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) ≥ 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 SP2 was most cost-effective up to a WTP of £39,800/QALY after which, bMAD superseded it.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 ≥ 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/m²; 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).

Design Systematic review and meta-analysis using individual participant data.

Data sources Individual patient data were obtained from eligible randomised controlled trials found by searching the electronic databases Medline, Embase and the Cochrane Central Register of Controlled Trials and reference lists of all identified articles.

Eligibility criteria for selecting studies Trials were eligible if they included patients with minimally symptomatic OSA, had randomised them to receive CPAP or either sham-CPAP or no CPAP, and had measured blood pressure at baseline and at a follow-up visit.

Results Five eligible trials were found (1219 patients) from which the necessary data from four studies (1206 patients) was obtained. There was some evidence that CPAP treatment was associated with a small increase in systolic blood pressure of 1mmHg (95% confidence interval -0.1 to 2.2), $p = 0.079$, with a larger increase in those patients using CPAP less than four hours/night ($+ 2.7\text{mmHg}$, 95% CI (1.1 to 4.2), $p = 0.001$). There was no overall effect on diastolic blood pressure (DBP), however, there was evidence of a reduction in DBP in patients using CPAP more than four hours/night (-1.2mmHg , 95% CI (-2.1 to -0.3), $p = 0.013$) and an increase in those using it less than four hours/night ($+ 1.2$, 95% CI (0.1 to 2.3), $p = 0.035$). CPAP treatment reduced both subjective sleepiness and OSA severity (both $p < 0.001$), with larger reductions in patients using treatment more than four hours/night.

Conclusions Although CPAP treatment reduces OSA severity and sleepiness, it seems not to have a beneficial effect on blood pressure (and possibly a detrimental effect on systolic BP) in patients with minimally symptomatic OSA, unless they use CPAP for more than four hours per night.

S4 SHORT TERM USE OF CONTINUOUS POSITIVE AIRWAY PRESSURE (CPAP) BY OBESE PATIENTS WITH OBSTRUCTIVE SLEEP APNOEA SYNDROME (OSAS) DIAGNOSED DURING ASSESSMENT FOR BARIATRIC SURGERY

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Around one in three patients with OSAS is unable to continue with CPAP. The reasons for this are still poorly understood. Patients being assessed for Bariatric Surgery are informed that untreated OSAS can increase peri-operative risk. We investigated whether this information had an effect on CPAP use. Over a six month period we identified 22 obese patients (Mean BMI 49.3) with OSAS discovered during assessment for Bariatric Surgery (OSAS Bar). Over the same period we identified a group of 33 obese patients (Mean BMI 42.1) with OSAS referred through conventional pathways by General Practitioners and Hospital Doctors (OSAS Conv) not under consideration for Bariatric Surgery. OSAS was diagnosed by overnight pulse oximetry, clinical interview and Epworth Sleepiness Score (ESS) using established criteria.

Results There were more women than men in the OSAS Bar group (41%) than in the OSAS Conv group (18%). Apart from this the 2 groups (OSAS Bar vs OSAS Conv) were well matched prior to CPAP for: Age (Mean 51.2 vs 48.3, $p = \text{ns}$), $>4\%$ Oxygen Desaturation Index (Mean 31.9/hour vs 42.3/hour, $p = \text{ns}$) and ESS (Mean 12.8 vs 14.8, $p = \text{ns}$). By 6 weeks after Out-

Patient CPAP initiation, 6(27%) of the OSAS Bar group and 7 (21%) of the OSAS Conv group had stopped using CPAP. In the patients continuing with CPAP there was no difference between the two groups in hours of CPAP used per night as measured from the CPAP device clock: CPAP Bar (Mean 5, Range 1–8, hours), CPAP Conv (Mean 6, Range 1.5–8.5, hours) or in the ESS on CPAP: CPAP Bar (Mean ESS 6.8), CPAP Conv (Mean ESS 5.8).

Conclusion This group of obese patients with OSAS under assessment for Bariatric Surgery had similar CPAP use to obese patients with OSAS not considering surgical intervention. Information on peri-operative risk does not appear to be a motivator in overcoming whatever inhibiting factors prevent patients from using CPAP. Pre-operative assessment clinics should be aware that CPAP prescription does not necessarily mean that CPAP is being used.

S5 VARIABILITY IN CLINICIAN'S PERCEPTION REGARDING FITNESS TO DRIVE IN PATIENTS WITH OBSTRUCTIVE SLEEP APNOEA SYNDROME (OSAS)- ON BEHALF OF THE BRITISH THORACIC SOCIETY SLEEP APNOEA SAG.

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Introduction Advice about driving is a key component of the management of OSAS patients. No objective tests have been shown to predict reliably whether an individual is safe to drive or not and therefore the advice given will depend upon the opinion of clinicians. We evaluated the current practice of advice given regarding fitness to drive in OSAS patients.

Methods Clinicians were invited to participate in a web-based survey. The questionnaire included six clinical vignettes describing a variety of OSAS patients. For each the respondent chose from options ranging from driving without restriction to advising not to drive at all. For ease of presentation the data are summarised as whether would allow driving or not.

Results 467 respondents completed the survey. The advice given by the respondents to various clinical vignettes was variable (figure-1). In the least contentious scenario (vignette-1) there was 1 in 14.6 chance and in the most (vignette-4) there was a 1 in 2 chance of an individual being told whether they could drive or not. Respondents were more likely to advise patients to refrain from driving if the AHI was worse ($P < 0.0001$, OR-3.9), if the Epworth sleepiness score was high ($P < 0.0001$, OR-23.5) and if

Abstract S5 Figure 1.