Management of the Sleep Patient: “Daytime Sleepiness: Clinical Implications, Diagnosis and Evaluation”  
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Disclosures  
- Inspire Medical  
- Medtronic  
- Siesta medical  
- Lingualflex  
- Cryosa  
- Zelegent  
  
  Research/consulting  
  Consultant/royalty  
  Consultant/options  
  Consultant  
  Consultant

ICSD3: Excessive Daytime Sleepiness (EDS, hypersomnia)  
- EDS as an inability to remain fully alert or awake when sedentary during the wake portion of the sleep/wake cycle. (3 months)  
- Symptom not disease  
- This is in contrast to Fatigue  
  - Tiredness unrelated to sleep/wake onset

Hypersomnia and Excessive Daytime Sleepiness  
- In Sleep Medicine Measured by  
  - ESS, Stanford Sleepiness Scale, Karolinska Sleepiness Scale  
  - MSLT Mean sleep latency <8 minutes  
  - Maintenance Wakefulness Test (MWT) assesses the capacity to maintain wakefulness four 40-minute sessions latency <19 minutes abnormal  
- Each measures a different process

Excessive Sleepiness (DSM-5)  
- Recurrent periods of irrepresible need to sleep within the same day or confusional arousals—sleep drunkenness despite “normal” sleep duration (7 hrs)  
- Prolonged (9 hours +) nonrestorative main sleep episode associated with distress/impairment  
- 3 X per week / 3 months

Fatigue  
- Fatigue is frequent in chronic medical conditions (cardiovascular, respiratory, renal, and hepatic diseases)  
- Improvement of the primary condition, exercise, sleep may positively affects fatigue
Epworth Sleepiness Scale

- 8 domains measured with 4 ordinals (maximum = 24)
- Attempts to measure the context of sleepiness
- Epworth meaningful if ≥ 15 or ≤ 5
- Evaluative not discriminative metric
- Scientifically valid for group analysis (not individuals)

STOP-BANG

- Score ≥3 (AHI ≥5/h, AHI ≥15/h, ≥30/h)
  - Sensitivities 94.9%, 96.5%, and 97.7%
  - Specificities 50.0%, 28.6%, and 17.9%
- Chin Med J 2014;127 (17): 3065-3070
- “If you have normal score you have very low likelihood of OSA abnormal score is not diagnostic”

Hypersomnia

- Insufficient sleep syndrome
- Non – Breathing intrinsic sleep disorders
  - narcolepsy
  - idiopathic hypersomnia
  - recurrent hypersomnia
  - Restless leg syndrome (Willis Ekblom), periodic limb movements
- Breathing related sleep disorders
- Extrinsic sleep disorders
  - Medication- and toxin-dependent sleepiness (alcohol, narcotics)
  - Psychiatric disorders
- Other
  - Neurological disorders (parkinson's ds), Posttraumatic, Infection (bacterial, viral, parasitic diseases), Endocrine/metabolic

Narcolepsy (Rare = 0.026%)

- 4 cardinal symptoms
  - Irresistible sleep attacks
  - Sleep Paralysis
  - Hypnogaginic Hallucinations
  - Cataplexy
- Other features
  - Onset in adolescence
  - Naps are refreshing
  - Nocturnal sleep may be very disturbed
- Narcolepsy without Cataplexy
  - Diagnosis based on abnormal MSLT

Narcolepsy

- Pathophysiology
  - Results from a combination of genetic and environmental factors
  - Alteration of the hypocretin system
- Related to HLA subtypes DR2-DQ1 HLA
  - 92% caucacians vs 20% general population
- CSF orexin levels
  - Low in patients with cataplexy
  - Normal in those having narcolepsy without cataplexy

Treatment Cataplexy

- Cataplexy = sudden loss of voluntary muscular tone without change in consciousness often related to strong emotion
- Traditionally treated with antidepressants: tricyclics (imipramine, desipramine, clomipramine, and protriptyline)
  - SSRI's (including fluoxetine and sertraline) and serotonin and noradrenaline reuptake inhibitors (venlafaxine)
- Xyrem (sodium oxyb= orphan drug) sedating drug
- high dose IGG 1 g/kg/day for 2 days, repeated three times at 4-week intervals
Idiopathic Hypersomnia

- EDS without other cause
  - Severe sleep inertia
  - Autonomic dysfunction (headache, orthostasis)
  - MSLT showing fewer than two SOREMPs and MSLT <8 min
  - 24-h sleep time 660 min on 24-h polysomnographic monitoring after 14 D sleep log showing normal sleep
- Differential DX
  - OSA with RERA's
  - Insufficient sleep syndrome in a long sleeper
- Treatment difficult (all of label)
  - Modafinil /methylphenidate effective in only 50%
  - Flumazenil / clarithromycin (negative allosteric GABA modulator)

Other Hypersomnia Treatments (off label)

- Excessive daytime sleepiness
  - Naps
  - Sleep hygiene
  - Other Stimulants (caffeine / nicotine patches)
  - Sodium oxybate (Xyrem) ineffective except narcolepsy with cataplexy
- Antidepressant Medications
  - bupropion or protriptyline associated with insomnia
  - melatonin

Insufficient Sleep

- Often gradual onset
- Symptoms worse in afternoon and after meals
- Sleep inertia (+/-)
- Sleep duration < 6 hrs (sleep history unreliable)
- Worse on workdays and better on vacations

