Research Review Speaker Series™

Diagnosis and management of sleep symptoms

Making Education Easy

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MD 1991 Philippines; Am Bd Cert Psych 1999

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Dr Tony Fernando is a consultant psychiatrist and academic from the University of Auckland. He is from the Philippines and obtained his MD from the University of the Philippines. He then pursued his psychiatry training at Columbia University in New York and University of Pennsylvania in Philadelphia.

He obtained his fellowship in Sleep and Psychopharmacology from the University of Pennsylvania. He is practicing psychiatry in Auckland District Health Board and sleep medicine at Practice 92 in Mt Eden, Auckland. He teaches mindfulness meditation and compassion meditation to medical students and doctors in NZ and overseas.

He conceptualised and developed the www.calm.auckland.ac.nz CALM website together with Dr Fiona Moir. In 2011, he commenced his PhD research on compassion among physicians. He is a keen cello player and is an inaugural member of the NZ Doctors Orchestra.

Research interests

- Diagnosis and treatment of insomnia and other sleep disorders
- Medical education
- Prevalence studies of sleep disorders (including insomnia) in various populations
- Psychopharmacology of mood disorders and schizophrenia

Dr Tony Fernando is a Psychiatrist and Sleep Specialist at the Department of Psychological Medicine, University of Auckland. He spoke in Auckland and Hamilton in September 2012 on the diagnosis and management of sleep symptoms, and the relevance of mood disorders in this patient population. Specifically, he discussed the three major groups of sleep disorders; insomnia, excessive daytime sleepiness and parasomnias. Dr Fernando recommended two useful sleep resources for patients and doctors: www.calm.auckland.ac.nz, www.yoursleep.aasmnet.org.

Insomnia

Dr Fernando explained that for many, insomnia is really a `wake' problem rather than a sleep problem, and that the awake brain is very potent. A high proportion of women in their prime years suffer from insomnia and this may be a consequence of their busy lifestyles and ruminating mindset. Individuals with insomnia may present with poor, non-refreshing sleep, may have difficulty falling asleep initially, have difficulty in falling asleep after waking during the night, or may wake early. To be classified as having insomnia, an individual needs to have experienced symptoms of the condition for more than a month (i.e. a chronic condition) and to exhibit a daytime consequence of their poor sleep pattern.

Approximately 50% of people with chronic insomnia have mood and anxiety disorders, while 30% have primary insomnia (no depression, anxiety or other diagnosable medical condition). Antidepressants don't tend to work in those with primary insomnia, but behavioural therapy is often beneficial. Other conditions, which cause insomnia include medical problems (i.e. chronic pain, gastro-oesophageal reflux, chronic fatigue syndrome/myalgic encephalopathy, hyperthyroidism, fibromyalgia), the use of recreational and prescribed substances, poor sleep hygiene (some individuals consume too much caffeine), circadian rhythm disorders (i.e. delayed sleep-phase disorder [DSPD], jet lag, shift work) and other sleep disorders (i.e. sleep apnoea, restless legs syndrome, parasomnias, nocturnal panic, nightmares).

Dr Fernando explained that individuals with circadian rhythm disorders, such as DSPD, appear to have permanent jet lag and gave the example of a 19 year old who only falls asleep at 3 am and wakes mid-morning (this is common among teenagers). These individuals exhibit normal sleep and sleep well, but the problem is with the timing. They may be sleep deprived and appear depressed if they have to wake early to go to work for example, but tend to make up for this sleep deficit in the weekend. Dr Fernando explained that while this condition is often not diagnosed, it is highly treatable.

The prevalence of sleep symptoms

Dr Fernando and colleagues evaluated the prevalence of sleep symptoms in university students using the Auckland Sleep Questionnaire, and revealed a surprisingly high prevalence (47-61%) of such symptoms in students in a variety of professional courses (Table 1). Interestingly, a high proportion had alcohol problems based on questionnaire answers, including 19% of medical students!

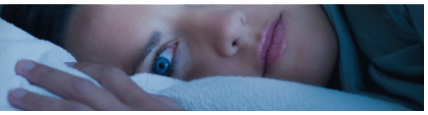


Table 1: Prevalence of sleep symptoms among university students using the Auckland Sleep Questionnaire [Fernando et al; Unpublished]

Preliminary results:	Medicine N=255	Others (architecture, health science, nursing) N = 339
sleep problems	47%*	61%*
sleep problems and depression (PHQ ≥ 10)	14%	19%
sleep problems + anxiety condition (GAD ≥ 8)	11%*	18%*
sleep problems and Delayed Sleep Phase Disorder	44%	4.1%
sleep problems and parasomnia	5%	3%
alcohol problem: CAGE ≥ 2	19%*	13%*

*statistically significant difference
GAD = Generalised anxiety disorder; PHQ = Patient Health Questionnaire

In another unpublished study of 1395 Year 12 and 13 high school students in New Zealand, approximately 37% had significant sleep problems (sleep apnoea 7.7%, delayed sleep phase 12%, parasomnia 18.8%), with depression (51.5%), anxiety (38.5%) and alcohol (12.2%) as the main probable cause. One girls' school in the North Island had a 40% rate of depression and one boy's school had 20-30% of students with diagnosable alcohol problems.

