Welcome to this edition of the APSR Research Review.

The main focus this month is obstructive sleep apnoea. We learn how obstructive sleep apnoea impairs vasodilatation and discover that sleep apnoea raises blood pressure in children. We also expand our understanding of the correlation between obstructive sleep apnoea (OSA) and motor vehicle accidents. The evidence is so overwhelming that it would be unethical to perform a randomised trial with this endpoint. This edition also includes articles of high scientific value that clarify the role of oral appliances in the management of OSA, the sobering observation that even significant weight loss does not resolve all OSA symptoms and a fascinating clinical trial that suggests that in stable, hypercapnic obesity hypoventilation syndrome continuous positive airway pressure (CPAP) may be as an effective treatment option as BiPAP.

Kind regards,
Dr Lutz Beckert
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Randomised trial of CPAP vs bilevel support in the treatment of obesity hypoventilation syndrome without severe nocturnal desaturation

Authors: Piper AJ et al

Summary: Daytime respiratory failure was investigated in 36 patients with obesity hypoventilation syndrome with respiratory failure and without severe nocturnal hypoxaemia who were randomised to receive continuous positive airway pressure (CPAP) or bilevel ventilatory support (BVS) over a 3-month period. Neither daytime CO2 level (primary outcome) nor compliance with the intervention differed significantly between the two treatment groups. Daytime sleepiness was reduced in both groups, but BVS was associated with better psychomotor vigilance performance and subjective sleep quality.

Comment: Intuitively one would assume that patients with a BMI in the range of 52–54, nadir of nocturnal saturation 53–55%, 19–33% of sleep time saturations <80% and significant daytime hypercapnia would do better with BVS than CPAP. The Sydney group recruited 36 of these patients, carefully excluded acute respiratory failure and prolonged hypoxaemia despite CPAP, and then randomised them to treatment with either CPAP or BVS. Patients treated with BVS reported greater improvement in sleep quality and reaction time. However, treatment with BVS was not superior to CPAP in improving daytime pCO2, awake SpO2, bodyweight, Epworth Sleepiness Score and Pittsburgh Sleep Quality Index.

http://thorax.bmj.com/cgi/content/abstract/63/5/395
Continuous positive airway pressure improves vascular function in obstructive sleep apnoea/hypopnoea syndrome

**Authors:** Cross MD et al

**Summary:** This RCT explored the hypothesis that continuous positive airway pressure (CPAP) can reverse impaired vascular function secondary to obstructive sleep apnoea/hypopnoea syndrome (OSAHS) with severe nocturnal hypoxaemia. Vascular function was compared between a ‘desaturator’ group of patients with OSAHS (>20 4% desaturations/hour; n = 27) and a ‘nondesaturator’ group (no 4% and <5 3% desaturations/hour; n = 19) who received 6 weeks of CPAP therapy or placebo in a crossover manner. Vasodilatation, as assessed by forearm venous occlusion plethysmography during endothelium dependent and independent vasodilator intra-arterial infusions, was significantly reduced in the desaturator group compared with the nondesaturator group regardless of the vasodilator used (p = 0.007). Both acetylcholine and sodium nitroprusside-induced vasodilatation were significantly inversely correlated with both apnoea/hypopnoea index and desaturation frequency. Forearm blood flow associated with vasodilator therapy was significantly better with CPAP therapy than with placebo (p = 0.001).

**Comment:** OSAHS is associated with hypertension in animal models, epidemiological surveys and interventional studies. However, the mechanism is not fully understood. This group from Edinburgh published an elegant paper showing that untreated OSAHS impairs vasodilatation. In addition, they conducted a second experiment in which they randomised patients with OSAHS to active treatment or treatment with a sham CPAP and demonstrated that the impaired vasodilatation was reversible with therapy. The authors concluded that OSAHS contributes to elevated endothelin-1 levels and has a severity-dependent effect on blood pressure, and that CPAP treatment may play a role in reducing cardiovascular complications associated with OSAHS.