Sleep Deprivation

**Sleep diary**
**Fitbit**

*May take several weeks to see if sleep extension has an effect*

Drugs / Medications

- Caffeine, nicotine
  - Variable effects (OK in normals)
- Alcohol interrupts sleep up to 6 hr prior
- Beta blockers
- Narcotics
- Anti-epileptics
- Anti-psychotics

Movement Disorders with EDS

- Restless legs (Willis Ekbom) (highly underdiagnosed)
  - Paresthesia/dysesthesia (Creepy crawly, burning, aching, bugs tunneling)
  - Strong desire (compulsion = akesthesia) to move
  - Better with movements worse with inactivity
  - Worse at night (circadian)
- Periodic Limb Movement Disorder
  - PSG diagnosis with repetitive stereotyped movements
  - Often asymptomatic
  - Controversy if it causes sleepiness in adults
Restless leg syndrome (Willis Ekbom)

- **Primary RLS**
  - Autosomal dominant (onset < 30y/o, + family history)
  - Associated with sleepiness
- **Secondary**
  - Pregnancy, uremia, myelopathy, iron deficiency, obesity
- **Treatment**
  - Avoid alcohol, caffeine, inadequate sleep
  - Gentle stretching exercises
  - Iron supplementation
  - Medications
    - Dopamine agonists
    - Gabapentinoids
    - Clonazepam
    - Narcotics

Post Traumatic Hypersomnia

- Sleep disturbances not correlation to loss of consciousness or cause of injury
- Residual headache, dizziness, anxiety, and/or depression was independently associated with the development of insomnia
- The Glasgow Coma Scale score was independently associated with hypersomnia

Recurrent Hypersomnia

- Episodes of long sleep duration (18 h a day, days to weeks).
- Kleine-Levin syndrome (adolescent boys)
  - Overeating sexual disinhibition,
  - Mental disturbances
  - May respond to prophylactic antiseizure meds (all off label)
  - (valproate, carbamazepine, or lithium carbonate)
- Menstrual hypersomnia
  - Estroprogestative ovulatory inhibitors (all off label)

Depression

- EDS common in mood disorders but atypical symptoms
  - Prolonged sleep episodes or daytime sleep time (> 10 hr/day or 2+ hrs more than normal sleep time)
  - (hypersomnia vs hypersomnolence)
  - MSLT findings are usually normal
- Impaired time-on-task, attentional, and/or motivational issues
- Rule out substance abuse or medications
- Associated with treatment resistance, relapse, increased risk of suicide

Mood Disorders and EDS

- no pharmacologic agents FDA approved
- Stimulant medications in patients with bipolar disorder is controversial
- Studies inconsistent whether medications improve sleepiness
- SSRIs associated with somnolence as a side effect (bupropion (norepi/dopamine) has more stimulating effects)
- Mirtazapine acutely worsened EDS but later improved (uniquely enhances slow wave sleep)

Depression, Sleepiness and OSA

- Depression
  - Correlates to OSA
  - Not correlated to AHI
  - Significantly correlated to ESS
Sleep Apnea AHI and EDS

- AHI correlates poorly with EDS
- Primarily associated with severe OSA

Hypersomnia after OSA Treatment Failure

- Non adherence
- Therapy failure
- Non-apneic sleep disorders
  - Sleep restriction
  - Depression
  - Obesity
  - Irreversible damage from OSA
  - Intrinsic hypersomnia
    - Narcolepsy
    - Idiopathic hypersomnia
    - Jet lag, Kleine-Levin syndrome, Menstrually related hypersomnia, Malingering

Upper airway resistance syndrome

- High upper airway resistance and increased work of breathing
- May not snore
- Polysomnography may not be of benefit assessment

Evaluation
- No consensus
- Nasal Pressure Sensors to see flow limitation
- Esophageal pressure (greater 20 cm H2O)
- Physical exam
- Empiric treatment
  - Cpap
  - Mad
  - No criteria to determine if surgery appropriate

- 28/70 with ESS > 10
- 25% with pat ahi > 15 hr
Modafanil/Armodafanil

- ‘Wakefulness promoting agent’
- Dopamine reuptake inhibitor
- Long half life with low addiction and abuse potential
- Indications: Improve wakefulness in patients with EDS associated with:
  - Narcolepsy
  - Shift work sleep disorder
  - Obstructive sleep apnea

Modafanil Side effects

- Headache, Dizziness, Nervousness
- Nausea, Insomnia, Rhinitis
- Interaction with metabolism of hormonal birth control pills
- Expense
- May be combined with short acting stimulants

Amphetamines

- Amphetamines (Simple derivatives of catecholamines)
  - Used for longer lasting formulations
  - High addiction potential
  - Need to monitor HR and HTN
  - Irreversible psychiatric complications can emerge
  - High dose induced psychosis
- Methylphenidate
  - Short acting
  - Do not exceed 60 mg day
  - Low cost compared to modafanil
  - Monitor for dose escalation
  - Side effect of facial tics

Xanthine Derivative-Caffeine

- Competitively antagonizes adenosine receptors (inhibitory neurotransmitter)
- Reduces drowsiness (increase RR, HR, anxiety, insomnia)
- Brewed coffee 200mg cup (recommend < 500 mg/day)
- Rapid tolerance and withdrawal effects

Behavioral Interventions

- Light therapy
- Raising core body temperature (vs extremities)
- Exercise/Posture
- Increase sleep duration
- Strategic napping