Improving Assessment of Sleep Disruption in Children with Atopic Dermatitis (Eczema)

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Background

• Eczema (atopic dermatitis) in 10-20% of US children\textsuperscript{1}
• 60% of children have sleep disturbance from AD, and up to 80% with flares\textsuperscript{2-5}
• Short stature in eczema, only occurs in kids with poor sleep\textsuperscript{6}
• Sleep disturbance in AD can induce ADHD and worsen behavior/school performance\textsuperscript{7, 8}
• Term to describe nighttime exacerbation of AD= Nocturnal Eczema\textsuperscript{7}

\textsuperscript{1} Shaw 2011, JID
\textsuperscript{2-5} Chamlin 2005, Arch ped & adol med; Hon 2008 Clin & Exp Derm; Camfferman 2010 Slep med rev
\textsuperscript{6} Silverberg 2015 JAMA dermatol
\textsuperscript{7} Fishbein 2015 JACI
\textsuperscript{8} Camfferman 2010 Sleep Med Rev
What sleep looks like in an 8 year old with severe eczema
### Wake After Sleep Onset (WASO): Key Objective Parameter of Sleep Disturbance in Atopic Dermatitis

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Atopic Dermatitis (n=19)</th>
<th>Control (n=19)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bedtime (hh:mm), mean (SD)</td>
<td>22:36 (1:15)</td>
<td>23:26 (1:37)</td>
<td>0.08</td>
</tr>
<tr>
<td>Waketime (hh:mm), mean (SD)</td>
<td>07:40 (0:37)</td>
<td>8:08 (1:21)</td>
<td>0.18</td>
</tr>
<tr>
<td>Sleep start time (hh:mm), mean (SD)</td>
<td>22:49 (1:13)</td>
<td>23:42 (1:47)</td>
<td>0.09</td>
</tr>
<tr>
<td>Sleep end time (hh:mm), mean (SD)</td>
<td>07:34 (0:38)</td>
<td>8:00 (1:22)</td>
<td>0.21</td>
</tr>
<tr>
<td>Time in Bed (minutes), mean (SD)</td>
<td>544.5 (73.0)</td>
<td>522.3 (53.5)</td>
<td>0.29</td>
</tr>
<tr>
<td>Sleep duration (minutes), mean (SD)</td>
<td>524.3 (72.1)</td>
<td>498.3 (61.6)</td>
<td>0.24</td>
</tr>
<tr>
<td>Sleep onset Latency (minutes), mean (SD)</td>
<td>13.7 (14.8)</td>
<td>15.7 (22.3)</td>
<td>0.74</td>
</tr>
<tr>
<td>Wake After Sleep Onset (minutes), mean (SD)</td>
<td><strong>103.4 (55.4)</strong></td>
<td><strong>49.8 (26.6)</strong></td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Fragmentation Index, mean (SD)</td>
<td>26.4 (19.2)</td>
<td>18.9 (6.9)</td>
<td>0.12</td>
</tr>
<tr>
<td>Sleep Efficiency, %, mean (SD)</td>
<td><strong>76.8 (12.7)</strong></td>
<td><strong>85.9 (4.9)</strong></td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

*Fishbein... Paller JAAD 2017*
Why Assess Sleep in Atopic Dermatitis?

• No official recommendations on how to assess or best way to assess

• No standardization in clinical trials

• AAAAI/ACAAI practice parameter: “The clinician should assess for sleep disturbances. Sleep might improve with treatment of inflammation, but the clinician might also consider therapeutic agents or referral to a sleep specialist or psychologist in severe cases or when sleep does not improve in remission.” ¹

• AAD guidelines: “Should query itch, sleep, impact on daily activity, and disease persistence”²

¹ Schneider et al 2013, JACI
² Eichenfield et al 2014, JAAD
Working Model To Test Circadian Mechanisms and Clinical Consequences of Nocturnal Eczema

- Skin Barrier Dysfunction
- Atopic Dermatitis Flare (itch/scratch cycle)
- Inflammatory Rhythms

Sleep Disturbance (sleep quality and objective sleep disturbance)

- Sleep-related impairment
- Itch
- Impaired Daytime Cognition
- Other health related quality of life measures (fatigue, pain, depression, anxiety, peer relationships, physical function)
Methods Summary

- 5-17 year olds with controlled asthma/allergic rhinitis
- English speaking
- Recruited prior to clinic visit
- Actigraphy watch and paper questionnaires
## Patient Characteristics (n=60)

<table>
<thead>
<tr>
<th>POEM_severity_rating</th>
<th>mild</th>
<th>moderate</th>
<th>severe</th>
<th>p=</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=17</td>
<td>n=23</td>
<td>n=20</td>
<td>0.41</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>11.7 (3.9)</td>
<td>10.9 (4.3)</td>
<td>12.5 (3.6)</td>
<td>0.20</td>
</tr>
<tr>
<td>Sex</td>
<td>male</td>
<td>6 12 13</td>
<td>0.08</td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td>0.08</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>4 3 1</td>
<td>0.08</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>0 5 6</td>
<td>0.08</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>9 11 11</td>
<td>0.08</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>4 4 2</td>
<td>0.08</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td>0.75</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Latino</td>
<td>6 6 5</td>
<td>0.75</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Aspects of sleep assessment to look at

- Sleep quality (by parent proxy and patient report)
  - PROMIS sleep disturbance
  - PROMIS sleep related impairment
- Sleep quality assessed by legacy measure of fatigue (by parent proxy and patient report)
  - Epworth Sleepiness Scale
- Sleep maintenance insomnia
  - WASO (wake after sleep onset)
  - Sleep efficiency
- Sleep initiation insomnia
  - Sleep onset latency
Sleep quality is not good in moderate/severe AD-parent proxy by self-reported disease severity

