

Management of Sleep Disorders in Psychiatry

Dr Hugh Selsick

Insomnia & Behavioural Sleep Medicine Clinic UCLH

Sleep Disorder Centre Guy's Hospital

Six Categories of Sleep Disorders

- Breathing disorders e.g. obstructive sleep apnoea.
- Insomnia – not able to get enough sleep.
- Movement Disorders e.g. restless legs, periodic limb movements.
- Circadian rhythm disorders – body clock out of sync with outside world e.g. delayed sleep wake phase disorder.
- Hypersomnolence e.g. narcolepsy, idiopathic hypersomnia.
- Parasomnias – unwanted experiences and behaviours in the night:
NREM - sleepwalking, night terrors; REM – REM sleep behaviour disorder, nightmares.

Insomnia

- Difficulty initiating or maintaining sleep.
- Despite adequate opportunity.
- Leading to daytime consequences.
- Such as tiredness, low mood, cognitive dysfunction, irritability.
- Significant risk factor for depression – both first episode (Ford, 1989) and relapse (Cho, 2008).
- Same impact on quality of life as congestive heart failure and major depressive disorder (Katz, 2002).

Chemicals and Sleep

Promote Wakefulness:

- Glutamate
- Noradrenaline
- Serotonin
- Acetylcholine
- Histamine
- Dopamine
- Orexin/hypocretin

Promote sleep:

- GABA
- Adenosine
- Melatonin

To Treat Insomnia

Reduce activity of:

- Glutamate
- Noradrenaline
- Serotonin
- Acetylcholine
- Histamine
- Dopamine
- Orexin/hypocretin

Enhance activity of:

