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Welcome to the latest issue of Sleep Medicine Research Review.

We report an important study that looked at the impact of CPAP treatment on cardiovascular outcomes in OSA patients with established cardiovascular disease, and Canadian findings that maternal SDB in the third trimester increases the risk of delivering small for gestational age infants. We also include a number of studies of the use of CBTi in adults (and 1 in school-age children) with chronic insomnia, and finish with a report of OSA in children with Down syndrome.

We hope you find these and the other selected studies interesting, and welcome your feedback.

Kind regards,

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Abbreviations used in this issue

AHI = Apnoea-Hypopnoea Index
CBT = cognitive behavioural therapy
CBTi = cognitive behavioural therapy for insomnia
CPAP = continuous positive airway pressure
OSA = obstructive sleep apnoea
PSG = polysomnography
SDB = sleep-disordered breathing


Abstract

CPAP for prevention of cardiovascular events in obstructive sleep apnea

Authors: McEvoy R et al., for the SAVE Investigators and Coordinators

Summary: This study examined whether the use of CPAP prevents major cardiovascular events in patients with OSA. 2717 adults aged 45–75 years who had moderate to severe OSA and coronary or cerebrovascular disease were randomised to receive CPAP treatment plus usual care (CPAP group) or usual care alone. After a mean follow-up of 3.7 years, the primary composite end-point (death from cardiovascular causes, myocardial infarction, stroke, or hospitalisation for unstable angina, heart failure, or transient ischaemic attack) had occurred in 17% of patients in the CPAP group and 15.4% in the usual care group (p=NS). No significant between-group differences were seen for any of the individual components of the end-point.

Comment (AN): This important study included 100 patients from 5 New Zealand sites recruited mainly from Cardiology and Neurology clinics. OSA disease severity by Kiwi sleep clinic standards was in the mild to moderate range as by study design those with severe sleepiness or desaturation were excluded. The bottom line is that this study did not provide support for CPAP as a mean of preventing further cardiovascular events in OSA patients with established cardiovascular disease. This may partly relate to CPAP adherence as high CPAP adherers matched by propensity score had a lower risk of stroke (relative risk, 0.56; p=0.02). Clear improvements in mood, days off work and accident rates were also seen with CPAP therapy.


MERRY CHRISTMAS AND A HEALTHY, HAPPY 2017!

Independent commentary by Associate Professor Alister Neill

Alister Neill is Associate Professor at the Department of Medicine, University of Otago, Wellington School of Medicine; and Respiratory and Sleep Physician at the Department of Respiratory Medicine, Capital and Coast Health. His research interests include the epidemiology and ethnic distribution of obstructive sleep apnoea in New Zealanders and its relationship to cardiovascular disease, new treatment technologies, sleep assessment pathways and the provision of home non-invasive ventilation for respiratory failure. He directs the University of Otago’s WellSleep Laboratory and Research Group and is an Associated Investigator of the Australasian Sleep Trials Network.
Prevalence and characteristics of central compared to obstructive sleep apnea: analyses from the Sleep Heart Health Study Cohort

Authors: Donovan L & Kapur V

Summary: This study determined the prevalence of central sleep apnoea (CSA) in a large community-based cohort, and compared its clinical characteristics with those of OSA. Baseline data from 5,804 participants in the Sleep Heart Health study were reviewed. 0.9% and 0.4% of participants were found to have CSA and Cheyne Stokes respiration (CSR), respectively. Those with CSA were older, had lower body mass index, lower Epworth Sleepiness Scale scores, and were more likely to be male than those with OSA. In patients with self-reported heart failure, CSA was more common than CSA (55.1% vs 4.1%).

Comment (AN): A New Zealand study by Kathy Ferrier of stable heart failure patients living in the community also showed that CSA is more common than CSA/CSR (63% vs 15%). The most important drivers were severity of heart failure, presence of atrial fibrillation and levels of obesity.

Abstract

Maternal sleep-disordered breathing and the risk of delivering small for gestational age infants

Authors: Pamidi S et al.

