(Over)USE of HYPNOTICS
in Acute Care

Alberta Sleep Forum

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Dr. G. Man has no conflict of interest to declare.
• Hypnotics use in general population and in hospital
• Impact of sleep on breathing
• Sleep and breathing in COPD
• Hypnotics use in patients hospitalized with AECOPD
PRESCRIPTION SLEEP AID USE
Among US Adults, 2005-2010

- Data from the National Health and Nutrition Examination Survey, CDC/NCHS

- About 4% of US adults (aged 20 and over) used prescription sleep aids in the past month
- More adult women (5.0%) used prescription sleep aid than adult men (3.1%)
- The percentage of adults using a prescription sleep aid increased with age and level of education

NCHS Data Brief No. 127, August, 2013.
SEDATIVE HYPNOTIC USE in Alberta

• Data from Alberta Mental Health Survey of 5383 adults (age 18 to 64 years)

• 3.0 % of adults used benzodiazepine and similar sedative-hypnotics in the past 2 days

• More adult women (3.8 %) used sedative-hypnotics than adult men (2.0 %)

• The frequency of use increases with age and unemployment status

USE of HYPNOTICS in Hospitalized Adult Patients

• 100 adult patients admitted to the general medicine or family practice ward (tertiary care hospital, Vancouver)

• 60% of patients were prescribed bedtime hypnotics while in hospital

• 29% had a hypnotic prescription initiated in hospital, with no evidence of pre-admission hypnotic use

• 31% had a continuation of their pre-admission hypnotic prescription while in hospital

BENZODIAZEPINE USE in Hospitalized Patients

- 444 patients admitted to department of internal medicine (Bordeaux, France)

- **33 %** used at least one benzodiazepine (BZD)
- **23.6 %** were using BZD at admission
- **17.6 %** used short half-life BZDs as hypnotic
- **6 %** used long half-life BZDs as anxiolytic

IMPACT of MEDICATIONS on Falls in Elderly Persons

• Meta-analysis of 9 medication classes
• 22 published articles; 79,081 subjects; age > 60

• Odds Ratio:
  Beta-blockers  1.01 (0.86-1.17)
  Diuretics  1.07 (1.01-1.14)
  Sedatives/hypnotics  1.47 (1.35-1.62)
  BZD’s  1.57 (1.43-1.72)

SEDATIVE-HYPNOTIC USE
Effect on Hospital Stay and Costs

• 856 consecutive medical and surgical admissions (university hospital, Philadelphia); age > 65

• 3 categories: (A) exceeded HCFA guidelines (19.9 %)
  (B) within guidelines (33.1 %)
  (C) no sedative-hypnotics (47.1 %)

• Hospital stay and hospital cost: (A) > (B) > (C)

21,489 adult patients admitted to a university hospital in Tokyo, Japan (55.1 % men; mean age 59.9 yrs)

BZD’s were prescribed in 19.9 %
Length of stay significantly longer in those prescribed BZD’s (even after adjusting for age, gender and ICD-10 diagnosis)

SLEEP and BREATHING in COPD
In normal individuals experiencing a typical sleep cycle, decreases in reticular activating system (RAS) activity, metabolic rate, and responsiveness to arterial PaO$_2$ and PaCO$_2$ along with increased airway resistance lead to decreased ventilation and subsequent changes in arterial blood gases during sleep (From Mohsenin, Semin Respir Crit Care Med; 26:109).
NOCTURNAL DESATURATION in COPD

Overnight oxygen saturation in a patient with chronic obstructive pulmonary disease. *Shaded areas* represent REM sleep during which marked oxygen desaturation occurs. (From Principles and Practice of Sleep Medicine, 2011)
MECHANISMS of Nocturnal Desaturation

- **Hypoventilation**: most important factor
- REM-related atonia causes loss of activity in accessory respiratory muscles
- Reduction in functional residual capacity with sleep onset
- Increased ventilation-perfusion mismatch
- Increased upper airway resistance
- Co-existing sleep apnea: in 12-15% of cases
- Impact of oxyhemoglobin dissociation curve
DISORDERED SLEEP ARCHITECTURE in COPD

- Delayed sleep onset
- Poor sleep efficiency
- Frequent arousals
- Frequent awakenings
CAUSES of AROUSALS/AWAKENINGS in COPD

- Cough, sputum, dyspnea
- Hypoxia, hypercapnia
- Medications: corticosteroids, B-agonists
- Apneas/hypopneas
- Depression
Impaired Sleep Quality

- Impaired daytime function
- Poor quality of life
EFFECTS of HYPNOTICS on Sleep & Breathing

**SLEEP**
- BDZ
  - Sleep latency
  - Arousal
  - Sleep efficiency
- non-BDZ
  - Sleep latency
  - Arousal
  - Sleep efficiency

**BREATHING**
- tidal volume
- Arousal response
- Hypoxia/hypercapnia
- Apneas
“Management of sleep problems in COPD should focus on minimizing sleep disturbances by measures to limit cough and dyspnea, and nocturnal oxygen therapy may be indicated for nocturnal hypoxemia.”

“Hypnotics should be avoided, if possible, in patients with severe COPD.”
Use of Hypnotics in Hospitalized Patients with Acute Exacerbation of Chronic Obstructive Pulmonary Disease

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Division of Pulmonary Medicine
Department of Medicine, University of Alberta
Research Questions

• What is the prevalence of hypnotics use in AECOPD patients admitted to UAH?

