To Sleep, Perchance to Dream…
Should sleep studies be included in the clinical management of MND/ALS?

Lee Guion MA, RRT
Forbes Norris MDA/ALS Research and Treatment Center
San Francisco, CA

December 10, 2010

Aims

- Briefly summarize what we know – and don’t know – about sleep in pALS
- Spark discussion about the best methods for evaluating and treating symptoms of sleep disordered breathing in MND/ALS

Background

- Diaphragm weakness exaggerates normal physiology during REM sleep
  - Suppression of intercostal and accessory muscles
  - Decreased lung volumes
  - Upper airway resistance
  - Decreased muscle tone in throat and upper airway
  - Diaphragm displacement by abdominal contents

Background

- Importance of restful, restorative sleep
  - Psychological and emotional well-being
  - Physiological health
    - Cardiovascular disease
    - Diabetes Mellitus
  - Quality of life

Evaluation of sleep quality

- Patient-reported symptoms
  - Feeling tired upon awakening
  - Difficulty staying awake during the day
  - Difficulty concentrating or with memory
  - Lack of energy or increased fatigue
  - Morning headaches
- Obtained on initial and all subsequent clinic visits

Evaluation of sleep quality

- Maintain high degree of suspicion of night time diaphragm weakness with daytime symptoms of poor sleep quality

Evaluation of sleep quality

- What is the best Symptom of early diaphragm weakness in MND/ALS?
- What is the best Method of identifying lung muscle weakness and night time hypoventilation in MND/ALS?
- Why is this important?

Treatment of hypoventilation

- Lung volume replacement with noninvasive ventilation (NIV)
  - AAN Updated Practice Parameter (2009)
  - EFNS Evidenced-based Guidelines and Practice Recommendations (2005)
  - Cochrane Review of nocturnal NIV in chronic hypoventilation (2009)
- Increasing support for early intervention with NIV to decrease morbidity and increase survival

What we don't know

- What physiological measures of sleep are the best predictors of hypoventilation in pALS
- And what is the significance of these measures in assessing sleep quality in MND/ALS

Effects of NIV on sleep outcomes in MND/ALS

- Methods
  - 12 subjects meeting CMS guidelines (US) for initiation of NIV (FVC < 50%, MIP < - 60 cmH2O)
  - Home sleep study before beginning NIV
  - Home sleep study with NIV
  - Total of 24 studies (adequately powered)

Katzberg, H. A pilot study of the effects of non-invasive ventilation on sleep outcomes in amyotrophic lateral sclerosis. 2010. Stanford University and Forbes Norris Center (unpublished)

Effects of NIV on sleep outcomes in MND/ALS

- Methods
  - Primary outcome
    - Change in minimum oxygen saturation
  - Secondary outcomes
    - Change in mean oxygen saturation
    - Apnea and hypopnea indexes
    - Sleep quality
      - Arousals
      - Restful sleep
      - Sleep architecture (stages)

Effects of NIV on sleep outcomes in MND/ALS

- Findings
  - Improvement in minimum oxygen saturation with NIV use (7%) throughout night and during REM
  - Non-significant improvement in mean oxygen saturation with NIV use (1.5%)
  - 8/12 patients had improved sleep efficiency

Effects of NIV on sleep outcomes in MND/ALS

- Outcomes
  - No statistically significant improvements in secondary outcomes with NIV use
    - Lack of stage 3 (restorative) sleep in MND/ALS *with* or without NIV use
    - Apnea index
    - Hypopnea index
    - NIV use did not improve sleep arousals, restful sleep, or overall sleep architecture

    (all patients able to use NIV $\geq$ 4 hours/night)

Effects of NIV on sleep outcomes in MND/ALS

- Outcomes
  - Orthopnea was the best predictor of respiratory impairment (hypoventilation)

Sleep in MND/ALS

- Summary
  - pALS appear to be unusual in response to nighttime decrease in oxygen saturation
  - Oxygen desaturations not directly tied to apnea and hypopnea indexes
  - Questionable usefulness of traditional measures of sleep quality (arousals, time in restorative sleep stages) in pALS

Sleep in MND/ALS

- Summary
  - pALS are heterogeneous and vary in response to diaphragm weakness and nocturnal hypoventilation
  - Apneas and hypopneas appear to be rare
  - pALS are able to maintain use of extra-diaphragmatic muscles (inspiratory neck muscles) during REM
  - Lack of consensus and insufficient data on the physiological significance of sleep changes in MND/ALS

Take home messages

- Detection of diaphragm weakness and night time hypoventilation can be accomplished by
  - Obtaining and recording subjective daytime symptoms of poor sleep quality at each visit
  - Lung function measures upright and supine (FVC, MIP)
  - Reported and observed orthopnea

Recommendations

- Develop international sleep diagnostic protocols for evaluating nocturnal hypoventilation in MND
- Develop international sleep treatment protocols for using NIV, insuring effective pressure support ventilation and volume-replacement therapy
- Expand training of technologists and physicians in sleep medicine to include scoring and interpretation of sleep changes in patients with diaphragm weakness