Rational diagnosis and management of insomnia

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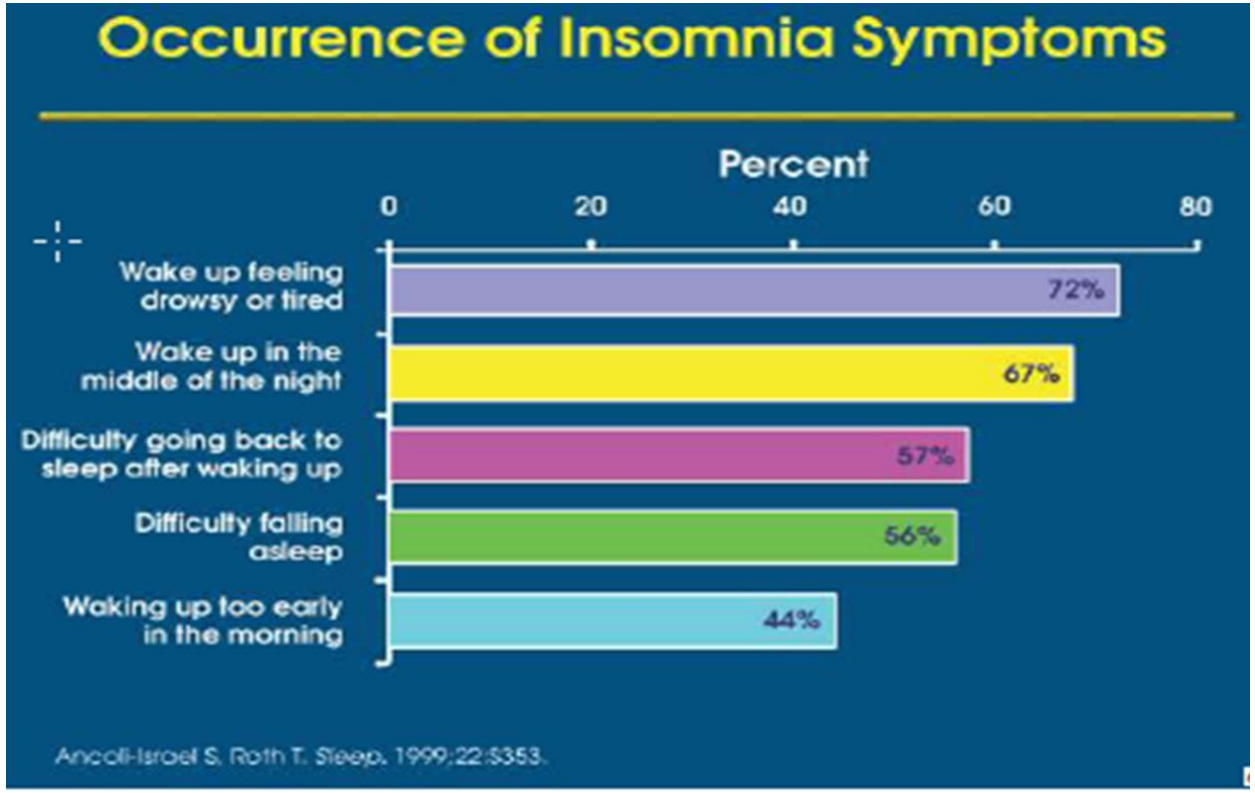
ABentleyInc – home studies

Overview

- What are we treating?
- Different types of non-hypnotic medications
  - OTC
  - Benzodiazepines
  - Antipsychotics and anti-depressants
- Hypnotics – use and abuse
- Appropriate use of hypnotics
- Cognitive behavioural therapy

Types of insomnia

- Different symptoms of insomnia
  - Difficulty falling asleep
  - Waking during the night
  - Waking too early in the morning
- Most patients have more than one symptom
- Symptoms often not specific for a particular diagnosis



