MedSleep

Sleep Matters®

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About MedSleep

MedSleep's network of clinics are committed to providing the highest quality sleep medicine services across Canada.

MedSleep is dedicated to improving health and promoting wellness by providing a comprehensive and patient-centered approach to the diagnosis and treatment of sleep disorders.

We strive to be pioneers in sleep medicine utilizing the latest in technology, promoting education, and participating in clinical research and the advancement of new treatments.

MedSleep clinics provide clinical consultation, diagnostic services (sleep testing) and treatment for the full spectrum of sleep disorders.

MedSleep's vision is to be Canada's leading provider of high quality sleep medicine services.

Recent Study links Obstructive Apnea to Cancer

THIS IS THE FIRST population-based cohort study documenting an association between baseline obstructive apnea and cancer mortality over a follow-up period lasting up to 22 years. The association remained significant after adjusting for possible confounding variables including age, gender, smoking, BMI, physical activity, diabetes, waist circumference, and sleep duration. The association remained evident when restricted to solid cancers only and persisted when patients treated with CPAP were excluded from the analyses.

It has been shown that cancer cells subjected to either chronic or intermittent hypoxia show increased resistance to therapy (e.g., radiation) and malignant progression. Furthermore, recent experiments in a melanoma-injected mice model demonstrate that intermittent hypoxia mimicking sleep apnea in humans increases tumor growth. This association might be explained by the increased angiogenesis associated with tissue hypoxemia. Newly formed vascular networks present structural and functional abnormalities that lead to reduced perfusion and oxygen delivery to the tumor tissue leading to necrosis, which is a predictor of aggressive cancer progression and poor prognosis.

Consistent with the experimental evidence from the intermittent hypoxemia models, this study showed that the association with cancer mortality was even stronger when, instead of the apnea-hypopnea index, the apnea was characterized using the hypoxemia index (percent sleep time below 90% oxyhemoglobin saturation).

Campos-Rodriguez F. et al. Association between obstructive sleep apnea and cancer incidence. Am J Respir Crit Care Med. *2013 Jan 1;187(1):99-105* ❖

Management of Acute Insomnia

REGARDLESS OF THE TYPE OF THERAPY, the primary goals of treatment are:

1) to improve sleep quality and quantity and
2) to improve insomnia related daytime impairments.

If possible, clinical reassessment should occur initially every few weeks until the insomnia appears stable or resolved, and then every 6 months, as the relapse rate for insomnia is high. When a single treatment or combination of treatments has been ineffective, other behavioural therapies, pharmacological therapies, combined therapies, or re-evaluation for comorbid sleep disorders should be considered.

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What's Inside?

What are the different types of sleep testing?

The American Academy of Sleep Medicine (AASM) classifies sleep study data acquisition systems into four categories: level I - in-laboratory attended full polysomnography (PSG); level II - unattended home sleep study with comprehensive portable devices incorporating the same channels as the in-laboratory standard PSG; level III - unattended devices that measure at least four cardiorespiratory parameters; and level IV - unattended devices recording one or two parameters, usually just oximetry.

Level I Studies

The "gold standard" level I study (or PSG) is monitored by a trained technician and consists of at least two channels of electroencephalogram (EEG), submental and tibialis electromyogram (EMG), two channels of electrooculogram (EOG), respiratory airflow (thermistor or pressure-flow transducer), respiratory effort (thoracic and abdominal breathing movements), oximetry, and electrocardiography. Body position and snoring (via microphone) are also typically recorded. Studies are still manually scored (with a bit of automated assist) and the apnea-hypopnea index (AHI), which is the number of apneas and hypopneas per hour of sleep used to quantify the severity of sleep-disordered breathing (SDB). This study in addition to diagnosing sleep apnea, can identify other sleep disorders and is also utilized to establish a wide range of respiratory therapy modalities (CPAP, BiPAP, Assisted-Servo Ventilators etc.). In most provinces there is an accreditation for free standing sleep labs providing PSG which is also provided in some hospitals.

Level II Studies

Level II systems measure the same sleep and respiratory parameters as standard PSG and thus potentially provide the same amount of information about sleep, respiration, and limb movements. The main disadvantage is the absence of a technician who can make observations about sleep-related phenomenon and detect and rectify technical difficulties, which otherwise may result in signal loss or inadequate data. Potential benefits for level II studies include reduced cost (ie, no technician or hospital fees), improved availability, and perhaps more "typical" sleep given that patients are sleeping in the home environment.

