Is screening for obstructive sleep apnea between 3 and 4 years of age in children with Down's syndrome too late?

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Summary:

Obstructive sleep apnea (OSA) is very common in children with Down's syndrome (DS), with potential negative consequences on neurodevelopment, behavior and quality of life. Current guidelines recommend a sleep study screening (PSG) in all infants with DS between the age of 3 and 4 years, but several studies show that OSA is highly prevalent and most often severe within the first months of life.
A recently published study showed that early screening and treatment of OSA in DS infants since the age of 6 months was associated with significantly better neurocognitive outcomes, which argues in favor of early screening and intervention for OSA during this critical period of cognitive development.
This implies the necessity to develop reliable, cost-effective screening methods for OSA screening in this young population.

Obstructive sleep apnea in children with Down syndrome:

OSA is a sleep disorder characterized by repeated total (apnea) or partial (hypopnea) obstruction of the upper airway during sleep, leading to decreased oxygen saturation or arousals. OSA is very common in children with DS, with reported prevalence of 50-79% (Bull et al. 2022). Untreated or persistent OSA in children with DS is associated with pulmonary hypertension and negatively affects neurocognitive development, behavior and quality of life.

What OSA screening in children with DS?

Detection of OSA is however not straightforward as symptoms and sleep questionnaires are poor predictors of OSA in infants with DS. Therefore, polysomnography (PSG) which monitors brain waves, blood oxygen and carbon dioxide levels, heart rate, and breathing during sleep remains the gold standard for diagnosing OSA. The apnea-hypopnea index (AHI) quantifies the severity of OSA and represents the mean number of apneas and hypopneas per hour during sleep with: no OSA: AHI < 1 event/hour, mild, OSA: AHI 1–5 events/hour, moderate OSA: AHI > 5–10 (Berry et al. 2012).

When to screen for OSA in children with DS?

Current guidelines recommend a sleep study (PSG) in young children with DS between the age of 3 and 4 years (Bull et al. 2022). However, because these recommendations are not evidence-based, the optimal timing of screening and treatment for OSA in children with DS remains an important unanswered clinical question.

Can early diagnosis, within the first months of life, and OSA treatment within this critical window of cognitive development in infants with DS, contribute to a significant improvement in neurocognitive outcomes as well as quality of life?

What do we know about the prevalence and severity of OSA in infant and young children with DS?

In fact, OSA, most often severe, has been observed in infants (0-1 years of age) and young children (1-3 years of age) with DS. Indeed, of 40 consecutive infants ≤ 12 months of age who underwent a PSG at a single academic center, all met criteria of OSA with a mean obstructive AHI of 34.6 events/hour (Cho et al 2023). Another large retrospective cohort study showed that 94% of 235 children younger than 7 years with DS had OSA with an inverse relationship between age and OSA severity, with 66% of infants < 6 months of age having severe OSA (Seither et al. 2023). These data are in favor of an earlier detection of OSA.

What can we expect from very early diagnosis and treatment of OSA on neurocognitive development?

There is a consensus in the literature that the first year of life is a critical window for optimal neurocognitive development of children with or without intellectual disabilities and that, untreated or persistent OSA in children with DS, negatively affects neurocognitive development, behavior and quality of life in children similar to findings in children without DS (Horne et al. 2019). Conversely, there were no studies demonstrating the potential benefits of a very early diagnosis and treatment of OSA on the neurocognitive development of infants (0-1 years of age) and young children (1-3 years of age) with DS.
A recently published study fills this knowledge gap. In this prospective, interventional, non-randomized study, 40 infants with DS underwent a systematic PSG every 6 months between 6 and 36 months of age (Screened Group). These screened infants were compared to a control group of 40 infants with DS receiving standard of care and a single, systematic PSG at 36 months of age (Standard Care Group). When present, OSA was treated. This study confirmed that prevalence of OSA was high in infants with DS both in the first year of life and at 36 months of age (>90%). At 6 months of age, OSA was present in 97.4% of infants and 53.8% had moderate or severe OSA (Fauroux et al. 2024). More importantly, overall neurocognitive outcome, measured by the total score of the Griffiths III at 36 months, was significantly higher in the Screened Group compared to the Standard Care Group (difference: 4.1; 95%CI: 1.3; 7.6; p = 0.009). A significative difference in favor of the Screened group was also observed on the VABS-II, a tool used to assess behaviour, adaptive functioning and communication (Fauroux et al. 2024).

Is it time to advocate screening for obstructive sleep apnea as early as 6 months of age in children with DS?