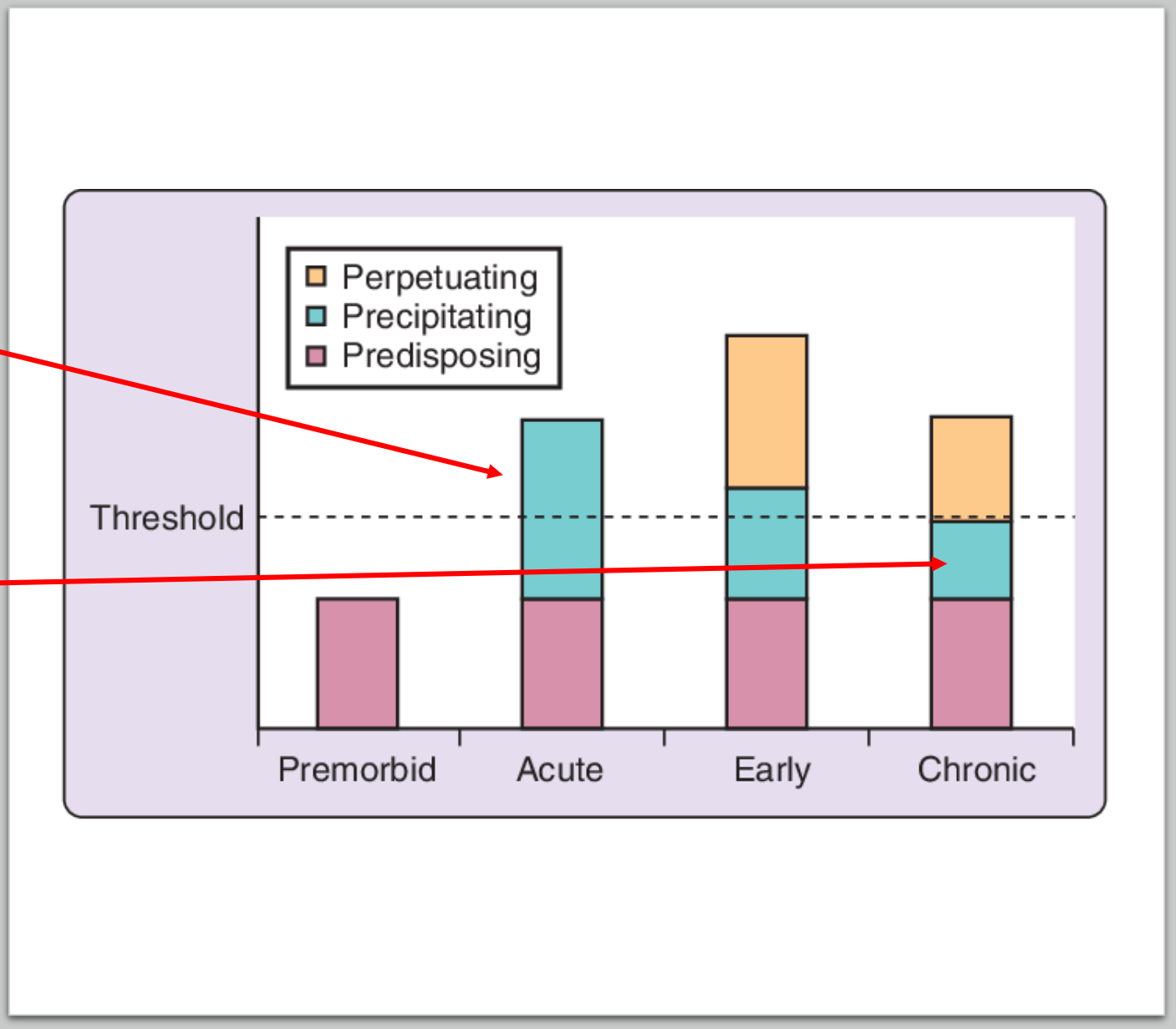
Prevalence and seeking treatment

- A substantial percentage of the population suffers from insomnia: estimates range up to 10% for insomnia disorder and 25% for insomnia symptoms .
- Even though insomnia is a very prevalent disorder, only 37% of those suffering from insomnia report consulting a healthcare provider for their sleep problems
- ? Because don’t want medications
- Don’t believe doctors can help them –
  - short consultations
  - Won’t listen to the story
- Rather go to pharmacist for ‘healthy’ alternative

Luik et al 2019

Insomnia

- Acute or short-term
  - Is a symptom
- Chronic – DSM-5:
  - Called insomnia disorder and it must be present for 3 months – is an independent disorder
- Insomnia other – usually secondary causes
  - Can be chronic - symptom



Chronic insomnia: Perpetuating factors

- Anxiety and errors of cognition then incorrect sleep behaviours – cognitive-behavioural origins
- Wrong sleep hygiene
  - Go to bed earlier – “if I get 5 hours of sleep when I am in bed for 8 hours then I will get more sleep if I spend more time in bed”
  - Lying in bed – “at least I am resting”
  - Finding external fault – “ the fridge is too loud, I need to go to the toilet”
  - Avoiding reality – “ I won’t look at the clock so that it doesn’t bother me”

What are the common causes of insomnia?

