Obstructive Sleep Apnea

Should All Children With Down Syndrome Be Tested?

Sally R. Shott, MD; Raouf Amin, MD; Barbara Chini, MD; Christine Heubi, BS; Stephanie Hotze, BS; Rachel Akers, MPH

Objectives: To determine the incidence of obstructive sleep apnea syndrome in children aged 2 to 4 years with Down syndrome and to determine parents’ ability to predict sleep abnormalities in this patient population.

Design: Prospective cohort study.

Setting: Tertiary care pediatric referral center.

Patients: Sixty-five children participating in a 5-year longitudinal study in which the otolaryngologic problems seen in Down syndrome were evaluated. Fifty-six completed overnight polysomnography (PSG) between 4 and 63 months of age (mean age, 42 months).

Interventions: Overnight PSG was performed. Parents also completed a questionnaire regarding their impressions of their child’s sleep patterns before PSG.

Main Outcome Measures: Polysomnograms were classified as abnormal if the obstructive index was greater than 1, if the carbon dioxide level was greater than 45 mm Hg for more than two thirds of the study or greater than 50 mm Hg for more than 10% of the study, and/or if there was unexpected hypoxemia less than 92% during sleep or repeated intermittent desaturations less than 90%. We also identified a group of children whose PSGs findings were normal except for an arousal index greater than 10 and were associated with increased work of breathing.

Results: The PSGs revealed that 57% of the children had abnormal results and evidence of obstructive sleep apnea syndrome. If we also include an elevated arousal index, 80% of the PSGs had abnormal results. Sixty-nine percent of parents reported no sleep problems in their children, but in this group, 54% of PSGs had abnormal results. Of the parents who reported sleep problems in their children, only 36% had abnormal sleep study results.

Conclusion: Because of the high incidence of obstructive sleep apnea syndrome in young children with Down syndrome, and the poor correlation between parental impressions of sleep problems and PSG results, baseline PSG is recommended in all children with Down syndrome at age 3 to 4 years.


Children with Down syndrome (DS) are at greater risk for development of obstructive sleep apnea syndrome (OSAS). The incidence of obstructive sleep apnea (OSA) is estimated to be between 30% and 60% in the DS population. Obstructive sleep apnea syndrome, a more encompassing term describing sleep abnormalities, consists of complete and partial upper airway obstruction (obstructive apnea and obstructive hypopneas), as well as chronic obstructive hypoventilation with hypercarbia and oxygen desaturation. In addition, the significance of sleep pattern abnormalities, such as sleep fragmentation and sleep arousals, are just beginning to be understood.

Although OSAS is seen in only 0.7% to 2.0% of the general pediatric population, Marcus et al retrospectively evaluated a group of 53 subjects with DS, ages ranging from 4 weeks to 51 years (mean age, 7 years), and found sleep abnormalities to be as high as 100%. With this high incidence, the question becomes whether all children with DS should be evaluated objectively for sleep abnormalities, especially OSAS, and at what age this evaluation should be performed.

This study prospectively investigates the incidence of OSAS in a group of young children with DS followed up prospectively from age 2 years for 5 years. In addition, we examine their parents’ ability to identify sleep abnormalities.

METHODS

Sixty-five children were enrolled in a 5-year longitudinal study, following the otolaryngologic problems seen in children with DS at Cincinnati Children’s Hospital Medical Center. The study design includes overnight polysomnography (PSG), or sleep study, performed in children aged 3½ through 4 years.

All of the children participating in this longitudinal study entered the study at aged 2 years or younger. If parental history and/or examina-
tion results suggested possible upper airway obstruction before the scheduled sleep study at age 3½ through 4 years, PSG was performed earlier. Twenty-two of the 56 children underwent multiple sleep studies. For reporting clarity, the initial sleep study results are analyzed separately from any subsequent studies.

