Sleep Disorders in Medically ill Patients

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Objectives

• Learn about the significance of sleep disorders in medically ill
• Sleep disorders in patients with Chronic Kidney Disease (CKD)
• No conflict of interest.
Sleep in medical illness

- Cardiovascular
- Immune
- Cancer
- Endocrine
- Gastrointestinal
- Movement disorders
- Pain, fibromyalgia
- Neurological and mental disorders
- Special populations: children, adolescent, elderly
Sleep in medical illness

• Coping, functioning, mental health, qol?
• Daytime functioning, sleep hygiene
• Special considerations: overlapping symptoms, dg, therapy (polypharmacy?)
• Effects of medications on sleep
• Role of hospitalizations, surgery
• Comorbidities, dementias
• Aging
• Gender differences?
Cytokines and sleep
Sleep and the Cardiovascular System

- Sleep deprivation increases concentrations of cytokines and C-reactive protein.
- This inflammation can lead to endothelial damage, leading to possible stroke or heart disease.
- Blood pressure and heart rate are higher following sleep deprived nights (Voelker, 1999).
- Sleep deprivation increases risk of heart disease in women (Josefson, 2003).
Sleep disorders in CKD – why is it important?

- Sleep problems are one of the most common complaints of patients in the dialysis unit
- Sleep Apnea Syndrome (SAS) may contribute to the pathogenesis of hypertension, CV morbidity
- Sleep disorders may impair quality of life
- Poor sleep is a predictor of morbidity and mortality in this patient population
- Sleep disorders are treatable – successful treatment may improve clinical outcomes
Sleep disorders in dialysis patients (30-80%)

• Insomnia
  – 4-29% vs 15-70%

• Sleep apnea syndrome (SAS)
  – 2-4% vs 20-70%

• Restless legs syndrome (RLS)
  – 5-15% vs 15-80%

Little is known about sleep problems in „predialysis” and transplanted patients
Would you be willing to do more frequent dialysis?

- If it increased your energy? – 94%
- If you had better sleep? – 57%
- If you lived 1-3 yrs longer? – 19%
Factors contributing to sleep disturbances in patients on dialysis

- **Treatment-Related Factors**
  - Premature discontinuation of dialysis
  - Cytokine production during treatment
  - Rapid changes in fluid electrolyte and acid-base balance
  - Abnormalities in melatonin
  - Alterations in thermoregulatory
  - Medications

- **Psychological Factors**
  - Anxiety
  - Depression
  - Stress
  - Worry

- **Disease-Related Factors**
  - General health status
  - Comorbid conditions
  - Anemia
  - Symptoms of uremia
  - Metabolic changes
  - Alterations in neurotransmitter production

- **Sleep Disturbances in Dialysis Patients**
  - Changes in sleep architecture
  - Sleep apnoea syndrome
  - Restless legs syndrome
  - Periodic limb movement disorder
  - Excessive daytime sleepiness

- **Lifestyle Factors**
  - ↑ Coffee intake
  - Cigarette use
  - Poor sleep hygiene

- **Demographic Factors**
  - ↑ Age
  - Male gender
  - White race

Diagnostic tools to detect sleep problems

- Sleep diaries
- Self administered questionnaires
  - Insomnia: Pittsburgh Sleep Quality Index, Athen Insomnia Scale
  - SAS: Berlin Questionnaire
  - RLS: Restless Legs Syndrome Questionnaire
  - Epworth Sleepiness Scale
- Clinical interview
- Actigraphy
- Polysomnography (SAS, PLMS)
  - MSLT, MWT – daytime effects
Polysomnography

- neurophysiologic variables (electrooculography, EEG, submental myogram) – sleep stages
- Measurement of resp. effort
- Art. O2 sat., pCO2 – transdermal pulsoxymetry
- ECG
- Limb movements
Restless legs syndrome (RLS)

- Restless legs syndrome (RLS) is characterized by an urge to move the legs that is often hard to resist and is usually but not always associated with disagreeable leg sensations.

- **Main symptoms:**
  - 1. An urge to move the legs, usually accompanied or caused by uncomfortable and unpleasant sensations in the legs.
  - 2. The unpleasant sensations begin or worsen during rest or inactivity.
  - 3. The unpleasant sensations are partially or totally relieved by movement.
  - 4. The unpleasant sensations are worse in the evening or night than during the day or only occur in the evening or night.
Restless Legs Syndrome

Predictors, etiology

- Altered CNS dopamin metabolism
- Iron deficiency (cerebral versus peripheral)
- Uremia – uremic toxins?
- Anemia
- Neuropathy

Consequences

- Fragmented sleep, „intitiation” insomnia
- Fatigue, tiredness
- Daytime sleepiness
- Impaired QoL
- Incr. mortality?
• Prevalence of RLS: 12-20% in dialysed\textsuperscript{1,2} and 4.5% in kidney transplanted populations\textsuperscript{3}

• **RLS is associated with increased risk of**

• insomnia and impaired quality of life (QoL) in dialysed patients\textsuperscript{4}

• There is **no data** regarding the association of RLS, poor sleep and QoL after renal transplantation

\textsuperscript{1} Winkelman et al. (1995)
\textsuperscript{2} Mucsi et al. (2004)
\textsuperscript{3} Molnar et al. (2005)
\textsuperscript{4} Unruh et al. (2004)
RLS in dialysis patients predicts mortality