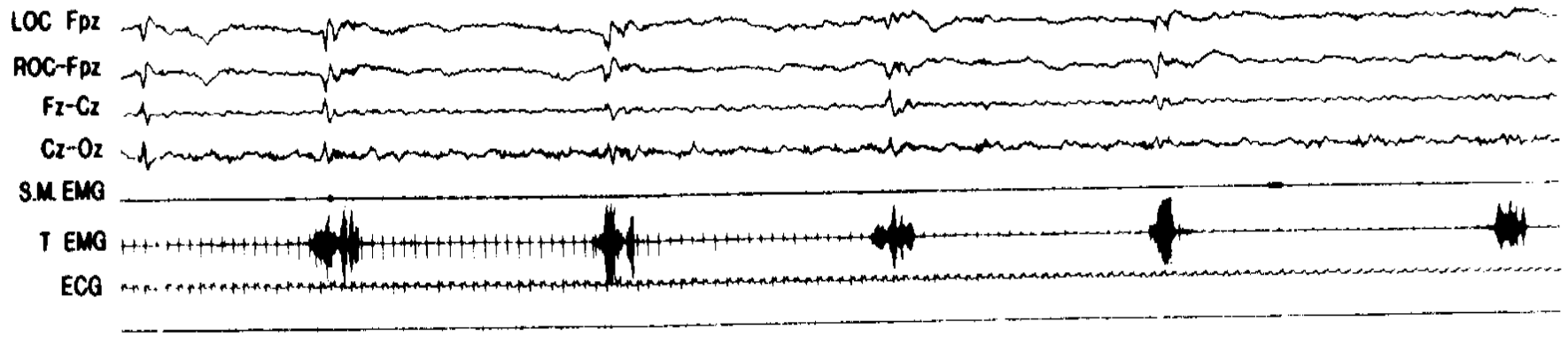
- Medical - Time of onset of insomnia and medical disorder or medical treatment is the same
- Environmental
- Sleep disorders
  - Restless legs syndrome and periodic limb movement disorder
  - Circadian rhythm disorders
  - Obstructive sleep apnea
- Psychiatric disorders
- Psychophysiological insomnia
  - Fall asleep on the couch but not when they go to bed

Restless legs syndrome

RLS – delayed sleep onset
PLMD – waking or non-restorative sleep

- An urge to move the legs often associated with an uncomfortable sensation
- Relieved by movement
- Worse at night
- Worse at rest

Periodic limb movement disorder



Use of melatonin: Circadian rhythm disorders

- Jet lag
- Shift work
- Delayed sleep phase syndrome
- Advanced sleep phase syndrome

Always about a normal sleep period and normal melatonin happening at the wrong time of the day

- Elderly
- Blindness
- Neurodevelopmental disorders
- Depression
- Alzheimers
- ?Delirium in ICU

Problem with reduced or irregular melatonin secretion

May need long term use – maybe life-long – safety data for 12 months

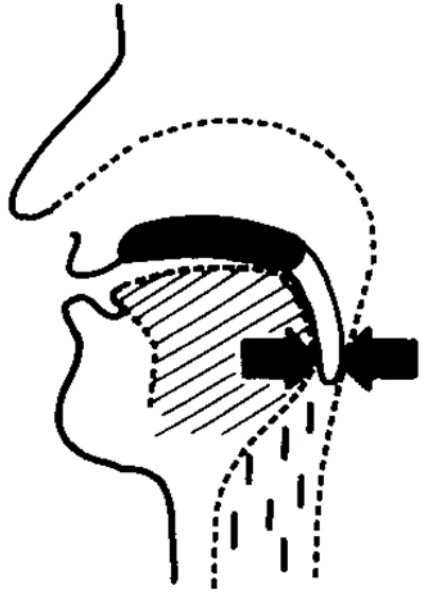
Obstructive sleep apnea and insomnia

- 2591 patients with insomnia – questionnaire on OSA confirmed on PSG
  - OSA≥5 = mild OSA 76.3%,
  - OSA≥15 = moderate OSA 53.1%
  - OSA≥30 = severe OSA 32.6%

