

Characteristics of Sleep Disturbance in CdLS

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Common sleep problems among individuals with CdLS consist mainly of insomnia (trouble going to sleep or staying asleep) and sleepiness. It appears that sleep apnea may also occur more commonly in CdLS than in the general population. Each of these can make for long nights for parents and leave children tired and grumpy during the day.

Since there is a known occurrence of behavioral problems in individuals with CdLS, a small number of studies looked at the relationship between behavior and sleep to try to uncover a link. This provided conflicting results as to why sleep disturbances occur, however studies suggest that 12 to 72 percent of individuals with CdLS have trouble going to sleep and staying asleep.

The articles published on sleep primarily studied the general occurrence of sleep difficulties among people with CdLS. The first by Berney et al. surveyed the families/caregivers of 49 children and adults with CdLS with mild versus severe intellectual disability (ID). They screened for irregular sleep patterns, insomnia, interrupted sleep and excessive daytime sleepiness. Out of those individuals, 55 percent demonstrated at least one symptom. Patients with mild ID were less likely to have sleep disturbance than those with severe ID. The second study by Hall et al. compared sleep disturbance in 54 children with CdLS and 46 children with ID but without CdLS. Sleep disturbance was found in 55 percent of the children in both groups and they found that sleep disturbance was not associated with self injurious behavior. A third study by Basille et al found sleep disorders in only 12 percent of 56 children with CdLS.

More recently, a study by Kline et al. of 18 adults and 46 children with CdLS noted that 51 percent had difficulty falling asleep; 65 percent had frequent night-time awakening; 30 percent had consecutive days without sleep; and 24 percent had frequent daytime napping. The onset of sleep disturbance in most occurred as infants or toddlers. Nearly 40 percent also noted an increase in the severity of sleep disturbance with increasing age. Unlike previous studies, a strong association was seen between sleep disturbance and self-injurious behavior (63 percent) as well as gastroesophageal reflux. About half of the respondents listed medications taken for sleep including melatonin, eszopiclone (Lunesta®), zolpidem (Ambien®), chloral hydrate, and temazepam.

Obstructive sleep apnea (OSA) is a condition characterized by snoring, witnessed pauses in breathing and night-time gasping and choking. Children with OSA often have problems with daytime focus and attention, increased behavioral problems including hyperactivity, and decreased school performance. Adults are more likely



to experience daytime sleepiness, morning headaches and moodiness. However, some patients present only with poor sleep quality or restless sleep. Treatment in children often starts with tonsillectomy and adenoidectomy, while adults are usually treated with a breathing machine during sleep called CPAP (continuous positive airway pressure). Weight loss can be critical. In those with persistent OSA or who cannot tolerate CPAP, dental devices and further surgical options are considered.

Sleep study evaluation is the primary method for diagnosis of OSA and has been successfully carried out in children with Down and Angelman syndromes. This demonstrates that it is a useful tool in the evaluation of sleep disturbances in patients with ID. However, there have been no studies reporting sleep study results or the frequency of snoring or OSA in individuals with CdLS.

To better characterize the nature and extent of sleep problems, we are using three validated sleep questionnaires to evaluate snoring, symptoms suggestive of OSA and sleepiness in children and adults with CdLS. Our results suggest that people with CdLS have an increased rate of possible OSA (35-36 percent) and sleepiness (25-35 percent). However, additional studies are needed with larger sample sizes and confirmation with sleep studies.

For problems with falling or staying asleep, behavioral therapy with consistent bedtime routines, minimizing bright light before bedtime and regular sleep schedules are important. For those in whom this is ineffective, sleep studies and sleep logs are often used to better characterize sleep patterns and breathing. Weighted blankets may help those with CdLS and autistic features. Medications for insomnia may also be used including melatonin, clonidine, zolpidem (Ambien®) and zaleplon (Sonata®). It is important to note, however, that most medications prescribed for insomnia are not FDA approved for children.

In conclusion, sleep disordered breathing, insomnia and sleepiness appear to be common in CdLS. As previous studies have shown, it is unclear if sleep disturbance correlates to behavioral and learning issues in this population. Further in-depth studies will help us learn more about this and should serve to improve quality of life for both those with CdLS and their families.

1. Basile E, Villa L, Selicorni A, Molteni M. The behavioral phenotype of Cornelia de Lange Syndrome: a study of 56 individuals. *J Intellect Disabil Res.* 2007 Sept;51:671-681.
2. Berney T, Ireland M, Burn J. Behavioral phenotype of Cornelia de Lange syndrome. *Arch Dis Child* 1999 Oct;81(4):333-336.
3. Hall SS, Arron K, Sloneem J, Oliver C. Health and sleep problems in Cornelia de Lange Syndrome: a case control study. *J Intellect Disabil Res.* 2008 Mar;52:458-468.
4. Kline A. Clinical delineation of sleep disturbance in Cornelia de Lange syndrome. American Society of Human Genetics, Annual meeting, Oct 2007.