Table 3. Adjusted Hazards of Severe Symptoms of Restless Legs and by Category of Restless Legs Symptom

<table>
<thead>
<tr>
<th>Severe Restless Legs Symptoms</th>
<th>Category of Restless Legs Symptom</th>
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<tbody>
<tr>
<td>Unadjusted hazard</td>
<td>1.31 (1.00-1.73)</td>
</tr>
<tr>
<td>Model 1, adjusted for age and race</td>
<td>1.42 (1.07-1.87)</td>
</tr>
<tr>
<td>Model 2, model 1 and adjusted for ICED, Karnofsky</td>
<td>1.39 (1.05-1.84)</td>
</tr>
<tr>
<td>Model 3, model 2 adjusted for clustering of clinics</td>
<td>1.39 (1.08-1.79)</td>
</tr>
</tbody>
</table>

Adjusted Differences in Quality of Life by Restless Legs Symptoms

Fig 2. Crude cumulative mortality according to severe symptoms of restless legs.

Unruh et al; AJKD; 2004
Restless Legs Syndrome and Mortality in Kidney Transplant Recipients

Miklos Zsolt Molnar, MD, PhD, Andras Szentkiralyi, MD, Anett Lindner, MD, Maria Eszter Czira, MD, Lilla Szeifert, MD, Agnes Zsofia Kovacs, MD, Katalin Fornadi, MD, Andras Szabo, MD, DSc, Laszlo Rosival, MD, DSc, Istvan Mucsi, MD, PhD, and Marta Novak, MD, PhD

Multivariate Cox-modell

<table>
<thead>
<tr>
<th>Presence of RLS</th>
<th>Mortality</th>
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<tbody>
<tr>
<td></td>
<td>HR</td>
</tr>
<tr>
<td>Presence of RLS</td>
<td>2</td>
</tr>
</tbody>
</table>

Adjusted for: age, gender, eGFR, albumin, hemoglobin, CRP, diabetes, hypertonia and transplant vintage

Clinical management of RLS in CKD

• Adequate dialysis/ renal transplantation
• Iv iron/ anemia management (Dose?)
• Non-pharmacological methods
• Medications
  – Ropirinole, pramipexole, carbidopa/levodopa,
  – Benzodiazepines - efficacy??
  – Gabapentin, carbamazepine – efficacy??
Sleep apnea syndrome

- intermittent episodes of breathing cessation during sleep,
  - airway collapse (obstructive sleep apnoea, OSA)
  - cessation of respiratory effort (central SA)
  - or both (mixed SA)

- The severity of the SAS is usually characterized by the number of apneic events per hour of sleep (AHI, RDI) (RDI>5 is considered pathological), severity of desaturation and by the presence and severity of daytime sleepiness.

- SAS is associated with disturbances of sleep initiation and maintenance as well as daytime sleepiness.

- A potential link is suggested between SAS and HTN, CAD, CHF and arrhythmias
OSAS

- Upper airway obstruction
- Anatomical problems
- Decreased muscle tone \( \downarrow \) + weakness of pharyngeal wall

\[ \{ \text{Dynamic collapse during inspiration} \} \]
Apnea leads to micro-arousals and fragmented sleep
Sleep Apnoe Syndrome

Predictors, correlates

- Age
- Obesitas (BMI, neck circumference)
- Male gender/menopause
- Alcohol
- Uremic toxins?
- Anemia
- Altered metabolic state

Consequences

- Daytime sleepiness
- Accidents
- Cognitive impairment
- Depression
- Sexual dysfunction
- Hypertension, LVH, CAD, arrhythmias
- Impaired QoL
- Increased morbidity, mortality?
Prevalence of OSA in CV diseases

- CHF: 25%
- HTN: 50%
- CAD: 30%
Mediating processes:
- Hypoxia
- Hypercapnia
- Change in the Intrathoracal pressure
- Micro-arrousals
- Sympathetic nervous system activity
- Endothelial dysfunction
- Oxidative stress
- Inflammation
- Hypercoagulability

Modifying factors:
- Hypertension
- Heart failure
- Arrhytmias
- CAD
- Cerebrovascular disease
- Obesity
- Gender
- Age
- Metabolic syndrome
- Smoking
- Medications

OSAS
Specific factors potentially contributing to the pathogenesis of SAS in patients with renal disease

- Hypocapnia, acid-base disorders
- Uremic toxins – effects on CNS
- Soft tissue edema
- Anemia
- Endocrine problems (menopause – gender difference)
- Dialysis modality (HD-cytokines, type of PD)
High risk of OSAS and graft failure

A. Szentkiralyi et al: Sleep medicine – in press
Clinical management of SAS in CKD

- Weight loss life style changes
- CPAP
  - Long term effects?
  - Compliance?
- Oral devices, Sx
- Transplantation?
- Intensified dialysis

photo courtesy of the American Sleep Apnea Association
Conclusions

- Sleep disorders are underdiagnosed and underreated in medically ill patients

- Overlap between somatic, mental and sleep-related symptoms needs careful assessment;

- Screening is simple, diagnosis might need polysomnographic sleep study and daytime testing;

- Management of these treatable disorders and may improve QoL, functioning, and maybe even survival of patients with medical illness.