Duarte 2019

- Male symptom phenotypes (Iceland):
  - excessive daytime sleepiness 42%,
  - disturbed sleep/insomnia 33% and
  - minimally symptomatic 25%

(Ye 2014)



- Should do a STOP BANG on persistent insomnia
- Daytime sleepiness not a good predictor
- CPAP resolves insomnia

When do patients start taking hypnotics?

- Patient requests:
  - Frequency of symptoms – the more symptoms the more likely to request medication
  - Difficulty falling asleep double the likelihood of being reported
  - Generally low level of reporting insomnia to doctors – pharmacists more likely
- Increasing age, increasing insomnia severity *Morin et al 2004*
- 16% take hypnotics in GP practices (prevalence of insomnia 55%)
  - Highest taking of hypnotics – older age group *Bjortvan 2017*
- Multi – morbidity – patient who have more than one disorder
  - OR for hypnotics use ranges from 7 (1-19 years old) to 20 (>70 years old)

What happens if you don’t treat? OTC use

- Herbal: Valerian, Lavender, Hops, Chamomile – some evidence they work
- Anti-histamines – some evidence but not consistent
- Alcohol – rapid tolerance and many side effects
- Cannabis:
  - Smoked dagga – rapid tolerance, severe rebound insomnia and nightmares on stopping
  - CBD oil – no real evidence in primary insomnia – does help in secondary insomnia related to pain and anxiety

Other Scripted medications

Tricyclic anti-depressants

- Amitryptaline – very little evidence in primary insomnia
- Doxepin – sleep maintenance but not sleep onset
- Trazadone - subjective improvement not objective. Side-effects
- Anecdotally - significant increase in total sleep time
- Increased daytime somnolence
- No evidence for use or continued efficacy in the long term

Anti-psychotics

- Quetiapine
- Failed to show any increase in total sleep time / reduction in sleep latency/ improvement in sleep satisfaction and its use for primary insomnia is considered low quality evidence
- Does improve sleep in treatment-resistant depression
- Some patients sleep well – very long acting – daytime somnolence
- No evidence for use or continued efficacy in the long term

Atkin 2018

Do hypnotics work? Do they give you normal sleep?

- Benzodiazepenes
  - Decreased stage 3 and 4 (slow wave sleep)
  - Decreased REM sleep
  - Increased light stages of sleep (stages 1 and 2)
- Z-drugs
  - No changes in sleep architecture

- **Do they work?**
- shortening the time it takes to fall asleep
- increasing total sleep time
- decreasing the number of awakenings
- improving sleep quality

Compared to insomnia sleep stages hypnotics improve sleep stages because of increased total sleep time

Studies over 6 months show continued efficacy and safety

Risk of hypnotics may be better than risk of ongoing insomnia

Starting patients on hypnotics

- Philosophy:
  - Aim for optimization of functioning which is more indicative of recovery and treatment effectiveness than reduction of symptoms (Guina 2018)
- Correct diagnosis
  - Manage any cause of insomnia first and see if any symptoms remain
- Pick most appropriate hypnotic
  - Short-acting for sleep onset difficulties
  - Longer-acting for waking during the night
  - Try not to use very long-acting sedatives
- Add some CBT to ensure maximal effect of hypnotic
  - Also creates focus on daytime function rather than symptoms

Intermittent versus nightly dosing

- Equivalent efficacy and no rebound insomnia when using between 3 and 5 tablets per week.
  - Rather script 3 tablets per week versus ‘use when desperate’
- Patients reported a similar improvement in sleep onset latency and total sleep time for nightly and non-nightly use of a hypnotic.
- There is currently no evidence that the intermittent strategy is equal or superior to nightly dosing but that it does create similar clinical outcomes which remain as stable over time as nightly dosing *Perlis et al 2008*
- In addition, there appears to be less dose escalation and adverse events.
- With the lack of rebound insomnia intermittent hypnotic use may lead to less remissions and less dependency on hypnotics in the long term.