Polysomnograms were obtained and analyzed by pulmonologists board certified in sleep medicine in a sleep center accredited by the American Academy of Sleep Medicine (Westchester, Ill). The PSG or sleep study was performed by using a computerized system (Grass-Telefactor; Astro-Med, Inc, West Warwick, Rl). Parents remained with their children throughout the night. Children were not sleep deprived before the study, nor were any sedatives administered. The following variables were recorded during the study: electroencephalogram (EEG; C3-A2, C4-A1, O1-A2, and O2-A1); right and left electrooculograms; submental, tibial, and intercostal electromyograms; electrocardiogram; nasal/oral air flow through nasal pressure sensor; end-tidal carbon dioxide, measured at the nose by means of infrared capnometry (N1000; Nelcor, Van Nuys, Calif); oxygen saturation measured with a pulse oximeter (N1000); oximeter pulse waveform; video monitoring using an infrared video camera and recorded on a videotape; and rib cage and abdominal volume changes recorded with a computer-assisted respiratory inductance plethysmograph (Somnostar; Noninvasive Monitoring System, Inc, Miami Beach, Fl). Sleep staging was performed according to the rules of Rechtschaffen and Kales.10 The following variables were generated from the PSG: study and sleep duration; percentage of sleep time spent in different stages of sleep; number of arousals from sleep—the standard definition of arousals recommended by the American Sleep Disorders Association, Rochester, Minn, was used; apnea index—the number of OSA episodes per hour of sleep; hypopnea index—the number of obstructive hypopneas per hour of sleep; apnea-hypopnea index or the obstructive index (OI)—the number of obstructive apnea and hypopnea episodes per hour of sleep; desaturation index—the number of episodes of oxygen desaturation by 4% or more per hour of sleep; time spent during sleep with oxygen desaturations less than 90%; peak and average end-tidal carbon dioxide greater than 45 mm Hg; and greater than 50 mm Hg. It can be technically challenging to perform full, overnight PSGs in young children with developmental delays, such as those with DS. Therefore, the Pediatric Sleep Laboratory at Cincinnati Children's Hospital Medical Center provided an extra sleep technician whenever a child with DS underwent PSG. With this added oversight, only 6 children were not able to adequately complete a PSG.

Before the sleep study, the parents completed a survey about their child's sleep behaviors. This questionnaire was developed from the Children's Sleep Habits Questionnaire, validated by Owens et al.11 One difficulty in evaluating sleep abnormalities in all children has been the use of adult definitions when describing this younger population. Children should not be evaluated using the standard adult definitions of sleep abnormalities. For instance, children have faster respiratory rates and smaller functional residual capacity, so significant oxygen desaturation can occur after shorter periods of apnea than in an adult population.8 The development of appropriate criteria for children has therefore been necessary.1,3-5,12,13 Because these definitions are inconsistent and because the science of pediatric sleep is still evolving, specific definitions used in data interpretation of the overnight PSGs are presented.

Obstructive apnea is defined as the presence of chest/abdominal wall motion in the absence or decrease of air flow and/or the sum channel of inductive plethysmography by more than 80% of the preceding breath. All obstructive events for 2 or more breaths are counted.

Obstructive hypopnea is a 20% to 50% reduction in the sum channel of inductive plethysmography and/or air flow, associated with oxygen desaturation of 4% or greater and/or an EEG arousal that follows the hypopnea. All obstructive events of 2 breaths or more are counted.

Central apnea is the absence of air flow, combined with absence of abdominal and thoracic movements for 2 or more breaths or respiratory cycles. Mixed apnea is central apnea, followed by obstructive apnea, for at least 2 respiratory cycles. The OI is the number of obstructive apneas, mixed apneas, and obstructive hypopneas per hour of sleep. Many writers refer to the OI as the apnea/hypopnea index or the AHI index or AHI.

Obstructive sleep apnea is defined, in part, by the OI. Mild OSA is defined by an OI of 1 to 5, moderate OSA is defined by an OI of 5 to 15, and severe OSA is defined if the OI is greater than 15 (Table 1).

The respiratory disturbance index is the number of obstructive apneas, mixed apneas, central apneas, obstructive hypopneas, and central hypopneas per hour of sleep. The respiratory disturbance index is different from the OI in that it includes central apneas and central hypopneas.

In hypoventilation syndrome, hypoventilation occurs when the end-tidal carbon dioxide is greater than 45 mm Hg for more than 66% of the total sleep time or if the end-tidal carbon dioxide is greater than 50 mm Hg for more than 10% of the total sleep time.

Arousals are defined by the following criteria: (1) An EEG arousal is an abrupt shift to a faster EEG frequency and must be 3 seconds or longer; (2) arousals in non–rapid eye movement (REM) sleep may occur without concurrent increases in submental electromyogram amplitudes, but if an arousal occurs during REM sleep, the arousal must be accompanied by concurrent increases in submental electromyograms.5,14,15 The arousal index is expressed as arousal events per hour of sleep. In our sleep center, the arousal index is abnormal if it is 10 or greater.

Hypoxemia, or oxygen desaturation, is considered abnormal if there are sustained oxygen desaturations less than 92% or intermittent oxygen desaturations less than 90%.

