/hour] were randomised to CPAP therapy or Best Supportive Care (BSC) for 6 months. Cognitive function was assessed at baseline and after 6 months, using a battery of 8 cognitive tests designed to examine attention, executive function and memory. MR brain scans were also completed however analysis is on-going.

**Results** The CPAP ( $n = 17$ ) and BSC ( $n = 17$ ) groups were well matched for age [mean (SD)] 70.8(4.1) vs. 70.8(3.3) years; BMI: 30.1(6.0) vs. 31.4(3.8) Kg/m<sup>2</sup>; Epworth sleepiness score (ESS): 9.4(4.3) vs. 9.4(4.8) and number of additional co morbidities/patient 2(1) vs. 2(1). ODI was higher in the CPAP group [35(22) vs. 19(15) events/hour  $p = 0.01$ ]. Baseline cognitive function was similar between groups for all tests. At 6 months the CPAP group had improvements in both of the attention and executive function compared to the BSC group [Trail Making B: 94(56) vs. 83(45) seconds,  $p = 0.047$ ; STROOP: 33(10) vs. 29(11) correct responses  $p = 0.03$ ]. Other measures of cognitive function were not statistically improved following 6 months of CPAP therapy. Subjective sleepiness did not improve significantly between groups [Change in ESS: CPAP -2.1(0.8) vs. BSC -0.7(0.7)  $p = 0.261$ ]; however the ODI was significantly reduced with CPAP: 20(18.3) vs. BSC 3(10.7) events/hour  $p < 0.01$ . The mean (SD) daily CPAP usage was: 3.4(2.2) hours.

**Conclusion** 6 months of CPAP therapy improved the ODI, attention and executive function but not subjective sleepiness or memory in this small group of older patients with SDB. We speculate the improvements in attention and executive function were due to a reduction in intermittent hypoxia. This may be reflected in changes in brain structure.

S3

**EFFECT OF CONTINUOUS POSITIVE AIRWAY PRESSURE ON BLOOD PRESSURE IN PATIENTS WITH MINIMALLY SYMPTOMATIC OBSTRUCTIVE SLEEP APNOEA: A META-ANALYSIS USING INDIVIDUAL PATIENT DATA FROM FOUR RANDOMISED CONTROLLED TRIALS**

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**Objective** To evaluate the effectiveness of continuous positive airway pressure (CPAP) in reducing blood pressure, sleepiness and sleep apnoea severity in patients with minimally symptomatic obstructive sleep apnoea (OSA).