**Reference:** Thorax 2008; 63(7): 578-83

http://thorax.bmj.com/cgi/content/abstract/63/7/578

Efficacy of the ‘tennis ball technique’ versus nCPAP in the management of position-dependent obstructive sleep apnoea syndrome

**Authors:** Skinner MA et al

**Summary:** The use of a thoracic antisupine band (TSAB; designed to mimic the ‘tennis ball technique’) was compared with nasal continuous positive airway pressure (nCPAP) in 20 adults with mild-to-moderate severe position-dependent obstructive sleep apnoea (OSA) in this randomised crossover trial. The mean proportion of sleep time in a supine position was significantly lower with the TSAB than with nCPAP (6.3% vs. 35.4%; p<0.001). A successful outcome of apnoea/hypopnoea index (AHI) ≤10/hour was achieved in less participants with the TSAB than with nCPAP (13/18 vs. 16/18 patients; p = 0.004); mean AHI scores were 12.0 and 4.9/h for the TSAB and nCPAP groups, respectively (p = 0.02). Sleep efficiency and subjective responses did not differ significantly between the treatment groups.

**Comment:** This Dunedin study investigated whether patients with positional sleep apnoea can be treated with a ‘tennis ball’ sewn to their pyjamas. Researchers recruited 20 adults with moderately-severe sleep apnoea and found that the ‘tennis ball technique’ reduces apnoeic episodes and improves daytime symptoms. Patients’ adherence was better with the ‘tennis ball technique’, but reduction in AHI and improvement of quality of life were better with nCPAP. The authors concluded that the ‘tennis ball technique’ may be appropriate for a minority of patients in whom nCPAP is not appropriate or acceptable, but the main treatment, even for patients with positional sleep apnoea, should still be nCPAP therapy.

**Reference:** Respirology 2008; 13: 708-15
http://www3.interscience.wiley.com/journal/120750309/abstract

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Acylated ghrelin level in patients with OSA before and after nasal CPAP treatment

Authors: Takahashi K-I et al

Summary: Low ghrelin levels have been linked to obesity, and weight gain prior to a diagnosis of obstructive sleep apnoea (OSA) is common, so the role of ghrelin in OSA was explored in this study. Plasma levels of acylated and unacylated ghrelin measured in 21 participants with OSA prior to and after 1 month’s treatment with nasal continuous positive airway pressure (nCPAP) were compared with levels from 14 untreated patients with OSA and 13 participants without OSA. Baseline ghrelin levels were significantly higher in patients with OSA than those without (acylated 11.4 vs. 7.19 fmol/mL; p = 0.03 and unacylated 84.2 vs. 48.3 fmol/mL; p = 0.02). The acylated ghrelin level was significantly decreased following treatment (p = 0.02), but the unacylated ghrelin level was not. The investigators suggested that treating OSA may have an important role in managing patients who are obese.

Comment: Ghrelin, a peptide that stimulates growth hormone release, food intake and weight gain, exists in both acylated (biologically active) and unacylated forms. This group of Japanese researchers measured both forms of ghrelin in patients with OSA before and after nCPAP treatment, patients with untreated OSA and patients without OSA. Unsurprisingly, they found increased ghrelin levels in the patients with OSA. After treatment with nCPAP, total ghrelin and active acylated were reduced. The authors speculated that increased ghrelin might be related to rapid weight gain prior to OSA diagnosis. The ongoing high ghrelin may be related to the fact that BMI was maintained after treatment. Will ghrelin become a therapeutic target for treatment of OSA and obesity?

Reference: Respir Physiol Neurobiol 2008; 166: 282-90
http://www3.interscience.wiley.com/journal/121393111/abstract

Risk and severity of motor vehicle crashes in patients with obstructive sleep apnoea/hypopnoea

Authors: Mulgrew AT et al

Summary: The relationship between obstructive sleep apnoea/hypopnoea (OSA/H) and motor vehicle crashes (MVCs) was explored in this study. Insurance records were used to obtain objective crash data for 783 patients with suspected OSA/H (mean age 50 years; mean apnoea/hypopnoea index 22 events/hour; mean Epworth Sleepiness Scale score 10), which were compared with 783 age- and sex-matched controls. Compared with controls, the relative risks of MVCs for patients with mild, moderate and severe OSA/H were 2.6 (95% CI 1.7, 3.9), 1.9 (1.2, 2.9) and 2.0 (1.4, 3.0), respectively, and the respective relative risks for MVCs associated with personal injury were 4.8 (1.8, 12.4), 3.0 (1.3, 7.0) and 4.3 (1.8, 9.9). The crash rates between controls and patients in whom polysomnography revealed no OSA/H were similar. Although the overall rate of head-on collisions and MVCs involving pedestrians or cyclists was low, 80% of such MVCs involved patients with OSA/H (p = 0.06).

