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Anatomy of Obstructive Sleep Apnea: An Evolutionary and Developmental Perspective

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Abstract

Aim: Our goal was to present obstructive sleep apnea (OSA) from evolutionary and developmental perspective by highlighting the different elements that predispose humans to develop this condition.

Background: The development of complex speech and bipedalism were some of the adaptations that resulted in changes that predispose humans as a species to the development of OSA. Laryngeal descent and regression of the maxillomandibular complex were some of the changes that took place and that led to a smaller and more collapsible airway. During development, reduction of the posterior airway space and suboptimal growth of the maxillomandibular complex further increase the risk of developing OSA as adults.

Review results: Treatment of OSA should be a continuous effort that starts early in childhood through the establishment of adequate nasal breathing. Chronic mouth breathing during active craniofacial development of a child may result in anatomical changes that directly affect the airway. Different strategies may be applied to optimize nasal breathing and that allow continuous interaction between the nasomaxillary complex and the mandible during development. Ultimately, this will guide the growth of the entire facial-skeletal complex in a forward and horizontal orientation. This will result in a lower risk of developing a narrow and collapsible airway later in life.

Conclusion: Treatment of OSA should be a continuous effort to establish adequate nasal breathing early in life that will maximize the growth and development of the facial-skeletal complex and the upper airway. In order to accomplish this, multiple strategies need to be considered and possibly combined.

Clinical significance: OSA is a common disorder characterized by repetitive upper airway narrowing during sleep with resulting hypoxemia, hypercapnia, sympathetic activation, and sleep disruption. Early intervention in children suspected to have OSA is essential to reduce the risk of developing more severe OSA as adults.

Keywords: Airway collapse, Craniofacial development, Evolution, Nasal breathing, Obstructive sleep apnea, Snoring, Upper airway.

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"Nothing in biology makes sense except in the light of evolution"
—Theodosius Dobzhansky

Obstructive sleep apnea (OSA) is a common disorder characterized by repetitive upper airway narrowing occurring solely while sleeping with resulting hypoxemia, hypercapnia, sympathetic activation, and sleep disruption.[1–6] Those afflicted with OSA often complain of excessive sleepiness and neurocognitive impairment and are at increased risk for systemic hypertension, pulmonary hypertension, myocardial infarction, cerebrovascular ischemic incidents, and death.[7,8] Pathophysiologic causes of OSA likely vary among patients. Age, gender, upper airway collapsibility, inadequate responsiveness of the upper airway muscles, exaggerated arousal responses to respiratory stimulation, and oversensitivity of ventilatory control mechanisms have been identified as putative mechanisms of OSA.[9,10] A comprehensive description of the recognized phenotypes of OSA is beyond the scope of this manuscript. Instead, we focus on the evolutionary and developmental aspects of upper airway anatomy that might predispose to collapsibility and ultimately OSA.

As homo sapiens, humans possess a unique set of anatomical characteristics that arguably makes them one of the few species at risk of developing OSA.[6] Several hypotheses including the development of bipedalism and binocular vision have been generated to explain how humans developed an oropharynx. As humans assumed an upright position, they began to rely more on vision than on olfaction. This led to the degeneration of the sense of smell and liberated the soft palate from the necessity to contact the epiglottis and allowed a gap to be interposed between the two known as the oropharynx.[7,8]

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Most animal species have a short upper airway where the oropharynx is non-existent and the epiglottis locks behind the palate.[7,8] The larynx can usually be found at the level of C2, and with respiration, air passes directly from the nasopharynx into

the larynx. Swallowing entails shuttling of food and/or saliva under the soft palate and around the epiglottis such that the bolus directly enters the hypopharynx.[7] Humans on the contrary have a floppy and distensible oropharynx that is partially supported by bone and is filled with soft tissue. Adult humans have a short palate with a 2–4 cm oropharynx and a larynx that has descended to the level of C6.[9,10] Air passes from the nasopharynx, through the oropharynx, and into the laryngeal inlet. Food also passes through the oropharynx before entering the hypopharynx. In most animals, the tongue is confined to the oral cavity, whereas in humans, the loss of epiglottis lock allowed the tongue to be incorporated into the upper airway in order to protect the descended larynx from aspiration and to modulate speech.[10]

Humans are also the only animals capable of producing complex speech. For optimal speech production, there needs to be a 1:1 ratio between the horizontal and vertical segments of the supralaryngeal vocal tract, which necessitates that the oral and pharyngeal cavities have an equal length.[11] In order to create this 1:1 ratio between the oral and the pharyngeal airway, there was an anterior migration of the foramen magnum and a regression of the maxillomandibular complex aiming to shorten the face.[6,11] The regression of the skeletal complex came at the expense of teeth. Compared to other monkey species such as the chimpanzee that can have up to 44 teeth, humans just have 32 teeth.[12] This adaptation led to retroposition of the tongue and narrowing of the airway, thereby facilitating upper airway obstruction by the tongue. Given the relatively smaller human upper airway, there may not be enough room to accommodate other structures such as the palatine and lingual tonsils, which may also become obstructive elements in the upper airways. This is particularly important during sleep as sleep induced loss of upper airway motor tone further narrows and may compromise the airway lumen.