WHAT ARE THE DIFFERENT TYPES OF SLEEP TESTING?

TESTS	Variables	Advantages	Limitations	Special Considerations
LEVEL 1 Laboratory Polysomnography	EEG, EOG, EMG, EKG, airflow, nasal pressure, respiratory efforts, snore sensor, leg EMG, Oximetry	comprehensive, can identify many sleep disorders beyond OSA and establish optimal therapy settings (i.e., PAP)	dedicated staff required, increased cost, not universally funded	gold standard for assessment and management of a variety of sleep disorders
LEVEL II Home Polysomnography	EEG, EOG, EMG, EKG, airflow, nasal pressure, respiratory efforts, snore sensor, leg EMG, Oximetry	absence of technicians, portability	no observations, no ability to detect and rectify technical difficulties	well suited to sleep studies for hospital in-patients
LEVEL III Cardiorespiratory Home Sleep Test	respiratory effort, airflow, oximetry and heart rate	very portable, relatively easy for patients to apply	no observations, no ability to detect and rectify technical difficulties, no sleep stage information	well suited for high pre-test probability OSA patients without cardiorespiratory co-morbidities
LEVEL IV Limited Home Test	Oximetry with or without airflow	very portable, inexpensive, easy to apply	data limited to SaO_2 only, high false negative results	good for estimating efficiency of CPAP, good for screening for OSA in pediatric patients

Level III Studies

Level III sleep studies require a minimum of four channels including an indicator of respiratory effort, airflow, oxygen saturation, and EKG. These studies do not record EEG, EOG, or chin EMG and, therefore, do not allow accurate determination of sleep efficiency or architecture. Without the ability to assess sleep versus wakefulness, the AHI cannot be accurately expressed as "events per hour of sleep" and instead is calculated as "events per hour in bed". For this reason, the AHI may be underestimated in subjects who are awake for a significant part of the night. Despite this concern, multiple studies have found well-correlated AHI measurements with simultaneous recording of level III tests and standard PSG in the laboratory. It should be noted that, as with level I studies, manual scoring by qualified PSG technologists has been found to be superior to automatic scoring. There has been much greater utilization of this study type for the diagnosis of OSA in regions where access to Level 1 studies is poor.

Level IV Studies

Most often, a level IV study is in-home overnight oximetry with a data down-load in the morning. This type of monitoring can be used as a quick and inexpensive screening tool when severe obstructive apnea or hypoventilation is suspected. However, these data are insufficient for a conclusive diagnosis, resulting in many false negative results. Level IV studies can also be useful for assessing a response to continuous positive airway pressure (CPAP) therapy. Lastly, level IV studies have been shown to be an accurate screening tool for the diagnosis of obstructive apnea in pediatric patients, especially those where there is question as to whether tonsillo-adenoidectomy surgery is warranted.

Choosing the Right Study

The search for a simple, inexpensive, and accurate diagnostic test for OSA continues. There are both potential advantages and disadvantages to using home sleep studies for diagnosis of OSA. In choosing a diagnostic strategy, local factors must be taken into consideration including access to service, disease prevalence, local funding, the availability of a sleep specialist with access to Level 1 (PSG) studies for evaluation of complicated, medically complex and/or equivocal home sleep test results.

Based on current literature, it seems reasonable to utilize portable sleep studies to medically stable patients with moderate to high clinical suspicion of obstructive apnea. Patients with significant co-morbid cardio-respiratory disorders and/or other suspected co-morbid sleep disorders should have Level 1 PSG. Patients with negative home sleep studies but persistent symptoms or failed or equivocal studies should undergo standard level I sleep study.

Reference: *Blackman, A. et al. Canadian Sleep Society/Canadian Thoracic Society position paper on the use of portable monitoring for the diagnosis of obstructive sleep apnea/hypopnea in adults. Can Respir J. 2010 Sep-Oct;17(5):229-32* ❖

On-line Tools for Managing Chronic Insomnia

RESEARCH CONTINUES TO SHOW that online cognitive behavioural therapy (CBT) may be an effective treatment for adults with ongoing insomnia. The internet provides a pervasive milieu for healthcare delivery. A recent study aimed to determine the effectiveness of a novel web-based cognitive behavioural therapy course called Sleepio, (please visit sleepio.com for more information) delivered by an automated virtual therapist, when compared with a credible placebo; an approach required because web products may be intrinsically engaging, and vulnerable to placebo response.

81% of the Internet group is still sleeping better at a six-month follow-up....