Summary: This prospective cohort study evaluated whether SDB in the third trimester is associated with the delivery of small for gestational age (SGA) infants. 234 participants in a multicentre pregnancy cohort study were evaluated in the third trimester for SDB based on symptoms and PSG. 27 (12%) participants delivered an SGA infant. SDB symptoms (snoring and/or witnessed apnoea) in the third trimester had a potential but not statistically significant association with delivering an SGA infant. However, the odds of delivering an SGA infant were significantly increased with PSG-based diagnosis of maternal SDB (odds ratio, 2.65; p=0.02).

Comment (AN): CSA/CSR (53% vs 15%). The most important drivers were severity of heart failure, presence of atrial fibrillation and levels of obesity.

Abstract

Effect of continuous positive airway pressure on airway reactivity in asthma

Authors: Holbrook J et al.

Summary: This study evaluated whether nocturnal CPAP decreases airway reactivity in patients with asthma. 194 patients were randomised 1:1:1 to use CPAP with warmed, filtered, humidified air at night at pressures <1cmH2O (sham), 5cmH2O, or 10cmH2O. The primary outcome was change in the provocative concentration of methacholine needed to reduce FEV1 by 20% (PC20) at 12 weeks. Despite low adherence to CPAP, all groups showed an improvement in PC20 at 12 weeks. However, there were no significant differences between active and sham groups. Changes in FEV1 and exhaled nitric oxide were minimal in all groups.

Comment (AN): CPAP treatment for OSA is thought to improve co-morbid asthma by reducing gastro-oesophageal reflux, upper airway inflammation and supine-related decline in lung volume. This study examined the effect of 5 or 10cmH2O of CPAP in comparison to sham PAP that delivered humidified air in asthmatics without OSA. CPAP proved difficult to use and had no effect on airway reactivity beyond that humidification.

Abstract

Pharmacotherapy for residual excessive sleepiness and cognition in CPAP-treated patients with obstructive sleep apnea syndrome

Authors: Avellar A et al.

Summary: This meta-analysis examined the effects of pharmacological treatment in adults with OSA who had residual excessive sleepiness despite adequate CPAP use. A search of MEDLINE, EMBASE, LILACS, Cochrane Central Register of Controlled Trials-CENTRAL, and PsycINFO electronic databases identified 8 randomised placebo-controlled trials that evaluated the effects of pharmacological treatments on residual excessive sleepiness, cognition, and quality of life, as well as treatment effectiveness and safety, in patients using CPAP for OSA. Pharmacotherapy with modafinil and armodafinil improved excessive daytime sleepiness, attention/alertness, and clinical condition. No improvements in quality of life or other cognitive domains (including memory, executive function, and language) were reported. Pharmacotherapy did not have any severe adverse effects, but was associated with significant drop-out rates compared with placebo.

Comment (AN): This meta-analysis examined the evidence for pharmacological treatment (with modafinil or the still in-patent isomer armodafinil) of residual sleepiness in CPAP-treated OSA. Modafinil is not available for this indication in New Zealand unless there is an additional diagnosis of narcolepsy. Although well tolerated I have concerns about adherence (drop-outs) and there were no comparative studies with less expensive central nervous system stimulants.

Abstract

Disclaimer: This publication is not intended as a replacement for regular medical education but to assist in the process. The reviews are a summarised interpretation of the published study and reflect the opinion of the writer rather than those of the research group or scientific journal. It is suggested readers review the full trial data before forming a final conclusion on its merits.

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Sexsomnia: a specialized non-REM parasomnia?

Authors: Dubessy A et al.

Summary: This study examined the clinical characteristics of patients with sexsomnia compared with healthy controls and sleepwalkers. Individuals referred for sexsomnia, sleepwalking and night terrors were interviewed and assessed using the Paris Arousal Disorder Severity Scale (PADSS). They were also monitored by video-PSG for up to 2 nights. Seventeen patients (70.6% male) were found to have sexsomnia, and their sexual behaviours were more direct during sleep than during wakefulness. Patients with sexsomnia had more N3 awakenings than matched controls and the same amount as regular sleepwalkers. Half of them presented evidence of cortico-cortical dissociation, including concomitant slow (mostly frontal) and rapid (mostly temporal and occipital) EEG rhythms. Of 89 sleepwalkers, 10% had previous episodes of amnestic sexual behaviour.