Evaluating insomnia

Evaluation of insomnia should be performed using clinical interview, sleep questionnaires (The Auckland Sleep Questionnaire developed by Bruce Arroll and Tony Fernando is available free from www.insomniaspecialist.co.nz) and by filling out a sleep diary for a couple of weeks (most insomniacs overestimate the severity of their insomnia). Sleep diaries can be very revealing not only in terms of the sleep data, but also in terms of the patient's personality type revealed by how they are filled out. Some of them have footnotes and Excel spreadsheets with analysis!

Overnight sleep studies are not usually required for insomnia. Indications for sleep studies are excessive daytime sleepiness or where the insomnia is severe and complicated medically.

The clinical interview should evaluate the following:

- When does the insomnia occur (early, middle or late)?
- Effects during the day? Are there safety issues (e.g. driving)?
- How did it start and how long ago?
- Are there any triggers?
- What is the sleep schedule – usual bed time, preferred bed time if on holiday, awakenings, time feeling really sleepy, final waking time, preferred waking time if on holiday?
- Daytime routines – meals, exercises, relaxation times, computer use, naps?
- Sleep conditions?
- Substances (caffeine, nicotine, recreational substances, prescribed drugs, over-the-counter agents)?
- Current and past sleep treatments?
- Other sleep symptoms?
- Psychiatric/medical/family history of sleep symptoms?

Non-drug treatments for insomnia

Most importantly find and treat the underlying cause if possible (i.e. depression). Improving sleep hygiene (avoiding caffeine, following routines) works occasionally in those with chronic insomnia, but it works better in those with occasional insomnia. The best recommended treatment is Cognitive Behavioural Treatment for Insomnia in which the most important factor is a sleep rescheduling protocol, which works in about 70% of chronic primary insomniacs. Dr Fernando and colleagues recently published instructions on undertaking a brief behavioural intervention protocol in the BMJ.[1] Another treatment that is worth considering is mind-training exercises to decrease hyperarousal at night (see www.calm.auckland.ac.nz).

Dr Fernando pointed out that while meditation on its own will not treat insomnia, it can improve the quality of sleep by developing a calm and relaxed mind. Patient meditation courses are also run free of charge at Auckland Hospital on Thursday evenings (see http://www.facebook.com/groups/295386480555708/). Furthermore, sleep rescheduling may be helpful and involves limiting the time spent in bed to the total duration of fragmented sleep. This forces the sleep period to be consolidated.

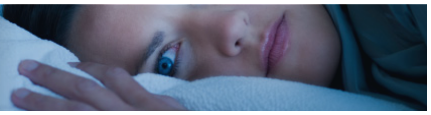
Bright light exposure can also help improve insomnia (5-10 000 lux in the morning before 9 am), although sun exposure is better. Such treatment has mild antidepressant effects, wakes the brain up and indirectly improves sleep the following night. Dr Fernando advises patients to have 30 minutes of sun exposure (without sunglasses) immediately after waking if possible. He also advises going for a walk in the morning towards, rather than away from, the sun.

Excessive daytime sleepiness

Excessive daytime sleepiness is very common, defined by difficulty in maintaining desired wakefulness, falling asleep at inappropriate times or an excessive amount of sleep.

A range of different conditions can present as excessive daytime sleepiness:

- Sleep deprivation
- Sleep apnoea (very loud snoring, observed apnoeic episodes, large neck, excessive daytime sleepiness, fatigue)
- Narcolepsy (sudden sleep attacks or dreaming) – not common 1/10000 people, <1000 patients in New Zealand
- Idiopathic hypersomnia (sleepy for excessive periods, e.g. 17 hours per day)
- Substances and medications including psychotropics (e.g. selective serotonin reuptake inhibitors [SSRIs] for depression – if excessive daytime sleepiness is observed check whether reducing SSRI dose resolves the problem, rather than assuming it's a symptom of depression)
- Circadian rhythm disorders
- Restless legs syndrome, periodic limb movements (can be violent movements), parasomnias (sleep talkers and sleep walkers)
- Depression
- Neurologic conditions



Evaluating excessive daytime sleepiness

Clinical interview should determine the degree of sleepiness versus fatigue. With sleepiness, individuals cannot keep their eyes open and keep nodding off, and they may yawn constantly. With fatigue there is just lack of energy. Dr Fernando stressed that it is also important to differentiate from normal circadian dip in alertness – It's normal to feel sleepy after lunch!