How do you know there's a problem?

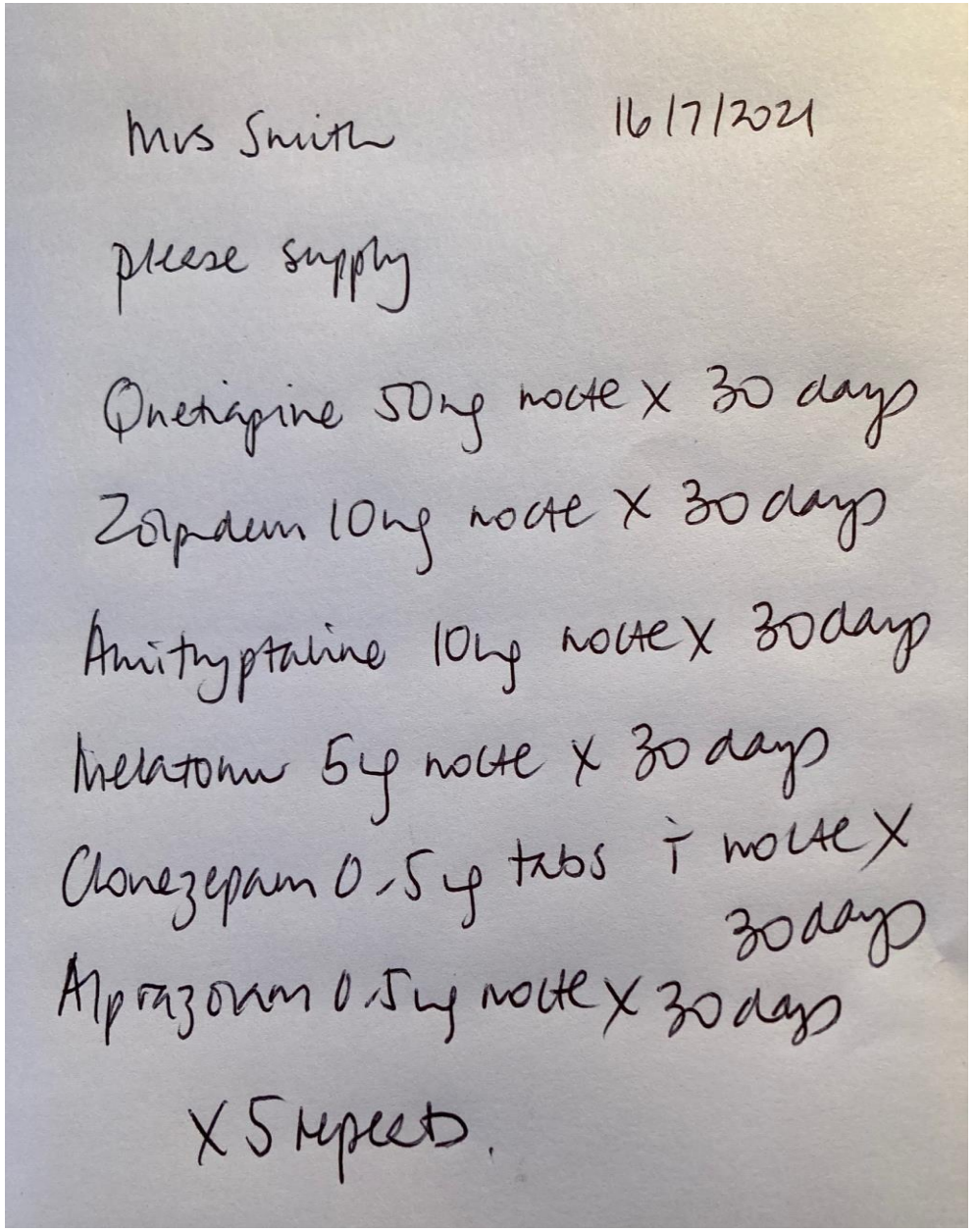
- Poor or no response to treatment
  - Rapidly increasing doses of hypnotics
  - Rapid changing of meds
- Multiple sedative medications required
  - Melatonin, anti-psychotic, hypnotics, tricyclic antidepressants
- Dependence / withdrawal symptoms

Poor response to medications

- Often seen as rapidly increasing doses of medications or rapid changing of medications
- Individual patient response to medications
- Incorrect diagnosis:
  - Lark / owl
  - Delayed sleep phase
  - Restless legs syndrome
  - Naturally short sleeper
- Patients taking them too early – ‘they take 2 hours to work’
- The danger is adding more medications.