ANOVA, p<0.01

ANOVA, p=0.01
Sleep quality is not good in moderate/severe AD-child report by self-reported disease severity

ANOVA, p=0.02

ANOVA, p=0.06
Correlation of PROMIS sleep measures with Objective sleep disturbance

PROMIS T-score

$r=0.30$, $p=0.019$, $n=60$
$r=0.34$, $p=0.022$, $n=44$
$r=0.23$, $p=0.075$, $n=60$
$r=0.22$, $p=0.15$, $n=44$
# Sleep Characteristics of the Cohort

|                          | POEM Mild (n=17) | Moderate (n=23) | Severe (n=20) | p=  
|--------------------------|------------------|-----------------|---------------|-----  
| Get_Up_Time              | 7:59:33          | 7:45:37         | 8:03:36       |     
| Time_in_Bed_hours        | 8:59:41          | 9:06:14         | 8:53:47       |     
| Total_Sleep_Time_hours   | 7:34:31          | 7:25:10         | 6:59:44       |     
| Onset_Delay__minutes     | 9.4 (5.4)        | 15.0 (12.0)     | 17.3 (17.4)   | 0.17  
| Sleep_Efficiency__percent| 84.2 (3.8)       | 81.7 (6.1)      | 79.7 (9.1)    | 0.14  
| WASO__minutes             | 67.6 (16.6)      | 77.9 (28.9)     | 90.2 (54.3)   | 0.19  
|                          |                  |                 |               |      
|                          | EASI Mild (n=24) | Moderate (n=22) | Severe (n=14) | p=  
| Time_in_Bed_hours        | 8:54:32          | 8:58:16         | 9:13:06       |     
| Total_Sleep_Time_hours   | 7:27:20          | 7:27:42         | 6:52:30       |     
| Onset_Delay__minutes     | 13.0 (11.7)      | 12.0 (10.0)     | 19.7 (17.8)   | 0.19  
| Sleep_Efficiency__percent| 83.6 (4.8)       | 83.7 (5.2)      | 75.4 (8.7)    | <0.01  
| WASO__minutes             | 66.7 (19.7)      | 69.8 (28.5)     | 114.8 (51.3)  | <0.01  

**Note:** The table above compares the sleep characteristics of mild, moderate, and severe groups across two conditions (POEM and EASI). The p-values indicate statistical significance between the groups.
Most strongly associated with WASO for **CHILD** \((p<0.01)\) or **PARENT**

<table>
<thead>
<tr>
<th>Sleep Disturbance</th>
<th>Never</th>
<th>Almost Never</th>
<th>Sometimes</th>
<th>Almost Always</th>
<th>Always</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. I had difficulty falling asleep</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. I slept through the night</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. I had a problem with my sleep</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. I had trouble sleeping</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. It took me a long time to fall asleep</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. I worried about not being able to fall asleep</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. I woke up at night and had trouble falling back to sleep</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8. I tossed and turned at night</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Clinician assessed disease severity correlates best with WASO

$r=0.31$, $p=0.016$, $n=60$

$r=0.57$, $p<0.001$, $n=60$
Sleep onset latency minutes not different by disease severity group

POEM_severity_rating
ANOVA, p=0.17

EASI_severity_rating
ANOVA, p=0.19
Sleep onset latency (assessment of sleep initiation insomnia) and disease severity assessment

Sleep onset latency (minutes it takes to fall asleep)

Disease severity assessment score

r = 0.27, p=0.04, n=60

r = 0.20, p=0.12, n=60
EASI (clinician assessed disease severity) versus POEM (patient oriented eczema measure)

<table>
<thead>
<tr>
<th>EASI_severity_rating</th>
<th>mild</th>
<th>moderate</th>
<th>severe</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>mild</td>
<td>12</td>
<td>9</td>
<td>3</td>
<td>24</td>
</tr>
<tr>
<td>moderate</td>
<td>4</td>
<td>8</td>
<td>10</td>
<td>22</td>
</tr>
<tr>
<td>severe</td>
<td>1</td>
<td>6</td>
<td>7</td>
<td>14</td>
</tr>
<tr>
<td>Total</td>
<td>17</td>
<td>23</td>
<td>20</td>
<td>60</td>
</tr>
</tbody>
</table>
Can we use the POEM sleep question for screening?

Over the last week, on how many nights has your child’s sleep been disturbed because of their eczema?
If you dichotomize POEM sleep question (any days of sleep disturbance vs. none), does it screen for sleep disturbance?

- 74% have sleep disturbance
- Picked up everyone with PROMIS score $\geq 60$ except for 1 on child and 2 on parent (SD and SRI)
- Picked up anyone with WASO $\geq 80$ (our published norm is $50\pm27$)
- Picked up everyone with SOL $\geq 17$ min (our published norm is $16\pm22$)
- Lots of false +, many people with good sleep, but they think they don’t
Key points about sleep assessment....

• PROMIS sleep disturbance scores differentiate by disease severity groups
• Parents report worse SD/SRI scores than children
• PROMIS sleep disturbance scores correlate with objective sleep disturbance, however disease severity correlates best with objective sleep disturbance
• Sleep maintenance insomnia (WASO and sleep efficiency) are poor in AD, and most prominently in severe disease assessed by the clinician
Limitations

• Many questionnaires filled out at home, sometimes not clear if child filled out parents, or parent filled out child's
• Varying ages, interpreting WASO differing by age/length of sleep, not enough patients in this cohort to analyze by age
• No babies, and they are the most affected... other issues in younger cohorts
• Missing data
• Correct choice of assessment for impaired daytime cognition?
• Assessing disease severity
Thank you

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