- GABA
- Adenosine
- Melatonin

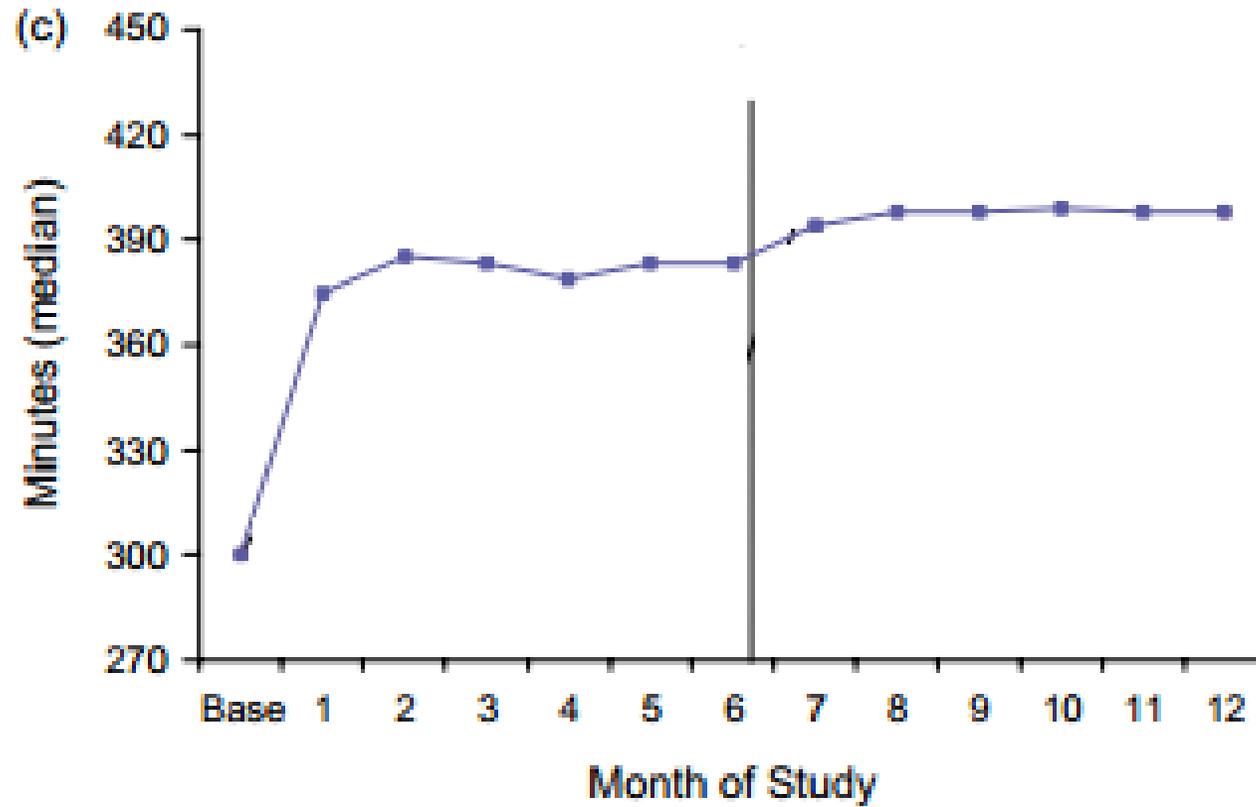
GABA-ergic Drugs

- Benzodiazepines and cyclopyrrolones (z drugs).
- GABA-A receptor positive allosteric modulators with varying degrees of specificity for the various alpha subunits.
- At hypnotic doses they are relatively similar, though the z drugs are more specific hypnotics with fewer muscle relaxant, respiratory depressant, anticonvulsive and anxiolytic effects.
- This may make them safer and less addictive.
- Despite their reputation addiction is not inevitable with these medications.

Do They Work?

Significantly different from placebo	Sleep onset latency		Total sleep time		Wake time after sleep onset		Sleep quality
	Self-rated	PSG	Self-rated	PSG	Self-rated	PSG	
Temazepam	(✓)*	(✓)*	✓	✓	✓	✓	✓
Zopiclone	✓	✓	✓	✓	✓	✓	✓
Zolpidem	✓	✓	✓	✓	✓	No	✓

Do they work in the long term?



(Roth, 2005).

Do They Work When You Stop Taking Them?

- If insomnia is acute and time limited this doesn't really matter.
- Once the medication is discontinued the effect is lost (Riemann, 2009).
- Therefore a “short course of hypnotics just to reset the sleep cycle” doesn't work.
- When the doctor discontinues the medication the patient will experience a recurrence of symptoms and will ask for more.
- This is often mistaken for addiction.

The Two Z's and some Pams

	T_{max} (hours)	T_{1/2} (hours)	Hangover
Zopiclone	0.5-2	5-6	Yes
Zolpidem	1.7-2.5	1.5-2.5	Probably not
Temazepam	1-3	8-20	Maybe
Clonazepam	1-2	35-40	Yes

Melatonin for Insomnia

- Reduces sleep onset latency.
- Improves sleep quality.
- Effect is modest compared to other hypnotics.
- Excellent safety profile.
- May be a good first choice if there is no urgency to treat insomnia.
- Licensed for over 55, and children.



Histamine Antagonists

- Pure antihistamines can be very effective and well tolerated hypnotics.
- Doxepin at low doses is a very pure antihistamine and 3-6mg doxepin is licensed as a hypnotic in USA.
- Peak sedative effect occurs about 90 minutes after the peak plasma level.
- Therefore really useful for sleep maintenance insomnia.
- Doesn't appear to raise the arousal threshold.

So Are OTC Antihistamines Advised?

- Antihistamines are frequently advised as they are perceived to be safer than benzos and z drugs.
- This may be due to the fact that they are not prescription drugs.
- But at therapeutic doses they all have significant anticholinergic effects.
- They will therefore add to the anticholinergic burden with all the attendant risks with regard to cognition, GIT and cardiac side effects.
- They also have long half lives which lead to daytime sedation.

Using Hypnotics in Depression

- Benzo receptor agonists commonly prescribed in early stage of antidepressant treatment.
- This is effective at improving sleep and does not interfere with antidepressant action (Howland, 2011).
- Eszopiclone led to improvements in sleep and an improved response to fluoxetine in depressed patients (maintained after discontinuation(Krystal, 2007)), an effect that has not been found with other non-benzodiazepine hypnotics (Fava, 2006).
- Studies have found benefit in combining antidepressants with benzodiazepine hypnotics, both in terms of sleep and antidepressant response (Jindal, 2009).

Using Hypnotics in Bipolar Disorder

- Ramelteon (melatonin agonist) does not improve sleep in mania (McElroy, 2011; Schaffer, 2011), but does halve relapse rates in euthymic bipolar patients with sleep disturbance (Norris, 2013).
- Zolpidem, zolpidem controlled release (CR), and eszopiclone were generally safe and effective (Schaffer, 2011).
- In bipolar patients at a Li clinic patients prescribed sedative antidepressants for their insomnia had a greater risk of manic relapse. Those patients prescribed anxiolytic or hypnotic medication for their insomnia had a lower risk of relapse and longer periods of mood stability (Saiz-Ruiz, 1994).

Using Hypnotics in Schizophrenia

- Low level evidence to suggest that Zopiclone may lead to greater improvements in sleep and negative symptoms than benzodiazepines (Naofumi, 1994).
- Eszopiclone improved sleep and cognitive function relative to placebo. On discontinuation of drug sleep remained better in eszopiclone group but cognitive benefits lost (Tek, 2014).
- Two studies showed benefit of melatonin in schizophrenic patients (Shamir, 2000; Suresh Kumar, 2007).