The insomnia mega script

- No justification for this type of script
- Very few studies using even two medications together:
  - Usually double up on sedation or other side effects
  - Use P450 cytochrome like many other drugs
- Rationale: using other sedative pathways:
  - Anti-histamine
  - GABA
  - Melatonin
  - No evidence that this works



Dependence – ‘addiction’

- Hypnotics not really addiction:
  - Defn: chronic pattern of compulsive drug-seeking associated with a loss of control, preoccupation and anticipation and continued use despite psychosocial dysfunction and distress.
- Dependence:
  - Defn: Physical dependence is the presence of tolerance or withdrawal
  - Psychological dependence – cannot fall asleep unless they have taken hypnotic with relief of anxiety after taking meds
- Tolerance: the dose stops working and there is a desire to increase the dose
  - Therapeutic effects subject to tolerance but not adverse events
- Risk of dependence: In a study in American veterans < 1% of men and 41% of women used high doses within 180 days of initiation, and 20% continued to use zolpidem long-term (Kim 2019)

Appropriate uses of hypnotics

Acute / short-term insomnia

Long-term medical causes of insomnia

- Pain especially terminal pain
- Tinnitus

May have to stay on hypnotics if primary disorder cannot be treated properly.

Particularly in terminal patients

Reduce dose:

Intermittent versus nightly

Gradual tapering

Assist with cognitive behavioural therapy

Brief Behavioural therapy (BBT) / CBT-I

- For use by clinicians with too little time
- Not enough CBT-I practitioners anywhere in the world
  - If BBT doesn't work can send for more intensive CBT-I
- Shown to be effective in many situations with insomnia
  - Older adults, co-morbid depression, hypnotic-resistant insomnia, HIV
- Assists in withdrawal from hypnotics
  - Improves sleep and reduces withdrawal symptoms
- Contraindications: ESS >10, unstable psychiatric conditions

Sweetman et al 2021 AJGP

Treatment concepts – BBT and CBT-I

- Reduce your time in bed to consolidate sleep period (bed/ sleep restriction)
- Get up at the same time every day, no matter how poor the sleep was
- Do not go to bed unless sleepy
- Do not stay in bed if you do not fall asleep quickly (Stimulus control)

- Then document it all with a sleep diary
  - No bloods / xrays/ and other means of collecting data (maybe Fitbits)

Cognitive behavioural therapy

'He's tired – he was up all night worring about his sleeping pill consumption'

- Giving patient on hypnotics a course of CBT

  decreases use of hypnotics
  - 23-39% drop in usage depending on product.
  - 77% complete drug cessation with combination versus

  38% just taper (maintained for 12 months)
- According to AASM and systematic reviews:

  treatment with CBT has better long-lasting impact than hypnotics alone – <u>CBT is recommended for treatment of chronic insomnia</u>
- Has the same impact whether secondary (e.g. chronic pain) or primary insomnia
- Usually in 8 x 1-hour sessions but can be done by nurses / internet

Patient information leaflet on hypnotics (18% reduction)

- How insomnia and normal sleep works and causes of insomnia
- Medications used to treat insomnia
- Side effects of drugs
  - Confusion between symptoms (waking up tired) and medication side effects
- Options:
  - CBT
  - Tapering / intermittent use
  - Withdrawal effects
- High percentage of patients can get off medications. Only 1/3 of patients have problems during withdrawal
- Patient doctor contract – doctor needs to take supportive role

Symptoms with hypnotic withdrawal

- Recurrence – symptoms are identical to the symptoms for which hypnotics originally prescribed
  - Check diagnosis
  - Add CBT
- Rebound – Mirror image of therapeutic effects of hypnotics
  - Usually worse anxiety, insomnia and restlessness
- Withdrawal – symptoms that are unique to the medication and were not present before drug was started
  - Timing – short acting – start within 6-24 hours, peak between day 1-4 and improve by day 4-5
  - Long acting – start within 1-7 days, paek at 5-14 days and improve by 3-4 weeks

