

Anti-inflammatory therapy for obstructive sleep apnea in children

Bat-Chen Friedman MD Ran D. Goldman MD FRCPC

Abstract

Question A 4-year-old child was diagnosed by polysomnography as experiencing mild obstructive sleep apnea (OSA). Despite the child being inattentive and distracted during the day at school, his parents prefer to avoid surgical treatment (adenotonsillectomy). Are there any non-surgical treatments for mild OSA in young children?

Answer Obstructive sleep apnea in children is caused mainly by adenotonsillar hypertrophy and can lead to considerable morbidities, including neurocognitive and behavioural disturbances. Surgical removal of the tonsils and adenoids is the treatment of choice. In recent years, however, a new understanding of the inflammatory components of OSA has led to the assumption that anti-inflammatory treatment can reduce adenotonsillar size and improve OSA symptoms. Evidence from a few studies suggests that intranasal steroids and oral leukotriene receptor antagonists have beneficial effects, but data from randomized controlled trials are still lacking.

Résumé

Question Un enfant de 4 ans a reçu un diagnostic d'apnée obstructive légère du sommeil (AOS). Même si l'enfant manque d'attention et est distrait durant la journée à l'école, ses parents préfèrent éviter un traitement chirurgical (adéno-amygdalectomie). Existe-t-il des traitements non chirurgicaux pour une AOS légère chez les jeunes enfants?

Réponse L'apnée obstructive du sommeil chez les enfants est causée principalement par une hypertrophie des adénoïdes et des amygdales, qui peut causer une morbidité considérable, y compris des troubles neurocognitifs et comportementaux. L'ablation chirurgicale des adénoïdes et des amygdales est le traitement privilégié. Toutefois, au cours des dernières années, de nouvelles connaissances sur les composantes inflammatoires de l'AOS ont mené à l'hypothèse qu'un traitement anti-inflammatoire peut réduire la taille des adénoïdes et des amygdales et améliorer les symptômes de l'AOS. Les données factuelles tirées de quelques études font valoir que des stéroïdes par voie intranasale et des antagonistes des récepteurs des leucotriènes par voie orale ont des effets bénéfiques, mais on ne dispose pas encore de données provenant d'études contrôlées randomisées.

Childhood obstructive sleep apnea (OSA) syndrome is characterized by episodic upper airway obstruction during sleep. The airway obstruction might be accompanied by episodic snoring, episodic hypoxia and hypercapnia, and sleep fragmentation due to repeated arousals.^{1,2} The prevalence of childhood OSA has been estimated at 2% to 3% of healthy children.¹ If not treated, OSA can lead to considerable morbidity, including neurocognitive and behavioural disturbances, systemic and pulmonary hypertension, endothelial dysfunction, enuresis, and failure to thrive.²

Surgical treatment of OSA

Adenotonsillar hypertrophy is the most common underlying cause of OSA, as the relative enlargement of the tonsils during the preschool years reduces pharyngeal space and promotes airway collapse during sleep.³ Adenotonsillectomy, the surgical removal of the tonsils and adenoids, is the treatment of choice. It is usually

well tolerated and leads to resolution of OSA symptoms in most cases.² However, adenotonsillectomy can be painful and carries the risk of complications, such as hemorrhage, postsurgical respiratory compromise, and adverse anesthetic events.⁴ The complication rates reported are in the range of 5% to 34%.⁵ Residual OSA is estimated to occur in more than 20% of children who go for adenotonsillectomy.⁵ Moreover, there are no definitive polysomnographic criteria for adenotonsillectomy, and the procedure is usually reserved for children with moderate to severe respiratory disturbance—mainly those with an apnea-hypopnea index (AHI) exceeding 5 events per hour of sleep.² No consensus exists on the appropriate management of children with an AHI of more than 1 but less than 5 events per hour of sleep, although such children are at risk of associated morbidity.⁶ Owing to the limitations of adenotonsillectomy, the interest in non-surgical treatment options for OSA has increased.