This study involved 144 participants. Data showed that CBT delivered using a media-rich web application with automated support and a community forum is effective in improving the sleep and associated daytime functioning of adults with insomnia disorder[1]. Members of the active treatment group showed a significant improvement in sleep efficiency, with a higher percentage of their total time in bed spent sleeping. The online treatment also had a long-lasting effect, with 81% of the Internet group still sleeping better at a six-month follow-up. These data are significantly better that those measuring the benefit of sedative-hypnotic medications.

Sleepio is highly interactive; it uses stories, quizzes and games to teach healthy sleep habits. It also gives personalized advice based on a completed sleep diary. The content is divided into core units that focus on specific methods for improving sleep. These include sleep restriction, stimulus control, sleep hygiene, cognitive restructuring and relapse prevention. These methods are based on traditional, face-to-face CBT. Also, expert and social supports. The American Academy of Sleep Medicine recommends CBT as an effective treatment for chronic insomnia in adults.

[1] *Espie, CA, et al. A randomized, placebo-controlled trial of online cognitive behavioral therapy for chronic insomnia disorder delivered via an automated media-rich web application. Sleep 2012 1;35(6):769-81.* ❖

WHAT IS MELATONIN?

Also known chemically as *N*-acetyl-5-methoxytryptamine, melatonin is a naturally occurring compound found in animals, plants, and microbes. In animals, circulating levels of the hormone melatonin vary in a daily cycle, thereby allowing the entrainment of the circadian rhythms of many biological functions. In humans, melatonin is produced by the pineal gland in the brain. Melatonin levels vary in 24-hour cycles and are controlled by the suprachiasmatic nucleus of the hypothalamus. Direct afferents from the retina convey light/dark information the SCN and then to the pineal gland. Normally, synthesis is inhibited by bright light, and is increased in the absence of light, which is why it is often called 'the hormone of darkness'. Melatonin communicates information about light to different parts of the body via this chemical transduction process. It helps regulate biological rhythms and plays an important role in the reproductive cycles of many animals. In humans it is best known for helping to regulate the body's circadian sleep-wake cycle. Though it does not actually induce sleep, melatonin can have sleep-promoting effects. Experiments have shown that at high doses melatonin lowers body temperature, decreases motor activity, and increases subjective sleepiness. Melatonin production starts falling after puberty, and it can virtually disappear in the elderly, a phenomenon which could help to explain why sleep disturbances are more prevalent among older adults. Marketed as a dietary supplement and touted as a cure-all for insomnia, jet lag, and even cancer and aging, the overall effects of melatonin on human health are still largely unknown.

Jet lag

Several human trials have suggested that melatonin taken by mouth, started on the day of travel (close to the target bedtime at the destination) and continued for several days, reduces the number of days required to establish a normal sleep pattern, diminishes sleep latency (the time it takes to fall asleep), improves alertness, and reduces daytime fatigue. Although these results are compelling, the majority of studies have had problems with their designs and reporting, and some trials have not found benefits. Overall, the scientific evidence does suggest benefits of melatonin in up to half of people who take it for jet lag. More trials are needed to confirm these findings, to determine optimal dosing, and to evaluate use in combination with prescription sleep aids.

Delayed sleep phase syndrome (DSPS)

Delayed sleep phase syndrome is a condition that results in delayed sleep onset despite normal sleep architecture and sleep duration. Although these results are promising, additional research with larger studies is needed before a stronger recommendation can be made.

Insomnia (in the elderly)

Several human studies have reported that melatonin taken by mouth before bedtime decreases sleep latency (the time it takes to fall asleep) in elderly individuals with insomnia. Improved sleep quality and morning alertness has also been reported. However, most studies have design flaws, and some research has found limited or no benefits. The majority of trials have been brief in duration (several days long), and long-term effects are not known.

Sleep disorders (children with behavioural, developmental, and intellectual disorders)

There have been multiple trials investigating melatonin use in children with various neuropsychiatric disorders, including mental retardation, autism, psychiatric disorders, visual impairment, or epilepsy. Studies have demonstrated reduced sleep latency (the time it takes to fall asleep) and increased sleep duration. Well-designed controlled trials in select patient populations are needed before a stronger or more specific recommendation can be made.

Sleep enhancement in healthy people

Multiple human studies have measured the effects of melatonin supplements on sleep in healthy individuals. A wide range of doses has been used, often taken by mouth 30-60 minutes prior to sleep time. Most trials have been small and brief in duration, and have not been rigorously designed or reported. However, the weight of scientific evidence does suggest that melatonin decreases sleep latency (the time it takes to fall asleep), increases the feeling of sleepiness, and may increase the duration of sleep. Better research is needed in this area.