Withdrawal of hypnotics

- Session 1: Take basic sleep history
  Give info on basic sleep biology and hypnotics
  Give sleep diary

If acute insomnia treat for 7 nights

To come back in two weeks

Session 2: Check diary
Screen for organic sleep disorders
Add sleep restriction and stimulus control and drop hypnotic by 25%

To come back in two weeks

Session 3: Check diary
Check progress
Tweak medication – drop by another 25% if patient ready

If improving to repeat and come back in two weeks

If not improving refer

Sleep diary

Date and day		8 p.m. 20:00		9 p.m. 21:00		10 p.m. 22:00		11 p.m. 23:00		12 p.m. 00:00		1 a.m. 01:00		2 a.m. 02:00		3 a.m. 03:00		4 a.m. 04:00		5 a.m. 05:00		6 a.m. 06:00		7 a.m. 07:00		Score 1-5
	Night 1																									
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Length awake																										
Details	Time to bed - B Time up – U Took meds - M Woke up - W																	Score 1-5 (1 bad and 5 good) for:								

Other options for CBT-I

- Digital CBT therapy
  - large short-term effects and smaller long-term effects up to 1.5 years after treatment across populations with various co-occurring health problems.
  - Overall, evidence has consistently been demonstrating that dCBT for insomnia is efficacious in treating insomnia
  - More support, whether via a human therapist or automated, is generally thought to have positive effects on adherence and efficacy of dCBT for depression and anxiety. By increasing guidance, the treatment effect for CBT-I was increased and the number of failed treatments reduced
  - Meta-analyses have suggested effect sizes of dCBT for other disorders are in a similar range as face-to-face CBT

- Luik AI, van der Zweerde T, van Straten A, Lancee J. Digital Delivery of Cognitive Behavioral Therapy for Insomnia. Curr Psychiatry Rep. 2019 Jun 4;21(7):50. doi: 10.1007/s11920-019-1041-0.

Conclusion

- Make sure diagnosis is correct to allow use of correct medication with best chance of working
- Hypnotics are appropriate for acute insomnia and secondary insomnia
- Cognitive behavioural therapy (CBT-I/BBT) is the treatment of choice for chronic insomnia
  - Can be combined with some hypnotics – doesn't have to be all-or-nothing
  - Intermittent hypnotics use useful and proven to work
  - Behavioural change always hard to continue
- Different medications for different symptoms – which ever is most distressing
- Focus on improving daytime symptoms and not sleep numbers

References

- Kim HM, Gerlach LB, Van T, Yosef M, Conroy DA, Zivin K. Predictors of Long-Term and High-Dose Use of Zolpidem in Veterans. J Clin Psychiatry. 2019 Feb 5;80(2). pii: 18m12149. doi: 10.4088/JCP.18m12149.
- Guina J and Merrill B. Benzodiazepines 1: Upping the care on Downers: The evidence of risks, benefits and alternatives. J Clin Med 2018; 7, 17. doi: 10.3390/jcm7020017.
- Guina J and Merrill B. Benzodiazepines 2: Waking up on sedatives: providing optimal care when inheriting benzodiazepine prescriptions in transfer patients. J Clin Med 2018; 7,20. doi: 10.3390/jcm7020020\
- Hintze JP, Edinger JD. Hypnotic Discontinuation in Chronic Insomnia. Sleep Med Clin. 2018 Jun;13(2):263-270. doi: 10.1016/j.jsmc.2018.02.008.
- Morin C, Valliéres A, Guay B, Ivers H, Savard J, Mérette C, Bastien C, Baillargeon L. Cognitive behavioural therapy, singly and combined with medication, for persistent insomnia: a randomized controlled trial. JAMA 2009;301(19): 2005-15, doi: 10..1001/jama.2009.682.
- Perlis M, Gehrman P, Riemann D. Intermittent and long-term use of sedative hypnotics. Curr Pharm Des 2008; 14(32): 3456-65.
- Lader M. Benzodiazepine harm: how can it be reduced? 2012 Br J Clin Pharm 77:2. 295-301
- Atkin T, Comai S and Gobbi, G. Drugs for Insomnia beyond Benzodiazepines: Pharmacology, Clinical Applications, and Discovery. Pharmacol Rev 2018 70:197–245

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