Antidepressants

- Using antidepressants and antipsychotics for insomnia is a common practice. This is all off label prescribing.
- This is despite a relatively small evidence base for this practice.
- But choosing a sedative psychiatric medication where there is comorbid insomnia is sensible.
- Of the antidepressants the best evidence (and clinical experience) is for Trazodone (anti-noradrenergic), doxepin and mirtazapine (antihistamine).

1. Krystal, A., 2010. *In Foundations of Psychiatric Sleep Medicine*
2. BAP consensus statement on evidence-based treatment of insomnia, parasomnias and circadian rhythm disorders 2010

Antipsychotics

- Switching from typical to atypical antipsychotics improves sleep parameters.
- Quetiapine (25-75mg) found to enhance sleep in insomniacs (open label) and olanzapine in healthy volunteers.
- Quetiapine improves sleep in patients with MDD, bipolar depression and schizophrenia.

Before You Prescribe For Insomnia – Check That They Have Insomnia!

Could they have restless legs?	The treatment is different. Antihistamines, antidepressants and antipsychotics can make it worse.
Could they have a circadian rhythm disorder?	Insomnia drugs will be of very limited benefit.
Could they have untreated obstructive sleep apnoea?	Treating with hypnotics could mask a disorder which has severe consequences.

Before You Prescribe For Insomnia – Check That You Haven't Caused It!

- Are they on:
 - An SSRI?
 - SNRI?
 - B-blocker?
- Are they taking these drugs at night?
- Are they on a slow release formulation?
- Could you switch to:
 - Mirtazapine/Trazodone/Pregabalin?

Pluck the Low Hanging Behavioural Fruit

- Are there any obvious and major maladaptive behaviours that I can correct.
- Excessive caffeine
- Daytime napping.
- Long lie-ins in the morning/inconsistent rising times.
- Going to bed way too early.

Choosing a Hypnotic – Things to Consider

- Are they a sole carer? Is it appropriate to use a hypnotic if they may need to attend to a child in the night? Histamine antagonists are theoretically preferable if medication is unavoidable.
- Have they developed tolerance to a particular drug, or not responded at all to that drug, in the past? If so, it may be better to choose a drug with a completely different mode of action.
- Always check for interactions – many drugs reduce the metabolism of widely used hypnotics. A dose adjustment may therefore be required.

Choosing a Hypnotic – Think About the Duration of Action

- Are they at risk of falls? If so, it is sensible to select shorter acting drugs (though hard evidence for this is lacking).
- When in the night do they have difficulty with sleep? If sleep initiation is the problem then consider a short acting drug e.g. zolpidem, if the problem is later in the night then use a longer acting drug e.g. zopiclone, histamine antagonist/antidepressant.
- Do they drive? One should not drive for at least 8 hours after zolpidem and 13 hours after zopiclone – so use melatonin or zolpidem if they drive in the morning.

CBT for Insomnia

- There is a large and growing evidence base for the efficacy of CBT for Insomnia (CBT-I).
- Unlike medication this often has durable effects and continues to work long after the therapy has finished.
- It can be delivered individually, in groups, in books, or online.
- It is composed of a number of individual, circumscribed techniques that can be taught quickly as part of a psychiatric consultation.
- But it is still not widely available.

CBT-I in Psychiatric Conditions

Condition	Improves insomnia	Improves Psychiatric Sx
Major Depressive Disorder	Yes	Yes (possibly as much as CBT for depression)
Bipolar Disorder	Yes	Yes (reduces likelihood of relapse)
Psychotic Disorders	Yes	Yes (reduces delusions)
PTSD (CBT-I + IHT)	Yes	Yes
Alcohol Dependence	Yes	No (no reduction in relapse rates)

Blom, K. *et al.* (2015) 'Internet treatment addressing either insomnia or depression, for patients with both diagnoses: a randomized trial.', *Sleep*, 38(2), pp. 267–77

Harvey, A. G. *et al.* (2015) 'Treating insomnia improves mood state, sleep, and functioning in bipolar disorder: A pilot randomized controlled trial.', *J of Consulting and Clinical Psychology*, 83(3), pp. 564–577.

Myers, E., Startup, H. and Freeman, D. (2011) 'Cognitive behavioural treatment of insomnia in individuals with persistent persecutory delusions: A pilot trial', *Journal of Behavior Therapy and Experimental Psychiatry*. Pergamon, 42(3), pp. 330–336. doi: 10.1016/J.JBTEP.2011.02.004.