The clinical interview should evaluate the following:

- Collateral information from family members as to what they have observed about the patient with regard to their sleep pattern is also very valuable.
- The most important quantitative measure is the Epworth Sleepiness Scale (see http://epworthsleepinessscale.com/about-epworth-sleepiness/).
- For excessive sleepers, Dr Fernando would normally do an overnight sleep study in order to rule out sleep apnoea for example.
- A Multiple Sleep Latency Test (MSLT) can also be conducted.

Treating excessive daytime sleepiness

Find out the cause of the excessive daytime sleepiness and treat the cause if possible. For sleep apnoea treatment, Continuous Positive Airway Pressure is gold standard therapy, though surgery may work in some people. Weight loss can work for mild sleep apnoea. Modafinil [Modavigil®] can also be used to wake people up. For idiopathic hypersomnia/narcolepsy, modafinil and/or traditional stimulants should be considered.

Jetlag/shift work

Dr Fernando suggests speeding up adaption by assuming the time of day in the new time zone, then one or two hours before sleep take melatonin (not just before sleep) – sometimes a benzodiazepine (zopiclone, triazolam) may be needed. This should be followed by bright light therapy in the morning. Modafinil can also be used to help wake up.

Parasomnias

These are undesirable physical or experiential events that occur during sleep and can be subdivided into non-rapid eye movement (non-REM) parasomnias and REM parasomnias. Non-REM parasomnias include sleep walking, sleep talking, sleep shouting, confusional arousals, sleep driving and sexual behaviours. REM parasomnias include nightmare disorder, REM behaviour disorder and sleep paralysis. Other parasomnias can include sleep related dissociative disorder, sleep enuresis and sleep-related eating disorder.

Dr Fernando recalled his experience of sleep paralysis as a student, which included unusual perceptual issues such as seeing a tree starting to move towards him and start strangling him.

Evaluating parasomnias

The clinical interview should evaluate the following:

- Sleep quality
- Unusual activities/events at night
- Duration, severity, frequency of events
- Effects the following day

It is important to ascertain if there is any collateral information such as video or audio recorded by family members on smartphones. There is a useful iPhone application, called `Sleep Talker', to record sleep talking or snoring. An overnight sleep study, which is the gold standard, is important, but if nothing significant is captured it does not necessarily mean that it does not occur on other occasions.

Treating parasomnias

As for the other types of sleep disorders, first find the cause. One common cause is obstructive sleep apnoea, so screen and treat for co-morbid sleep apnoea if identified. For those with primary parasomnias decrease stress, cut back on alcohol (alcohol has been involved in parasomnias who have committed crimes during sleep), think about environmental safety (for sleep walkers take ground floor rooms and put obstructions in place etc), and use low-dose hypnotics in moderate to severe cases (clonazepam). Anticonvulsants and antidepressants are also used.

Sleep in depression

Insomnia is a major symptom of mood disorders, it is observed in 60-80% of cases of depression. Dr Fernando explained that if one has a patient who they think has depression, but they sleep normally, chances are they do not have clinical depression. A small number of patients with depression have hypersomnia (about 20%). When one looks at the sleep of depressed people, they have a different EEG pattern to normal people. Polysomnogram of depression indicates sleep disruption (initial, middle and late), REM sleep changes (onset is earlier) and reduction of slow-wave (deep, refreshing) sleep. Treatment of insomnia is important in the context of depression, because insomnia can be an early warning sign of depression and residual insomnia in treated depression increases the risk of relapse.

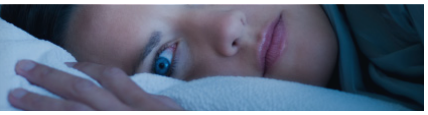
Medications to treat insomnia

Medications include sleep promoters such as gamma-aminobutyric acid (GABA) promoters (benzodiazepines,`Z drugs' [zopiclone]), melatonin and analogues (melatonin needs to be taken 1-2 hours before the target sleep times and does not treat chronic insomnia), tricyclic antidepressants and antipsychotics. Tricyclic antidepressants and sedating antipsychotics are not sleep promoters so much as wake blockers and have more side effects than the GABA promoters which enhance sleep. Other wake blockers include quetiapine and antihistamines. Antipsychotics should not be used as first-line treatments for insomnia, the primary concern is tardive dyskinesia and weight gain. Tardive dyskinesia is not that common anymore with the newer agents, but if you're using antipsychotics to treat insomnia, make sure its' use can be justified (i.e. other agents have been tried).