Comment (AN): The paper reports clinical, polysomnographic features and forensic consequences of sexsomnia – a prior history of sleepwalking and PSG features may prove helpful in evaluation. Concomitant OSA should always be carefully looked for as a reversible cause of arousal from sleep that can reduce parasomnia occurrence.

Reference: Sleep 2016; published online Oct 28

Cognitive-behavior therapy singly and combined with medication for persistent insomnia: impact on psychological and daytime functioning

Authors: Morin C et al.

Summary: This study evaluated the impact of CBT, alone and combined with medication, on various indices of daytime and psychological functioning in adults with chronic insomnia. 160 patients with chronic insomnia were given CBT alone or with medication (zolpidem) for an initial 6-week treatment period, followed by an extended 6-month period. After the initial 6-week treatment period, significant improvements of fatigue, quality of life (mental component), anxiety, and depression were seen in the CBT alone group but not in the CBT + medication group. Improvements were well maintained at the 6-month follow-up.

Comment (KF): This group previously published results of the sleep outcomes in the same study which showed that CBT alone and CBT combined with medication produced similar improvements in nighttime sleep after the 6-week acute treatment phase. Bearing in mind that patients mostly seek treatment for insomnia due to the daytime effects (e.g. fatigue, mood symptoms), my take away points from this very useful additional study were: 1) that following acute treatment (six weekly 90 minute group sessions), significant improvements of fatigue, quality of life (mental component), anxiety, and depression were obtained in the CBTI alone condition but not in the combined CBTi plus medication condition; and 2) that maintenance CBTI (e.g. monthly for 6 months) leads to additional improvements in psychological well-being, fatigue, and quality of life.

Reference: Behav Res Ther 2016;87:109-116

Independent commentary by Dr Karen Falloon

Dr Karen Falloon completed her medical training at the University of Auckland Medical School in 2001. She became a fellow of the Royal New Zealand College of General Practitioners in 2009. In 2014 Karen completed her PhD in General Practice for which she investigated the effectiveness of a behavioural treatment for insomnia. She works as a GP specialising in insomnia and as a senior lecturer in the Department of General Practice and Primary Health Care at the University of Auckland. Karen is a member of the Australasian Sleep Association and serves on the GP education subcommittee.


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RACP MyCPD Program participants can claim one credit per hour (maximum of 50 credits per year) for reading and evaluating Research Reviews.
Effect of a web-based cognitive behavior therapy for insomnia intervention with 1-year follow-up

Authors: Ritterband L et al.

Summary: This study evaluated the use of a web-based CBTi intervention in adults with chronic insomnia. 306 adults were randomised to undergo an internet CBTi programme or receive online patient education. The internet CBTi (Sleep Healthy Using the Internet [SHUTi]) was a 6-week fully automated, interactive, and tailored web-based programme that incorporated the primary tenets of face-to-face CBTi. Patients in the patient-education group received nontailored and fixed online information about insomnia. Outcomes were significantly in favour of the CBTi group for Insomnia Severity Index, sleep-onset latency, and wake after sleep onset during follow up, and treatment effects were maintained at 1-year. 56.6% of patients in the CBTi group achieved remission status and 69.7% were deemed treatment responders at 1 year based on Insomnia Severity Index data.

Comment (KF): Internet-based CBTi is a promising option to achieve improved sleep outcomes in those with chronic insomnia. It may help to address the issues of access and affordability that hinder the widespread use of CBTi to treat insomnia. However, it does still come with a cost (SHUTi costs approximately $190 for 16-week access) and won't be acceptable to all. It is important also to remember that the participants in this particular trial were predominantly female, white, highly educated and comfortable with internet use. The accompanying editorial to this article reminds us that restraint is called for – the study was essentially unblinded so the true effect size (SHUTi vs control) remains unknown and all internet CBTi programmes are not equal. It is also important to remember that individual behavioural components of CBTi given in the primary care setting can be effective (improving the access and affordability of insomnia treatment).