Comment: This Canadian study adds to our understanding of OSA and MVCs. Based on the insurance company records of 783 patients 3 years prior to their OSA diagnoses, the authors found a significant increase in the rates of MVCs and also a ‘dose-response curve’ (i.e. the higher the AHI the more severe the accident). In the excellent accompanying editorial (Thorax 2008; 63(6): 481-3), John Stratifying reflects on the quality of the data and expresses his opinion that a prospective randomised controlled study would now be unethical. He suggests that our role should be to empower GPs to have strategies for early diagnosis of at-risk patients and access to rapid, funded CPAP treatment.

Reference: Thorax 2008; 63(6): 536-41
http://thorax.bmj.com/cgi/content/abstract/63/6/536

Persistence of obstructive sleep apnea after surgical weight loss

Authors: Lettieri CJ et al

Summary: The effect of surgical weight loss on obstructive sleep apnoea (OSA) was investigated in 24 consecutive patients (mean age 47.9 years) with OSA who underwent bariatric surgery. Polysomnography (PSG) was performed before surgery and one year later. At follow-up, most patients (71%) still had moderate-to-severe OSA, and only one patient (4%) had experienced complete resolution. Baseline apnoea/hypopnoea index (AHI) was correlated with follow-up AHI (R² = 0.603). All patients who continued to experienced OSA also continued to require CPAP treatment, although the mean required pressure decreased from 11.5 to 8.4cm H₂O (p = 0.001).

Comment: In this fascinating study from Washington, researchers compared sleep studies of 24 patients before and one year after bariatric surgery. The patients managed to lose about 50kg of weight, dropping their BMI from 51.0 to 32.1 kg/m² and their AHI from 48 to 25 events/hour. However, even after this substantial weight loss, 23 patients still had persistent OSA. Interestingly, 70% of patients reported that they no longer snored, yet 96% of them still snored during their repeat PSG. The authors observed that the resolution of subjective snoring was a strong predictor of discontinuation of CPAP therapy. Bottom line: bariatric surgery leads to significant weight loss and an improvement in AHI and Epworth sleepiness scale, but not a complete reversal of OSA.


Association of sleep-disordered breathing with postoperative complications

Authors: Hwang D et al

Summary: The association between obstructive sleep apnoea (OSA) and postoperative risk was investigated in 172 elective surgical patients with clinical features of OSA who underwent home nocturnal oximetry. Participants with ≥5 oxygen desaturations/hour (defined as oxygen desaturation ≥4%) were compared with those with <5 oxygen desaturations/hour. The rate of postoperative complications was significantly greater in those with ≥5 desaturations/hour than those with <5 desaturations/hour (adjusted OR 7.2; 95% CI 1.5, 33.3; p = 0.012). The postoperative complication rate was also significantly higher for ≥15 desaturations/hour compared with 5–15 desaturations/hour (17.5% vs. 13.8%; p = 0.01).

Comment: Resources to diagnose sleep disordered breathing are limited and often not available in the allocated time frame prior to elective surgery. In this study, researchers from New York performed home-based overnight oximetry on 172 patients prior to surgery. They found a prevalence of SDB of 57% with a mean oxygen desaturation index (ODI) of 22. Most importantly, they discovered that the higher the ODI, the greater the risk of postoperative complications. The authors suspected that an increased ODI >5 is associated with increased complications; however, the causality would need to be proved through a randomised trial of perioperative CPAP treatment.

Reference: Chest 2008; 133(5): 1128-34
http://www.chestjournal.org/cgi/content/abstract/133/5/1128

Independent commentary

By Dr Lutz Beckert, Respiratory Physician at Christchurch Hospital, New Zealand.
Health belief model predicts adherence to CPAP before experience with CPAP

Authors: Olsen S et al

Summary: The degree to which preconceived beliefs and expectation surrounding treatment with continuous positive airway pressure (CPAP) affect adherence to treatment was investigated in 77 consecutive patients with newly diagnosed obstructive sleep apnoea (OSA). Data were obtained from questionnaires administered before the participants received CPAP therapy, standard sleep studies and adherence assessments at 4 months' follow-up. While psychological health belief model constructs and biomedical indices combined explained 31.8% of the variance in adherence to CPAP therapy, 21.8% of the overall variance was explained solely by the health belief model constructs. Higher treatment outcome expectancies, lower risk perceptions and greater functional limitations due to sleepiness explained the greatest proportion of CPAP adherence.