Ulmer CS, Edinger JD, Calhoun PS. A multi-component cognitive-behavioural intervention for sleep disturbance in veterans with PTSD: a pilot stud. *J Clin Sleep Med*. 2011;7(1):57-68.

Arnedt, J. T. *et al.* (2011) 'Cognitive-Behavioral Therapy for Insomnia in Alcohol Dependent Patients: A Randomize Controlled Pilot Trial', *Behavior Research and Therapy*, 49(4), pp. 227–233.

Restless Legs Syndrome

- Uncomfortable sensation – can be anywhere in the body, but usually the legs.
- Worse at night.
- Worse at rest.
- Temporarily relieved by movement.
- Easy to localise but hard to describe.
- Manifests as sleep onset insomnia.

Diagnosing RLS

- General physicians correctly diagnose RLS in less than 10% of patients (Hening, 2004).
- It is surprisingly rare for patients to volunteer RLS symptoms. You need to specifically ask about them.
- A single question has been shown to have 100% sensitivity and 96.8% specificity for RLS in a neurology outpatient population (Ferri, 2007):
- “When you try to relax in the evening or sleep at night, do you ever have unpleasant, restless feelings in your legs that can be relieved by walking or movement?”

Aetiology

- Dopamine antagonists.
- Histamine antagonists
- Peripheral nerve irritation.
- Iron deficiency
- Pregnancy
- Diabetes
- Renal Dysfunction
- Peripheral neuropathy
- Psychiatrists

Psychiatrists?

- Many psychiatric drugs promote RLS:
- SSRI's
- SNRI's
- Mirtazapine
- Tricyclics
- Antipsychotics
- B-blockers
- Lithium

RLS & Depression

- Symptoms of depression are common in RLS (Hornyak, 2010).
- Some data to suggest treating RLS improves depression (Pichiatti, 2005).
- 35% of patients with Restless Legs and Depression report suicidal ideation as a result of their restless legs (Becker, 2006).

Treating RLS

- Iron (if ferritin < 75 mcg/L).
- Change their medication if possible.
- Dopaminergics e.g. ropinirole, pramipexole, rotigotine – low doses, but risk of psychosis & compulsive behaviours.
- Anticonvulsants – pregabalin, gabapentin
- Clonazepam
- Opiates

Practice Points

- Always ask about restless legs.
- Always ask again after changing medication.
- Be aware of the risk of exacerbating or causing RLS when prescribing, particularly drugs with anti-histamine action.
- RLS is a clinical diagnosis. You can diagnose it and initiate treatment in your clinic.

Nightmares - Definition

- Repeated occurrences of extended, extremely dysphoric, and well remembered dreams that usually involve threats to survival, security or physical integrity.
- On awakening the person becomes rapidly oriented and alert.
- The dream or the sleep disturbance causes significant distress or impairment in social, occupational or other areas of functioning e.g. mood disturbance, sleep resistance, cognitive impairment, sleepiness.
- Broadly divided into idiopathic and PTSD related. Most research has been done in PTSD.

Nightmares and Suicide



- Nightmares are associated with a 5 fold increase in risk for high suicidality.
- This relationship remains after adjusting for psychiatric diagnosis and symptom severity. (Sjostrom, 2007)

Treatment Strategies:

Prazosin

Alpha 1 antagonist.

- Prazosin is recommended for treatment of PTSD related nightmares in military and civilian patients.
- Average dose of 3mg, although in military populations may be as high as 10-13mg.

Clonidine

- Alpha 2 agonist.
- Dose range: 0.2-0.6mg

Trazodone

- Alpha1 antagonist.
- Survey of 74 PTSD pts: reduced nightmares in 79% of patients with complete remission in 50%.
- 91% of full responders were on 100mg.

May Also Consider:

- Atypical antipsychotics – Olanzapine, risperidone and aripiprazole
- Topiramate – civilians with PTSD. Final dosage 100mg or less in 91% of full responders.
- Gabapentin – mean dose of moderate to marked improvement 1344mg.

Imagery Rehearsal Therapy

- Recall the nightmare.
- Write it down.
- Alter the theme, ending etc.
- Rehearse the new version.
- Effective in PTSD and idiopathic nightmares.
- Lucid dreaming therapy where the patient learns to rescript the dream from within the dream may be effective in PTSD and idiopathic nightmares, especially if delivered individually. (Level C)

Progressive Muscle Relaxation

- Idiopathic nightmares.
- Progressively tense and relax muscles.
- Really easy to teach and do.
- May be useful to practice it during day a few times if bedtime is very stressful.
- Soundcloud: search “sleepresources”, click on PMR and let my dulcet tones chill you out.

Questions?

- hugh.selsick@nhs.net