With this is mind, we should visualize the problem of OSA as a continuum that starts early in childhood and may continue into adulthood if the appropriate steps are not taken to address different problems that contribute to the development of this condition. The current practice guidelines for the treatment of pediatric OSA recommend adenotonsillectomy as the first line treatment for children with OSA and adenotonsillar hypertrophy.[13] Treatment with continuous positive airway pressure (CPAP) is recommended if adenotonsillectomy is not performed of if OSA persists postoperatively.[13] These practice guidelines make no mention of other anatomical issues that also need to be addressed in order to optimize craniofacial and airway development of the child and to prevent OSA relapse after successful adenotonsillectomy.

Several studies that have looked at the recurrence of OSA after adenotonsillectomy in children have shown that a significant number of patient experience recurrence of their OSA after initial normalization of the apnea-hypopnea index (AHI) postoperatively.[14] Age has been identified as the most important risk factor for OSA recurrence, which can be partly explained by the significant reduction in the posterior airway as the child transitions into puberty.[15] The nasomaxillary complex continuously grows from infancy through the prepubertal period and until the completion of puberty. In fact, maximal orofacial growth takes place during the first 2 years of life, and already by 6 years of age, nearly 60% of the adult face has developed.[16,17] Since the human upper airway and all its components are directly connected to the maxillo-mandibular complex of the face, it is essential to create the right conditions for optimal growth and development of the facial-skeleton in order to reduce airway instability and collapsibility.

Chronic mouth breathing during active craniofacial development of a child may result in anatomical changes that directly affect the airway.[17,18] Prior investigations of children with chronic mouth breathing have shown a correlation with abnormal orofacial growth. The continuous interaction between the nasomaxillary complex and the mandible during nasal breathing is important to guide the growth of the entire facial-skeletal complex in a forward and horizontal orientation. This interaction lessens the angulation of the occlusal plane, which shortens the vertical airway length, creates intraoral space to accommodate the tongue, leads to a shorter soft palate, and potentially improves the function of airway dilator muscles to help maintain the airway open.[19,20] Therefore, it is reasonable to consider that continuous nasal breathing might favorably affect craniofacial and airway development in a child which in turn would enhance upper airway size and collapsibility.

Nasal obstruction is related to OSA in several ways: (1) reduces airflow through the collapsible airway, therefore increasing upper airway resistance, (2) forces patients to become oral breathers during sleep, which leads to narrowing of the airway, and (3) interferes with the nasal reflexes that stimulate ventilation.[21,22] Systematic evaluation of nasal obstruction remains challenging due to the high number of factors that contribute to this problem. In most settings, nasal examination is limited to the evaluation of the anterior septum, internal nasal valve angle, and inferior turbinate size. Frequently, there will not be any findings in this limited examination of the anterior nasal cavity that correlate with the severity of the symptoms seen in patient complaining of nasal obstruction.

Traditional approaches to maximize nasal breathing in the pediatric patient include medical treatment of nasal allergies, reduction of the inferior turbinates' size, adenoidectomy, and septoplasty. However, it is also important to consider that continuous oral breathing often leads to a transverse maxillary skeletal deficiency that deepens the palatal arch. The resulting narrow maxilla with a high arched palate has been correlated with increased nasal airflow resistance and with increased potential of developing OSA as an adult.[23]

Chronic mouth breathing leads to a repetitive cycle where "under-ventilation" of the nose leads to the accumulation of inflammatory cells in the nasal mucosa and further promotes nasal resistance.[24] The same anatomic disturbances in orofacial growth that result from chronic oral breathing, in particular the narrowing of the dental arches, may also compress the nasal septum in a cephalocaudal orientation, thus causing further nasal obstruction as a result of deviation of the nasal septum.[25] It is for this reason that other approaches such as non-surgical maxillary expansion and frenuloplasty in combination with myofunctional therapy may play an important role in the management of pediatric OSA. These therapies help reduce the potential for mouth breathing and encourage craniofacial skeletal development that enhances upper airway size and stability of the child.