Table 1. Obstructive Index and Degree of Obstructive Sleep Apnea

<table>
<thead>
<tr>
<th>Degree of Obstructive Sleep Apnea</th>
<th>Obstructive Index</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Mild</td>
<td>1-5</td>
</tr>
<tr>
<td>Moderate</td>
<td>&gt;5-15</td>
</tr>
<tr>
<td>Severe</td>
<td>&gt;15</td>
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</table>

Of the 65 children who started the 5-year longitudinal study, 56 were able to complete the full sleep study. In 4 cases, the study was discontinued at the parents’ insistence. Two other patients completed the sleep study, but the results were incomplete because of patients pulling monitors off or too little study time. Three patients moved out of state and dropped out of the study before their sleep study was complete. Therefore, the following results reflect data from the 56 completed studies (Table 2).

The age of the children undergoing the sleep studies ranged from 20 to 63 months (mean age, 42 months). Four children were younger than 24 months, and 4 children were older than 60 months. Children younger than the study protocol of 3½ to 4 years underwent PSG if there...
the parent says the child does not have a problem. Sensitivity was 0.45, indicating the chance the child does not have a sleep problem if the parent says the child has a problem. Negative predictive value was 0.36, indicating the chance the child has a sleep problem if the parent says the child does not have a problem. Specificity was 0.61; in children with abnormal sleep studies, 11 (60%) of 18 parents will report it, indicating how well the parent questionnaire identifies children without a problem. Positive predictive value was 0.53, indicating the chance the child has a sleep problem if the parent says the child has a problem. Negative predictive value was 0.45, indicating the chance the child does not have a sleep problem if the parent says the child does not have a problem.

was a strong parental concern about sleep problems. Parental hesitancy and concern about the overnight PSG accounted for some children who did not undergo PSG until they were older than the study protocol age.

Total sleep time divided by total study time, or sleep efficiency, ranged from 48% to 95% (mean, 80%). This percentage reflects some of the technical difficulties encountered when performing sleep studies in young children with developmental delays.

The number of REM sleep cycles ranged from 0 to 12 (mean, 5.2). Percentage of REM sleep ranged from 0% to 35% (mean, 18.3%).

Arousal indexes ranged from 4 to 35.2 (mean, 12.9). The arousal index was elevated in 34 (61%) of the 56 children.

Obstructive indexes ranged from 0 to 17.8. The OI was greater than 1 in 21 (38%) of the children. Abnormal carbon dioxide retention occurred in 17 children (30%). Hypoxic events occurred in 11 children (20%). Thirty-two children (57%) had abnormal sleep study results, as defined by an abnormal OI, hypercarbia, and/or hypoxemia. The REM sleep percentage and number of cycles was similar for all groups, despite sleep study results.

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The current recommendations for health care guidelines for children with DS, published by the American Academy of Pediatrics in 2001, acknowledge that children with DS may have an increased risk of sleep abnormalities and recommend that primary care physicians

### Table 2. Summary of Polysomnographic Results Overall and According to Group*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Group 1 (n = 21)</th>
<th>Group 2 (n = 11)</th>
<th>Group 3 (n = 24)</th>
<th>Overall (N = 56)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at study, mo</td>
<td>40.8 ± 7.5</td>
<td>44.8 ± 9.3</td>
<td>43.5 ± 7.4</td>
<td>42.8 (20-63)</td>
<td>.33</td>
</tr>
<tr>
<td>Arousal index</td>
<td>15.0 ± 7.8</td>
<td>10.1 ± 3.6</td>
<td>12.3 ± 5.0</td>
<td>12.9 (4-35)</td>
<td>.14</td>
</tr>
<tr>
<td>Rapid eye movement, %</td>
<td>17.5 ± 7.5</td>
<td>15.9 ± 7.6</td>
<td>20.2 ± 7.3</td>
<td>18.3 (0-35)</td>
<td>.06</td>
</tr>
<tr>
<td>Rapid eye movement cycles, No.</td>
<td>5.2 ± 1.6</td>
<td>4.1 ± 1.8</td>
<td>5.6 ± 2.6</td>
<td>5.2 (0-12)</td>
<td>.14</td>
</tr>
<tr>
<td>Sleep efficiency, %</td>
<td>82.2 ± 7.9</td>
<td>81.1 ± 7.6</td>
<td>78.0 ± 10.4</td>
<td>80.2 (48-95)</td>
<td>.30</td>
</tr>
</tbody>
</table>

*Data are given as mean ± SD or mean (range).