OSA and inflammation

Nasal and oropharyngeal inflammation is present in children with OSA and might contribute to the pathogenesis of breathing disturbances during sleep.^{7,8} Local and systemic inflammatory markers and pro-inflammatory cytokines are increased in these children and promote lymphoid tissue proliferation.⁹ Thus, systemic or topical anti-inflammatory agents were suggested to have a potential role in reversing tonsillar enlargement.¹⁰⁻¹⁵

Intranasal corticosteroids

Although an earlier study demonstrated no beneficial effects of systemic corticosteroids on OSA,¹¹ in 2001 Brouillette et al conducted the first randomized, triple-blind controlled trial comparing 6 weeks of treatment with nasal fluticasone versus placebo in 25 children between the ages of 1 and 10 years with polysomnography-based diagnosed OSA. There was a substantial decrease in the frequency of apnea and hypopnea events among children treated with fluticasone; however, there was no improvement in parents' symptom scores or reduction in tonsillar and adenoidal size.¹² In another open-label study, polysomnographic parameters and symptom scores of snoring children with mild OSA improved after 4 weeks of treatment with nasal budesonide, and the effect was sustainable for several months after treatment.¹³ In 2008 a double-blind randomized crossover trial compared intranasal budesonide (32 µg per nostril at bedtime) with placebo in a 6-week treatment period in 62 children. Polysomnographic measures of sleep quality and respiratory disturbance improved and adenoid size decreased after treatment. Normalization of sleep measures was obtained in 54% of treated children. Furthermore, sleep studies of 25 children 8 weeks after cessation of treatment revealed a sustained effect.¹⁴ The authors concluded that the findings justified the use of intranasal steroids as the initial therapeutic option in otherwise healthy children with mild OSA. However, the optimal dosage and duration of therapy are still unclear. It also remains unclear which subgroups of patients are more likely to benefit from this therapeutic option.

Leukotriene receptor antagonists


Several studies suggest that the inflammatory processes in OSA involve leukotriene expression and regulation.^{7,8,16} Leukotriene levels were higher in adenotonsillar tissue of children with OSA compared with children with recurrent infectious tonsillitis.¹⁶ When leukotriene concentrations were quantified using exhaled breath condensate collected from children with OSA, a disease severity-dependent increment was observed.⁷ Therefore, leukotriene receptor antagonists, which are proven to be safe, well tolerated, and effective in the preventive treatment of inflammatory conditions such as asthma

or allergic rhinitis, could serve as an alternative intervention to adenotonsillectomy in children with OSA. In a preliminary open-label intervention study, Goldbart et al¹⁵ administered montelukast therapy daily for 16 weeks to 24 children between 2 and 10 years of age with mild OSA. Sleep parameters and adenoid size were compared with those of 16 children with mild OSA who did not receive montelukast. Considerable reduction in adenoid size and in respiratory-related sleep parameters was observed in the treated group.¹⁵

Combined therapy for residual OSA

Adenoidal regrowth might occur in children after surgical intervention and is associated with recurrent symptoms.⁵ Kheirandish et al¹⁷ reported an open trial exploring the effect of a combined anti-inflammatory approach in children with persistent OSA after a surgical treatment. Twenty-two children with residual mild OSA postsurgery were offered a combined therapy consisting of intranasal budesonide and oral montelukast for a period of 12 weeks. Compared with the 14 children receiving no therapy, there was considerable improvement in the polysomnographic respiratory measures (ie, AHI, nadir of arterial oxygen saturation, and respiratory arousal index) and in the radiographic measures of airway size, thus suggesting a new approach to residual OSA after adenotonsillectomy.¹⁷

Conclusion

Anti-inflammatory treatment of childhood OSA is a promising approach that might replace surgical treatment in children with mild OSA in the future or be used as postsurgical therapy for residual OSA. Although a few studies indicate that intranasal corticosteroids and oral leukotriene receptor antagonists have beneficial effects, more information is needed on dosing, duration, and long-term effects of these treatments. 

Competing interests

None declared

Correspondence

Dr Ran D. Goldman, BC Children's Hospital, Department of Pediatrics, Room K4-226, Ambulatory Care Bldg, 4480 Oak St, Vancouver, BC V6H 3V4; telephone 604 875-2345, extension 7333; fax 604 875-2414; e-mail rgoldman@cw.bc.ca

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