Patients respond differently to different benzodiazepines, they may do well on triazolam, but not respond to lorazepam or do fine on diazepam. Dr Fernando explained that this phenomenon doesn't make any sense and one can't write off the whole family of drugs because the patient did not respond to one member.

Antidepressants

Antidepressants and their effect on sleep are outlined in Table 2. All of the classes of antidepressants have different mechanisms of action and therefore have different sleep effects. A couple of examples are the sedating tricyclic antidepressants (TCAs), which are good in terms of sleep. The SSRIs on the other hand,



are notorious for causing sleep problems so they tend to be administered in the morning. However, some patients prefer to take SSRIs at night because they find it helps them sleep. So there is no overall rule and therapy needs to be individualised for each patient.

Mirtazapine, a noradrenergic and specific serotonergic antidepressant, is a newer agent, which has potent antagonist properties at presynaptic α-2 receptors to increase release of 5-hydroxytryptamine (5HT) and norepinephrine (NE), and an ability to increase slow-wave sleep. Mirtazapine can cause weight gain and extreme sedation. Dr Fernando would not continue to treat a patient with this agent if it caused them to gain weight.

Table 2: The effect of antidepressants on sleep

Drug	Mechanism relevant to sleep	Effect on sleep
Sedating TCAs: amitriptyline, doxepin	H1 antagonist, 5HT reuptake inhibition, NE reuptake inhibition, α-1 antagonist, M1 antagonist	Shorten sleep latency, increase TST, increase deep sleep, REM suppression
Activating TCAs: desipramine, protriptyline	NE reuptake inhibition	Increase sleep latency, increase awakenings, decrease TST
Trazodone	5HT2 antagonist, 5HT1A/C antagonist, H1 antagonist, α-1 antagonist, weak 5HT reuptake inhibition	Increase TST, increase SWS, +/- REM suppression
SSRIs	5HT reuptake inhibition	Increase sleep latency, decrease sleep continuity, increase awakenings, decrease TST, REM suppression
Nefazodone	5HT2 antagonist, 5HT reuptake inhibition	Increase sleep continuity, no REM suppression, preserved sleep architecture
Bupropion	DA and NE reuptake inhibition	Increase sleep efficiency, decrease REM latency, increase REM sleep time
Venlafaxine	5HT and NE reuptake inhibition	Increase awakenings, decrease stage 2 and 3, REM suppression, increase PLMs
Mirtazapine	5HT2 (a,c), H1, 5HT3 antagonist	Decrease sleep latency, increase total sleep time, increase deep sleep

DA = dopamine; NE = norepinephrine (noradrenaline); PLMs = periodic limb movements; REM = rapid eye movement; SSRIs = selective serotonin reuptake inhibitors; SWS = slow-wave sleep; TCAs = tricyclic antidepressants; TST = total sleep time; 5-HT = 5-hydroxytryptamine receptor

Antipsychotics

Antipsychotics include quetiapine, a $5HT_2$, H1 antagonist, which is commonly used in psychiatry for sleep and substance abuse to increase sleep continuity and total sleep time. Dr Fernando would not use quetiapine in general practice as a first- or second-line agent for sleep, because of the risks of weight gain and tardive dyskinesia. It can be used in patients with mood disorder and chronic fatigue, who can't sleep.

Benzodiazepines

Benzodiazepines (including zopiclone, temazepam, triazolam and lorazepam) are used to decrease sleep latency and awakenings, but the quality of sleep is not normal on these agents. EEG indicates it's not deep sleep, and most patients stay in stage 2 sleep (the best sleep is in stage 3 and 4). However, in those who have really bad sleep, stage 2 sleep is better than no sleep. These agents also have a range of issues such as tolerance and dependence, which are thought to occur in less than 10% of patients, but those are the ones we remember! Dr Fernando reported on one of his patients who was taking 32 zopiclone tablets per night! Other issues include psychological dependence, rebound insomnia and new-onset automatism (unusual behaviour while asleep).

One must balance the risks with medication (dependence, tolerance, falls, lack of coordination) against those without medication (sleep, worsened depression, anxiety, poor memory, falls, lack of coordination). Dr Fernando commented that from his personal experience, British, New Zealand, South African and Australian people are generally "benzophobes", while Americans are "benzophiles" He pointed out that some doctors here will even prescribe barbiturates rather than benzodiazepines. He believes that benzodiazepines do have a place and the risk/benefit for each patient needs to be weighed up.

Natural remedies

Natural remedies that have been reported to be of some benefit for sleep symptoms include melatonin, kava, valerian and tart cherry juice.

References

1. Falloon K et al. The assessment and management of insomnia in primary care. BMJ. 2011;342:d2899.