An example is sleep scheduling (sleep restriction) advice which has been shown to lead to significant improvements in sleep quality and fatigue at 6 months for those with chronic primary insomnia (Simplified sleep restriction for insomnia in general practice: a randomised controlled trial. Br J Gen Pract 2015).

Reference: JAMA Psychiatry 2016; published online Nov 30

Abstract

Obesity may be the common pathway for sleep-disordered breathing in women with polycystic ovary syndrome

Authors: Suri J et al.

Summary: This case-control study in India investigated the cause of the increased prevalence of SDB in women with polycystic ovary syndrome (PCOS). 50 cases with untreated PCOS were compared with 100 controls. 66% of cases and 4% of controls had SDB (odds ratio, 46.5; p<0.001). After adjustment for body mass index (BMI) and waist circumference, the between-group difference was not significant. Free testosterone levels were significantly higher in the PCOS group than in controls (p<0.001).

Comment (KF): Increased testosterone predisposes to central obesity presumably leading to increased risk of SDB in this PCOS group. Obesity in these Indian women was defined as BMI>25 so it is important not to overlook our Indian women patients in the BMI 26–30 range (rather than just considering obesity to be BMI>30). It was interesting to note that there was notable under-reporting of snoring so there is a real drawback in using this as a surrogate marker of risk for SDB (in Indian women at least). The other notable point from this study is that the women were relatively youngish. So perhaps be mindful of the young Indian patient with PCOS who does not look obviously obese and doesn’t snore as she may still have SDB.


Abstract

Prevalence and predictors of obstructive sleep apnoea in young children with Down syndrome

Authors: Hill C et al.

Summary: This study examined the prevalence and predictors of OSA in children with Down syndrome. 202 children with Down syndrome aged from 6 months to <6 years were recruited; 188 out of 202 (93%) children were successfully evaluated. 59% of them were found to have mild to moderate OSA and 14% had moderate to severe OSA. Male sex and habitual snoring predicted OSA, whereas age, body mass index and tonsillar size did not.

Comment (KF): It is very important to appreciate the high prevalence of OSA in young children with Down syndrome and to ensure this population is routinely screened. Importantly, body mass index and tonsillar size did not predict OSA so objective screening is required. Recognition and treatment of OSA is important to help ensure optimal cognitive functioning and quality of life. This study used domiciliary cardiorespiratory polygraphy as a more feasible alternative to polysomnography.


Abstract

Short- and long-term effects of CBT-I in groups for school-age children suffering from chronic insomnia: the KISS-Program

Authors: Schlarb A et al.

Summary: This study evaluated the short- and long-term effects of CBTi (the KISS-Program) in school-age children with chronic insomnia. 112 children with chronic insomnia were randomly assigned to a wait-list control group or to the KISS-program (3 sessions for the children and 3 sessions for their parents). Children who received CBTI reported greater improvements in sleep behaviour immediately after treatment compared to the control group. Improvements persisted at the 3-, 6-, and 12-month follow-up assessments.

Comment (KF): This study showed improved sleep (compared to wait-list control) over the 6-week treatment period. Education and strategies were given to both children and parents. Therapy puppet Kalimba (a leopard with magical spots for good sleep) also helped introduce and reinforce concepts. The treatment seems quite intensive with multiple strategies. It would be great to know which of these might be the more magical ingredients (apart from the leopard’s spots) so that the treatment could be replicated more easily. Sleep improvements were maintained over the long follow up but there was no control group (after the 6-week period) for comparison so the true long term effect of the CBTi is unclear. A similar study in children with mental disorders or attention deficit hyperactivity disorder would be valuable.

Reference: Behav Sleep Med 2016;1-21

Abstract