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Management of Acute Insomnia

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Compensatory Behaviours

When patients begin to experience insomnia, they will often make adjustments in order to compensate for sleep loss. Unfortunately, these compensatory behaviours often become perpetuating factors which hold them over the insomnia threshold. Correcting these maladaptive behaviours is the first step in management.

Common Compensatory Behaviours

1) Increased daytime caffeine consumption
2) Increased evening alcohol consumption
3) Earlier bedtimes
4) **Increased time in bed**
5) Late rise times on days off
6) **Daytime napping**
7) Reduction of social activities
8) Reduced exercise due to daytime tiredness

Although a sleep diary is the most effective way to document these maladaptive behaviours, a good sleep-history may also pick-up most of them. This is where the patient can be engaged in the treatment process. The gathering of this information on a sleep diary, and then the implementation of behavioural adjustments will be the most important part of the initial and long-term management of insomnia.

The patient should be advised to reduce (or eliminate) consumption of caffeine and alcohol. They should estimate their ideal total sleep time, and then spend that amount of time in bed each night (plus about 1 hour – at the most). They should choose an ideal rise time that restricts their time in bed to 7.5-8 hours per night, and then strictly adhere to it, even on weekends and holidays. A regular meal schedule may have also been abandoned, if the insomnia is severe enough, and they should be advised in this regard. Although napping can be part of a cultural norm, and a good strategy for some shift-workers, napping should be completely eliminated in any patient presenting with a complaint of insomnia. Lastly, patients should be encouraged to resume (or start) a program of improved physical fitness, as exercise has been shown to have a beneficial influence on sleep and mood.

Medications for Sleep

Pharmacological treatment should be accompanied by patient education regarding: (1) treatment goals and expectations; (2) safety concerns; (3) potential side effects and drug interactions; (4) other treatment modalities (cognitive and behavioural treatments); (5) potential for dosage escalation; (6) rebound insomnia. Patients should be followed on a regular basis (every few weeks initially) to assess for effectiveness, possible side effects, and the need for ongoing medication.

Principles of Treatment

Pharmacotherapy is generally recommended at the lowest effective dose as short-term treatment lasting less than 7 days. Although long-term use of hypnotic agents is discouraged due to the potential for tolerance and dependence, there are specific situations and circumstances under which long term use of hypnotics may be appropriate.

Short term (<7 consecutive nights)

This can be used to break the cycle of insomnia and allow the patient to implement and adapt to behavioural adjustments/suggestions.

Long term intermittent

This can be a self-administered therapy to decrease arousal and prevent relapse. Often patients will be able to initiate sleep just knowing that the medication is in the bathroom cabinet. Patients can be encouraged to use the medication on a limited PRN basis (<3 times/week) for occasional bouts of insomnia to prevent relapse.

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Long term continuous

Chronic hypnotic medication may be indicated for long-term use in those with severe or refractory insomnia or chronic comorbid illness (especially mood and anxiety disorders). It may also be appropriate for patients with a prominent family history of insomnia, and/or childhood onset insomnia. Whenever possible, patients should receive an adequate trial of cognitive behavioural treatment during long-term pharmacotherapy. Long-term prescribing should be accompanied by consistent follow-up, ongoing assessment of effectiveness, monitoring for adverse effects, and evaluation for new onset or exacerbation of existing comorbid disorders. Long-term administration may be nightly, intermittent (e.g., three nights per week), or as needed.

First-line pharmacotherapy: highest level of evidence supporting efficacy & safety		
Zolpidem (Sublinox)	5-10 mg	Tmax ~ 30+ mins; T1/2 ~ 2-3 hrs
Zopiclone (Imovane)	5 & 7.5 mg	Tmax ~ 30+ mins; T1/2 ~ 4-6 hrs
Temazepam (Restoril)	15 & 30 mg	Tmax ~ 60+ mins; T1/2 ~ 8-10 hrs

Second-line pharmacotherapy: Moderate level of evidence; extent of present use and favourable tolerability support use as second-line agent		
Trazodone (Deseryl)	50-100 mg	Tmax ~ 60+ mins; T1/2 ~ 8-10 hrs

Variable evidence		
L-tryptophan	500 mg-2 gm	Evidence supporting efficacy is variable and insufficient. May be requested by individual patients looking for a "natural source" agent.
Melatonin	0.3-6 mg	
Valerian	400-1000 mg	