Comment: Approximately 15–30% of patients do not adhere to CPAP treatment, which is not explained by biological variables like the apnoea/hypopnoea index, Epworth sleepiness score, BMI or age. This group of researchers from Queensland showed that a patient's health beliefs prior to commencement of CPAP will influence their adherence to CPAP therapy. Following investigations in 77 newly diagnosed patients with sleep apnoea, the authors showed that adherence to CPAP therapy was best explained by outcome expectancies, functional limitations and risk perception. If this model were to be accepted, we may be able to improve adherence to CPAP by outcome expectations, functional limitations and biomedical indices combined explained 31.8% of the variance in adherence to CPAP therapy. If this model were to be accepted, we may be able to improve adherence to CPAP by outcome expectations, functional limitations and risk perception. If this model were to be accepted, we may be able to improve adherence to CPAP by outcome expectations, functional limitations and risk perception. If this model were to be accepted, we may be able to improve adherence to CPAP by outcome expectations, functional limitations and risk perception. If this model were to be accepted, we may be able to improve adherence to CPAP by outcome expectations, functional limitations and risk perception. If this model were to be accepted, we may be able to improve adherence to CPAP by outcome expectations, functional limitations and risk perception. If this model were to be accepted, we may be able to improve adherence to CPAP by outcome expectations, functional limitations and risk perception.

http://eri.ersjournals.com/cgi/content/abstract/32/3/710

Comparison of a custom-made and a thermoplastic oral appliance for the treatment of mild sleep apnea

Authors: Vanderveken OM et al

Summary: A prefabricated thermoplastic oral appliance was compared with a custom-made device in 35 patients with a mean apnoea/hypopnoea index (AHI) of 13 events/hour in this RCT. Following use of both devices for 4 months in a crossover manner, it was found that the overall success rate was 60% for the custom-made device, compared with 31% for the thermoplastic device (p = 0.02). The custom-made device was the only one that reduced AHI, and the reduction in snoring was also greater than it was with the thermoplastic device. The compliance rate was also poor with the thermoplastic device, due mainly to insufficient overnight retention, and the overall failure rate associated with this device was 69%. Moreover, the custom-made device was preferred by 82% of the participants.

Comment: This elegantly designed study from Belgium compared two different oral appliances for treatment of snoring or mild sleep apnoea. The authors performed a randomised cross-over trial on 35 patients (AHI 13). They confirmed that thermoplastic oral appliances are indeed cheaper and faster to fit. However, when compared with custom-made appliances obtained from a dentist/dental technician, the thermoplastic devices showed no reduction in AHI, less reduction in snoring and worse user rates. Furthermore, 82% of patients preferred the custom-made device. The bottom line: oral appliances are a treatment alternative for selected patients with sleep apnoea, but thermoplastic devices are not recommended.

http://ajrccm.atsjournals.org/cgi/content/abstract/178/2/197

An evaluation of a titration strategy for prescription of oral appliances for obstructive sleep apnea

Authors: Krishnan V et al

Summary: In order to help elucidate the best practice for oral appliance titration for mild-to-moderate obstructive sleep apnoea (OSA), patients from a dental sleep clinic were fitted with such an appliance and instructed to titrate their treatment until their symptoms resolved or they experienced discomfort. Successful treatment (defined as an apnoea/hypopnoea index (AHI) score of <10 events/hour and AHI decrease of ≥50% from baseline) was achieved with self titration, and without the need for additional titration during follow-up polysomnography (PSG), in 55% of the participants in whom data were available (n = 49). The best responders were male and younger participants. The investigators concluded that the titration protocol for oral appliance use is beneficial as an initial step in OSA management.

Comment: This American study compared home versus PSG titration of an oral appliance in a cohort of 57 patients with OSA (AHI 25). Although this study has some methodological weaknesses, it does provide clinically meaningful insights: 1) patients referred for oral appliance are less obese (BMI 27); 2) men and younger patients respond better; 3) baseline severity did not impact on treatment efficacy; and 4) most patients (55%) were able to self titrate at home without PSG-guided titration. Bottom line: this study supports the role of oral appliances in the treatment of OSA and the titration protocol offers a simple initial method to titrate treatment.

Reference: Chest 2008; 133(5): 1135-41
http://www.chestjournal.org/cgi/content/abstract/133/5/1135

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