We are convinced that the very high prevalence of moderate to severe OSA in infants and young children with DS, and the promising results of screening and OSA treatment as early as 6 months of age, argue in favor of a systematic early screening and intervention for OSA during this critical period of cognitive development.
However, there is still much to be done. Above all, we need to ensure that the benefits of screening and early intervention on neurocognitive development and behavior persist over time. Furthermore, it is evident that the access to PSG is extremely limited worldwide. There is thus an urgent need to develop reliable, cost-effective and noninvasive screening methods for OSA in infants and young children, which should preferably be used at home.

In conclusion:

Current data suggest that children with DS should be screened for OSA as early as 6 months of age. However, such a recommendation can only be implemented once we are certain that the medium- and long-term benefits of this intervention are sustained, that there are no adverse effects, and that it is feasible in current practice. In the meantime, it is important that parents and caregivers of children with DS are aware of the high prevalence and very early onset of OSA and its negative impact on neurocognitive development, behavior, and quality of life in these children.

Take home messages in three bullet-points

- High frequency of obstructive sleep apnea in infants with Down syndrome.
- A screening and treatment of OSA in infants with Down syndrome, as early as 6 months of age, may contribute to a significantly better neurocognitive outcome and behavior at the age of 3 years.
- There is a need to develop reliable, cost-effective screening methods for OSA in infants.

References

Berry RB, Budhiraja R, Gottlieb DJ, Gozal D, Iber C, Kapur VK, Marcus CL, Mehra R, Parthasarathy S, Quan SF, Redline S, Strohl KP, Davidson Ward SL, Tangredi MM; American Academy of Sleep Medicine. Rules for scoring respiratory events in sleep: update of the 2007 AASM Manual for the Scoring of Sleep and Associated Events. Deliberations of the Sleep Apnea Definitions Task Force of the American Academy of Sleep Medicine. J Clin Sleep Med. 2012 Oct 15;8(5):597-619. doi: 10.5664/jcsm.2172. PMID: 23066376; PMCID: PMC3459210.

Bull MJ, Trotter T, Santoro SL, Christensen C, Grout RW; COUNCIL ON GENETICS; Burke LW, Berry SA, Geleske TA, Holm I, Hopkin RJ, Introne WJ, Lyons MJ, Monteil DC, Scheuerle A, Stoler JM, Vergano SA, Chen E, Hamid R, Downs SM, Grout RW, Cunniff C, Parisi MA, Ralston SJ, Scott JA, Shapira SK, Spire P. Health Supervision for Children and Adolescents With Down Syndrome. Pediatrics. 2022 May 1;149(5):e2022057010. doi: 10.1542/peds.2022-057010. PMID: 35490285.

Cho Y, Kwon Y, Ruth C, Cheng S, DelRosso LM. The burden of sleep disordered breathing in infants with Down syndrome referred to tertiary sleep center. Pediatr Pulmonol. 2023 Apr;58(4):1122-1126. doi: 10.1002/ppul.26302. Epub 2023 Jan 13. PMID: 36588294; PMCID: PMC10349798.

Fauroux B, Sacco S, Couloigner V, Amaddeo A, Ravel A, Prioux E, Toulas J, Cieuta-Walti C, Walti H, Luscan R, Falquero S, Clert M, Caillaud MA, De Sanctis L, Khirani S, Marey I, Mircher C. Early detection and treatment of obstructive sleep apnoea in infants with Down syndrome: a prospective, non-randomised, controlled, interventional study. Lancet Reg Health Eur. 2024 Aug 21;45:101035. doi: 10.1016/j.lanepe.2024.101035. PMID: 39262447; PMCID: PMC11387522.

Horne RS, Wijayaratne P, Nixon GM, Walter LM. Sleep and sleep disordered breathing in children with down syndrome: Effects on behaviour, neurocognition and the cardiovascular system. Sleep Med Rev. 2019 Apr;44:1-11. doi: 10.1016/j.smrv.2018.11.002. Epub 2018 Nov 22. PMID: 30576943.

Seither K, Helm BM, Heubi C, Swarr D, Suhrie KR. Sleep Apnea in Children With Down Syndrome. Pediatrics. 2023 Mar 1;151(3):e2022058771. doi: 10.1542/peds.2022-058771. PMID: 36762410.

Further reading:

https://ndss.org/resources/sleep-down-syndrome

https://t21learning.institutlejeune.org/le-syndrome-des-apnees-obstructives-du-sommeil-saos/