### Table 3. Sleep Problems as Rated by Parents or Polysomnography*

<table>
<thead>
<tr>
<th>Parent</th>
<th>Polysomnography</th>
<th>Yes</th>
<th>No</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>4</td>
<td>7</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>13</td>
<td>11</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>17</td>
<td>18</td>
<td>35</td>
<td></td>
</tr>
</tbody>
</table>

*Sensitivity was 0.23; in children with abnormal sleep studies, 4 (23%) of 17 parents will report it, indicating how well the parent questionnaire identifies children with a problem. Specificity was 0.61; in children with normal sleep studies, 11 (60%) of 18 parents will report it, indicating how well the parent questionnaire identifies children without a problem. Positive predictive value was 0.53, indicating the chance the child has a sleep problem if the parent says the child has a problem. Negative predictive value was 0.45, indicating the chance the child does not have a sleep problem if the parent says the child does not have a problem.

PARENTAL QUESTIONNAIRE

Thirty-five of the 56 parents completed the questionnaire before the sleep study (Table 3). Parents were asked if their child snored, if the child stopped breathing while sleeping, and if there were snorts or gasps for air during sleep. Overall, 11 (31%) of 35 parents reported that their child had sleep problems, but these parents were correct about a sleep abnormality in only 4 (36%) of 11 cases. The other 7 (64%) children had normal PSGs. Of the 24 (69%) parents who reported no sleep problems, 13 (54%) of their children had abnormal PSGs.

In groups 1 and 2, the children with abnormal sleep study results, 13 (77%) of the 17 parents said their child had no sleep problems. Only 4 (23%) were concerned about their child's sleeping. In the children from group 3, in whom the sleep study results were normal, 11 (61%) of the 18 parents correctly reported no sleep problems, but the other 7 (39%) said their child had sleep problems.

OTHER HEALTH PROBLEMS: OBESITY AND CARDIAC DISEASE

The mean body mass index and the presence or absence of underlying cardiac disease for each group were evaluated. Table 4 shows no statistical significance between the groups in regard to body mass index, and there was also no statistical difference when the children were evaluated for cardiac disease (Table 5).

### Table 4

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Group 1 (n = 21)</th>
<th>Group 2 (n = 11)</th>
<th>Group 3 (n = 24)</th>
<th>Overall (N = 56)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body mass index, kg/m²</td>
<td>18.2 ± 2.3</td>
<td>18.7 ± 2.8</td>
<td>18.4 ± 2.5</td>
<td>18.5 (16-23)</td>
<td>.63</td>
</tr>
<tr>
<td>Heart index, %</td>
<td>2.5 ± 0.9</td>
<td>2.3 ± 1.0</td>
<td>2.4 ± 0.8</td>
<td>2.4 (1-6)</td>
<td>.14</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>2 (10%)</td>
<td>1 (9%)</td>
<td>5 (21%)</td>
<td>4 (14%)</td>
<td>.10</td>
</tr>
<tr>
<td>Hypertension</td>
<td>4 (20%)</td>
<td>2 (18%)</td>
<td>7 (29%)</td>
<td>6 (21%)</td>
<td>.13</td>
</tr>
</tbody>
</table>

The current recommendations for health care guidelines for children with DS, published by the American Academy of Pediatrics in 2001, acknowledge that children with DS may have an increased risk of sleep abnormalities and recommend that primary care physicians...
question parents about possible sleep disorders when the children are 5 years and older. However, no recommendations are made for specific testing.

In general, parents of children with DS significantly underestimate the severity of their child’s sleep disturbances. Overall, 69% of the parents in this group of children reported no sleep problems, yet 54% of these children had abnormal PSGs. In the children who had abnormal sleep study results, only 23% of parents correctly predicted a problem. Marcus et al had similar findings; in their study, only 32% of the parents reported a clinical suspicion of OSAS, despite a 100% incidence of abnormal study results.

This inaccuracy of reporting may be a characteristic more common in parents of children with DS. If we look at similar questionnaires completed by parents with healthy or typical children, the results show a better correlation. Bruzellette and colleagues developed a questionnaire in an attempt to detect OSA without the use of sleep studies in healthy children; when questioning the parents of healthy or typical children with PSG-proved OSA, 96% of the parents correctly reported snoring and difficulty breathing during sleep, and 78% correctly reported apnea. The lower accuracy in parents of children with DS is further illustrated by their tendency to assume that their child’s irregular breathing at night is normal for a child with DS, frequently expressed comment.