• What are the characteristics of patients who received hypnotics & those who did not?

• Are there any differences in the clinical outcomes between these two groups?
Methods

• Design: Retrospective hospital chart review

• Setting: University of Alberta Hospital

• Subjects: Patients admitted to GIM and Pulmonary with diagnosis of AECOPD between Jan 1st and Dec 31st 2010

• Exclusion Criteria:
  – Primary diagnosis of other pulmonary diseases such as pneumonia, empyema, cystic fibrosis, asthma and lung cancer
  – Direct admission from ER to ICU
  – Major psychiatric illness
  – Length of stay < 1 day or > 30 days
  – “Palliative Care” designation
Hospital admissions with diagnosis of AECOPD
n=247

Number of charts reviewed
n=215

Number of patients eligible
n=202

Patients included for analysis
n=178

Excluded due to LOS < 1 day
n=32

Excluded due to designation of “palliative care”
n=13

Excluded due to other significant diagnoses
n=24

Figure (1): The selection of patients. AECOPD = Acute Exacerbation of Chronic Obstructive Pulmonary Disease. LOS = Length of stay. Other significant diagnosis: Major psychiatric illness, lung cancer, interstitial lung disease, acute coronary syndrome, etc.
Results - Hypnotics used in AECOPD

Total patients
n = 178

Patients received hypnotics
n = 102

Of 102 patients 72 were taking hypnotics at home and 30 started in hospital

Benzodiazepine
(BZD, n=64)

Non-benzodiazepine
(NBZD, n=70)
## Results

### Characteristics of study subjects (n=178)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total</th>
<th>Hypnotics</th>
<th>No Hypnotics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>69.43 ± 12.49</td>
<td>69.19 ± 12.49</td>
<td>69.74 ± 12.55</td>
</tr>
<tr>
<td>Gender, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>88 (49.4)</td>
<td>46 (45)</td>
<td>42 (55)</td>
</tr>
<tr>
<td>Female</td>
<td>90 (50.6)</td>
<td>56 (55)</td>
<td>34 (45)</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>26.79 ± 8.07</td>
<td>26.52 ± 7.87</td>
<td>27.15 ± 8.36</td>
</tr>
<tr>
<td>Length of stay in hospital, days</td>
<td>8.94 ± 6.54</td>
<td>10.26 ± 6.88*</td>
<td>7.21 ± 5.54*</td>
</tr>
</tbody>
</table>

Values are presented as mean ± SD, unless otherwise indicated.

*p=0.001, hypnotics vs no-hypnotics group.*
Results - Length of Stay and Age Distribution

**Length of stay in days**

- **< 70 years**
  - Hypnotics: 8 (49 patients)
  - No hypnotics: 6 (33 patients)
  - *P = 0.006*

- **> 70 years**
  - Hypnotics: 14 (53 patients)
  - No hypnotics: 12 (43 patients)
  - *P = 0.004*

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**Age in years**

- < 70
  - Hypnotics: 49
  - No hypnotics: 33

- > 70
  - Hypnotics: 53
  - No hypnotics: 43
Results - Length of Stay and Gender Distribution

Results - Length of Stay and Gender Distribution

P=0.004

P=0.017

No. of patients

Gender

Male

Female

0
12
14
16
18
Length of stay in days

P=0.004

P=0.017
Results – Length of Stay and Severity of COPD

<table>
<thead>
<tr>
<th>No. of patients</th>
<th>Hypnotics</th>
<th>No hypnotics</th>
</tr>
</thead>
<tbody>
<tr>
<td>GOLD 1 Mild</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>GOLD 2 Moderate</td>
<td>11</td>
<td>10</td>
</tr>
<tr>
<td>GOLD 3 Severe</td>
<td>21</td>
<td>17</td>
</tr>
<tr>
<td>GOLD 4 Very Severe</td>
<td>24</td>
<td>12</td>
</tr>
</tbody>
</table>

- **GOLD 1**: Mild Severity
- **GOLD 2**: Moderate Severity
- **GOLD 3**: Severe Severity
- **GOLD 4**: Very Severe Severity

- Hypnotics: p = 0.083
- No hypnotics: p = 0.036
- No hypnotics: p = 0.003
Summary

- **57.3 %** of AECOPD patients received hypnotics in the hospital.

- Length of stay was significantly longer (by **3 days**) in patients who received hypnotics compared to those who did not.

- The difference in LOS was seen regardless of age group, gender or severity of COPD.
Limitations

• Retrospective chart review

• Reason for hypnotics prescription not clearly documented

• A causal relationship cannot be firmly established
Next Steps?

- Collect more data to confirm findings
- Raise awareness about hazards of hypnotics use
- Promote non-pharmacological approaches
- Broaden scope of cost-effectiveness analysis in evaluation of newer hypnotics
"We're out of sleeping pills. I'm going to read you a bedtime story."
MORTALITY with HYPNOTICS

<table>
<thead>
<tr>
<th>HYPNOTIC DOSES / YEAR</th>
<th>HAZARD RATIO</th>
</tr>
</thead>
<tbody>
<tr>
<td>NONE</td>
<td>1.0</td>
</tr>
<tr>
<td>0.4 - 18</td>
<td>3.2 (±1.1)</td>
</tr>
<tr>
<td>18 - 132</td>
<td>4.8 (±1.7)</td>
</tr>
<tr>
<td>&gt; 132</td>
<td>5.9 (±2.0)</td>
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</tbody>
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