It is estimated that 4.8% of newborns are born with a short lingual frenulum also known as ankyloglossia.[26] Limited tongue mobility as results of a short lingual frenulum prevents the tongue from elevating and pushing against the palate during deglutition, thus preventing it from acting as natural maxillary distractor to maximize palatal width and shape.[27] Different oral functions such as sucking, swallowing, and mastication are also critical to continuously stimulate the inter-maxillary cartilage from birth until 13–15 years of age. While active, this synchondrosis will allow facial growth through an osteochondral ossification mechanism.[28] By restricting tongue mobility, ankyloglossia may have a negative

impact on these critical oral functions and further reduce palatal width, which may lead to a constricted nasal cavity that forces patients to breathe through their mouth and subsequently develop OSA.[29,30]

Identification of a high arched/narrow palate and the different elements that may contribute to this anatomical configuration is critical in the management of pediatric OSA. Rapid maxillary expansion (RME) has been shown to be highly effective in the management of pediatric OSA, alone and in combination with other procedures.[31,32] Camacho et al. published a large systematic review of 314 children with high arched palates where he showed significant reduction in the AHI and improvement in the lowest oxygen saturation (LSAT) following RME. They also noted that the AHI improved more in children with previous adenotonsillectomy or with small tonsils.[33] In another study published by Pirelli et al.,[31] pediatric patients with OSA experienced normalization of their AHI after a mean cross-sectional expansion of the maxilla of 4.32 ± 0.7 mm.[31] In a follow-up study of these same patients 12 years later, 23 of them demonstrated maintenance and stability of the expansion and no recurrence of OSA.[32] Additionally, other studies have used rhinometry to show how maxillary expansion reduces nasal airflow resistance.[34,35] When RME is done in combination with adenotonsillectomy, the order of the procedures has not been shown to affect the outcome.[36]

Equally important is to address other problems such as ankyloglossia and poor oral functions that may have originally contributed to narrowing of the palate, and that if not addressed may lead to relapse of the expansion achieved after RME completion.[30] Skeletal development that may impact upper airway size and collapsibility continues until the end of puberty, which is why correcting these other issues is so important.[37] Previous studies have shown that the release of a short lingual frenulum in combination with myofunctional therapy may provide some benefits in the management of OSA.[38] Functional classification of ankyloglossia based on tongue range of motion has previously been described.[39] The potential benefit of releasing a short lingual frenulum may be in that it facilitates the execution of myofunctional therapy exercises, which target the facial and tongue muscles used to perform critical oral functions such as chewing, sucking, and swallowing that help maintain the normal width and shape of the palate. In addition, these exercises help reinforce the normal position of the tongue in the mouth, which normally rests with its tip placed against the hard palate, just behind the front teeth.[29]

Previous studies have shown that myofunctional therapy in children also reduces mouth breathing, which in turn helps control OSA.[40] Nasal breathing during sleep is essential to stimulate adequate ventilation, to activate reflexes that help maintain the tonicity of the muscles that stabilize the upper airway, and to avoid the airway instability that results from mouth breathing.[41] Addressing mouth breathing during sleep is essential. Especially, when at birth the child spends nearly 80% of the time asleep, and at 6 years of age, they still continue to spend up to 25% of the time sleeping.[42] Normal individuals spend 96% of their sleep time breathing through the nose.[43] Studies in normal children between 4 years and 6 years of age showed that mouth breathing comprised an average of 4% (range 0–10%) of their sleep time.

As humans enter adulthood, factors such as obesity and histological changes of the airway tissues may further compromise the size and collapsibility of the airway.[44] These are coupled to the comprised development of the airway during childhood, which facilitate the development of OSA as an adult. Some of the craniofacial variables commonly found in patients with OSA include: (1) increased distance of the hyoid bone from the mandibular plane, (2) decreased mandibular and maxillary projection, (3) downward and posterior rotation of facial development, and (4) increased vertical length of the upper airway.[19,20] All these result from normal human evolution leading to laryngeal descent and development of the oropharynx, but also from not properly addressing issues that impair craniofacial growth and development early in life.

In conclusion, early intervention in children suspected to have OSA is essential to reduce the risk of developing more severe OSA as adults. It is important to note that in pediatric patients with adenotonsillar hypertrophy and OSA, adenotonsillectomy will likely correct the problem in the short term, but that other issues also need to be addressed to prevent recurrence of the problem as the child continues to grow. With this in mind, treatment of OSA should be a continuous effort to establish adequate nasal breathing early in life that will maximize the growth and development of the facial-skeletal complex and the upper airway. In order to accomplish this, multiple strategies need to be considered and possibly combined.

Author Contribution

All authors met the four criteria for authorship established by the International Committee of Medical Journal Editors: Carlos Torre was responsible for the conception, design, and drafting the work, revising the work and reviewing the manuscript. Alejandro Chediak, Alberto Ramos, Salim Dib, and Alexandre Abreu had substantial contributions drafting the work, revising the work and reviewing the manuscript. All authors provided final approval of the version to be published and agreed to be accountable for all aspects of the work in ensuring including the accuracy and/or integrity of the work.

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