The OSAS has been linked to various morbidities, including pulmonary hypertension and cor pulmonale. Although these morbidities are less common today because of medical advances, children with DS and cardiac anomalies are at higher risk for developing these life-threatening complications. The OSAS also has been associated with neurocognitive abnormalities. The hypoxemia associated with OSAS is correlated with lower IQ performance testing. Anomalies are at higher risk for developing these life-threatening and possibly a disorder of neurotransmitters. All of these factors contribute to the children’s abnormal sleep.

Sleep fragmentation, associated with increased arousals and decreased REM sleep, is also an important component of sleep pathology. Sleep staging and evaluations of arousals are not considered in the OI but should be included in the overall analysis of the test results. Rapid eye movement sleep should make up 25% to 30% of sleep time for children younger than 5 years. In children older than 5 years, the percentage of REM is similar to adult levels of 20% to 25%. In this group of children with DS, only 9 [16%] of the 56 children spent more than 25% of their sleep time in REM sleep. Decreased REM sleep has been associated with an immaturity of the inhibitory system of the central nervous system and possibly a disorder of neurotransmitters. All of these factors contribute to the children’s abnormal sleep.

An abnormal or elevated arousal index alone was not considered an abnormal PSG result in this study. The significance of an elevated arousal index alone, with the other measured components of the PSG being normal, has not yet been fully established. However, 34 (61%) of the children had an elevated arousal index.

The arousal response is usually regarded as a protective mechanism. When one experiences obstructive breathing during sleep, this protective reflex helps to curtail the upper airway obstruction and reestablish a patent airway. Arousals occur secondary to hypoxemia, hypercarbia, and increased upper airway resistance. In addition, repetitive sleep fragmentation can lead to a blunted arousal response to respiratory stimuli, which can cause a delay in apnea termination, resulting in more severe adverse effects of the obstruction, particularly oxygen desaturation and carbon dioxide retention. Some have speculated that a defect in this protective reflex could lead to life-threatening asphyxia or even death. Many effects of increased arousals during sleep are just beginning to be understood. There is concern that an excessive number of arousals may lead to fragmented sleep and sleep deprivation. Excessive sleep arousals and sleep fragmentation have been linked to symptoms usually associated with sleep deprivation such as daytime sleepiness, lack of energy, and lack of initiative. Increased arousals have been associated with decreased neurocognitive abilities and lower results on IQ tests. The increased arousal rate in children with DS may affect their daytime function and could exacerbate learning or behavior disorders. In children with DS, the resultant behavior and learning disabilities may be overlooked and assumed to be caused by the limited intellectual abilities commonly assigned to children with DS.
If we examine only the OI, hypoventilation with hypercarbia, and hypoxemia, 32 (57%) of 56 PSGs were abnormal (groups 1 and 2). If we also include an abnormal or elevated arousal index, the incidence of abnormal PSGs in this population increases to 80% (45 of 56). As more is learned about the consequences of an elevated arousal index, we may need to become more stringent in our test interpretation.

Frequent risk factors associated with OSAS in adults, but not as commonly seen in children, were examined. There was no correlation between underlying cardiac disease and sleep study results (P = .37) (Table 5). Evaluation of each child’s body mass index at the time of their sleep study shows that obesity also was not a risk factor (Table 4).

Polysomnography in children is still an evolving and developing discipline. Similar to the field of pediatric otorhinolaryngology, PSG in children initially started with the use of adult criteria superimposed on this younger population. However, results of numerous studies attest to the need for different pediatric standards. In addition, testing environments and techniques need to be better standardized. For instance, nap studies cannot be correlated with data obtained during nighttime sleep. Along with the recent interest on the effects and implications of sleep fragmentation, how best to define sleep arousals is controversial. Mograss et al suggested the use of a simple montage using cardiorespiratory channels and videotaping as an alternative to EEG in measuring arousals; they found that this system accurately indicated 84% of the arousals that an EEG would indicate. Different methods of calculating arousals lead to different normal values. This issue is not yet resolved. Therefore, in interpreting different studies and their data, it is important to evaluate the methods and the techniques of data interpretation used in the particular sleep laboratory performing the studies.

CONCLUSIONS

This study is a prospective evaluation of the incidence of OSAS in young children with DS. A recent publication by Dyken et al was also prospective but was performed in a group of 19 children with DS, aged 3 to 18 years (mean age, 9 years). Seventy-nine percent of the children in their study had an abnormal OI. Results of the study by Dyken et al and the study by Marcus et al show a high incidence of OSA in these elementary-school-age children with DS. Our results point to the need for objective testing for OSAS in children as young as 3 or 4 years. Because there is a high incidence of sleep disorders in children with DS, baseline studies, using full overnight PSG, are recommended even if the parents report no sleep problems in their child.

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