Other non-prescription products		
Diphenhydramine: • Benadryl® • Sleep Eze • Simply Sleep • Nytol® • Unisom®	25–50 mg	Potential for serious side effects arising from anticholinergic properties (especially in elderly); residual daytime sleepiness, diminished cognitive function, dry mouth, blurred vision, constipation, urinary retention, etc.
Dimenhydrinate: - Gravol®	25–50 mg	These products are not intended for long term use and tolerance to sedative effects likely develops rapidly (~3 days) Gravol not approved in Canada as a sleep aid
Doxylamine: - Unisom 2®	25– 50 mg	

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What is Melatonin? / *Continued from page 4*

Bottom line

Normal physiologic levels of melatonin convey information about time of day and time of year to all parts of the body. It is likely that it helps regulate the time of the sleep-wake cycle, as well as other circadian rhythms. However, as humans, we largely ignore the melatonin "signaling", by over-ridding it with artificial light, voluntary sleep restriction and deprivation, trans-meridian jet travel, and shift work. It is no wonder that the results of studies looking at the clinical benefit of exogenous melatonin (taken orally) for the treatment of insomnia are so equivocal. Also, the doses provided in over-the-counter preparations generally range from 1 to 6 mg. This produces a serum melatonin peak that is tens or hundreds of times greater that naturally occurring melatonin. Thus, the effect on sleep induction is probably more pharmacologic than physiologic. A few studies have even suggested that these supra-physiologic doses exert an effect by weakly binding at the benzodiazepine receptor. Also, since this molecule cannot be patented, there have no multicentre trials proving efficacy and safety. There are no specific guidelines with regard to dose or dose timing, so information provided to patients is usually quite vague. To date, the most convincing evidence for efficacy has been in developmentally delayed children, often residing in institutions. Perhaps this is because these children have not yet lost sensitivity to the relevant biological signaling conveyed by melatonin. At this time, the use of melatonin for the treatment of primary insomnia in normal adults remains controversial and is generally not recommended. ❖

Management of Acute Insomnia – *Continued from page 6*

Not recommended	
Antidepressants - mirtazapine, fluvoxamine, tricyclics	Relative lack of evidence
Amitriptyline	Relative lack of evidence and significant adverse effects (such as weight gain)
Antihistamines - chlorpheniramine	Relative lack of evidence or excessive risk of daytime sedation, psychomotor impairment and anticholinergic toxicity
Antipsychotics (Conventional or 1st-Generation) - chlorpromazine, methotrimeprazine, loxapine	Relative lack of evidence and unacceptable risk of anticholinergic and neurological toxicity
Antipsychotics (Atypical or 2nd generation)- risperidone, olanzapine, quetiapine	Relative lack of evidence and unacceptable cost and risk of metabolic toxicity and psychotic behaviours
Benzodiazepines (Long- acting): diazepam, clonazepam, flurazepam, lorazepam, nitrazepam, alprazolam	Excessive risk of daytime sedation and psychomotor impairment
BDZs (Intermediate-acting): oxazepam	Very slow absorption: Tmax ~ 180 mins
BDZs (Ultra-short-acting): triazolam	Unacceptable risk of memory disturbances, rebound insomnia, and rebound anxiety

Conclusion

Effective assessment and management of acute insomnia can prevent the development of a more problematic pattern of psychophysiologic (chronic) insomnia. The assessment phase involves the identification of the particular stressor or other environmental factor that is the likely precipitant of the sleep complaint. The next step is to identify how the individual is adapting to that stressor, as the insomnia is likely to persist until there is some resolution, adjustment or acceptance of the stressor. In the meantime, compensatory behaviours and beliefs may quickly develop, which will leave the individual stuck in a more chronic pattern of insomnia (>3 months) if they are not effectively checked. Having the patient help identify any perpetuating factors, either with a sleep diary or a detailed sleep history, is an essential part of the management process.

The patient must be advised about behaviours that would lead to hyper-arousal, impair the normal process of sleep onset and maintenance, and/or alter normal circadian influences on the sleep-wake cycle. Once the patient has been engaged to implement the necessary changes, then the use of safe short-acting sedative-hypnotic medications can be considered. The patient should be advised that the medications are only to temporarily augment and/or accelerate the benefits of behavioural and psychological changes, which should be of continued benefit after the course of medication is complete. ❖

MedSleep

DEDICATED TO ACHIEVING EXCELLENCE

in both the diagnosis and treatment of the full spectrum of sleep disorders, providing comprehensive evaluation and integrative treatment.

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