



Boletín Médico del Hospital Infantil de México

www.elsevier.es/bmhim



TOPICS IN PEDIATRICS

Midface alterations in childhood as pathogenesis of obstructive sleep apnea syndrome[☆]



José de Jesús Rangel Chávez^{a,b}, Cynthia Espinosa Martínez^{a,b},
Aldo Uzziel Medina Serpa^{a,*}

^a Hospital de Especialidades Médicas de la Salud, San Luis Potosí, San Luis Potosí, Mexico

^b Hospital Lomas de San Luis Internacional, San Luis Potosí, San Luis Potosí, Mexico

Received 14 April 2016; accepted 28 June 2016

Available online 14 November 2017

KEYWORDS

Midface;
Aeration;
Childhood;
Obstructive sleep
apnea syndrome
(OSA).

PALABRAS CLAVE

Tercio medio facial;
Aireación;
Infancia;
Síndrome de
apnea-hipopnea
obstruktiva del sueño
(SAHOS)

Abstract The onset of nasal breathing sets a genetically determined impulse to aerate the face cavities or paranasal sinuses, which in turn initiate their growth creating a useful trafficable space for air during the development of the midface. Considering the evidence that the upper airway obstruction has a primary role in the pathogenesis of respiratory sleep disorders, any condition that causes a permanent difficulty to nasal airflow during breathing will cause hypo-development of the required amplitude in this passage, reducing the growth stimulation of the sinus cavities and altering the development of the whole midface.

© 2016 Hospital Infantil de México Federico Gómez. Published by Masson Doyma México S.A. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Alteraciones del tercio medio facial en la infancia como patogénesis del síndrome de apnea obstructiva del sueño

Resumen El inicio de la respiración nasal marca un impulso genéticamente determinado para airear las cavidades de la cara o senos paranasales, que a su vez inician su crecimiento y forman el espacio útil transitado desde el punto de vista respiratorio durante el desarrollo del tercio medio facial. Considerando la evidencia de que la obstrucción de la vía aérea superior tiene un rol primordial en la patogénesis de los trastornos respiratorios del sueño, cualquier

[☆] Please cite this article as: Rangel Chávez JJ, Espinosa Martínez C, Medina Serpa AU. Alteraciones del tercio medio facial en la infancia como patogénesis del síndrome de apnea obstructiva del sueño. Bol Med Hosp Infant Mex. 2016;73:278–282.

* Corresponding author.

E-mail address: aldomedinas@gmail.com (A.U. Medina Serpa).

patología que cause dificultad permanente al flujo aéreo nasal durante la respiración llevará a un hipodesarrollo de la amplitud requerida en esta vía, disminuyendo la estimulación del crecimiento de las cavidades sinusales y alterando el desarrollo del tercio medio facial en su conjunto.

© 2016 Hospital Infantil de México Federico Gómez. Publicado por Masson Doyma México S.A. Este es un artículo Open Access bajo la licencia CC BY-NC-ND (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

1. Introduction

Human breathing is a basic function of life. The human being is born conditioned to breathe through the nose and to feed through the mouth, and the process of breathing requires the free passage of air through the nasal and naso-oro-pharyngeal spaces. An adequate respiratory function associated with a correct masticatory, swallowing and labial and lingual muscular action will stimulate facial growth and development in its whole given that bone growth responds to the adequate functioning of the muscles and facial soft tissues, as it is described in Moss' theory.¹ Growth of the midface and the conformation of the dental arcade initiate from the first respiration and finalize at the end of the second childhood,² linked to the adequate ventilation of the paranasal sinuses in relation to the volume of air that can pass through the nose.³ The midface is integrated by the bones that form the roof of the mouth, the floor and the lateral walls of the orbit, a large part of the nasal cavity, which accommodates the nasal septum, the inferior, middle and superior turbinates, as well as the multiple cavities of the maxillary and ethmoidal sinuses, which serve as a support and give shape to the soft tissues from which the external configuration of the face will depend. Therefore, these tissues have a great physiological and esthetic relevance. Any disease that involves these structures can contribute to an alteration of their growth and development.

2. Biomechanics of the upper airway

Previous research has outlined the dynamic alterations of permeability as a function of the intraluminal pressure throughout the flexible segments of the cardiovascular, gastrointestinal and genitourinary biological conduits.⁴⁻⁸ In the case of the upper airways, the permeable and flexible segment, which corresponds to the pharynx, is connected through two rigid segments. The upstream segment corresponds to the nose and the downstream segment to the trachea (Fig. 1A).

The air conduits of the upper and lower segments of the flexible site have fixed diameters and resistances: upstream segment resistance (R_{US}) and downstream segment resistance (R_{DS}); and variable pressures—upstream segment pressure (P_{US}) and downstream segment pressure (P_{DS}). It is important to mention several characteristics of this model, known as Starling's model of resistance, highlighting the following concepts:

- A) The pressure outside the rigid conduits and the flexible conduit is positive; inside, the pressure is negative, which allows the air current to flow freely through the conduits
- B) The components of the system generate resistance to the passing of air; by increasing resistance, more pressure is required for the air to flow to the interior of the system
- C) The rigid segments of the conduit do not have a risk to collapse, only the flexible portion. Based on this, a new concept is generated: the critical pressure (P_{CRIT}), which represents the risk of total or partial collapse of the flexible portion, and results in a greater or lesser obstruction
- D) When the upper portion of the segment is obstructed, the pressure inside the conduit is modified, which increases the usual pressure from -18 to -10 cmH₂O to $+4$ cmH₂O, which closes or collapses the airway in the flexible segment during sleep.¹⁰ When the P_{CRIT} is greater than the P_{US} and P_{DS} , which connect with the flexible segment, the intramural pressure is positive, the airways close and airflow ceases (Fig. 1B).

Flow can be reestablished by elevating the P_{US} above the P_{CRIT} . If the P_{US} and the P_{DS} are greater than the P_{CRIT} , the intramural pressure is negative, the airways open and allow an adequate airflow (Fig. 1C). In these conditions, flow through the upper airway is proportional to the pressure gradient through the entire airway, and it can be described by the tension-current relation of Ohm's law:

$$V_{IMAX} = \frac{P_{US} - P_{DS}}{R_{US} + R_{DS}}$$

where V_{IMAX} represent the maximal inspiratory volume.

In contrast, when the P_{US} is greater than the P_{CRIT} and the P_{DS} is lower than the P_{CRIT} , the airways operate in a flow-limited condition (Fig. 1D). Since the inspiratory cycle varies rapidly between closed and opened status, the pressure in the flexible segment remains almost constant in relation to the P_{CRIT} . If the pressure in the flexible segment is constant, airflow also remains constant. Under these circumstances, airflow becomes independent of the P_{DS} and reaches a level of V_{IMAX} . Given that the P_{CRIT} replaces the P_{DS} , this favors an effective inspiratory flow return. Therefore, the level of V_{IMAX} is determined by the gradient of the P_{US} and P_{CRIT} divided by the resistance through the upstream segment in accordance with the following equation:

$$V_{IMAX} = \frac{P_{US} - P_{CRIT}}{R_{US}}$$

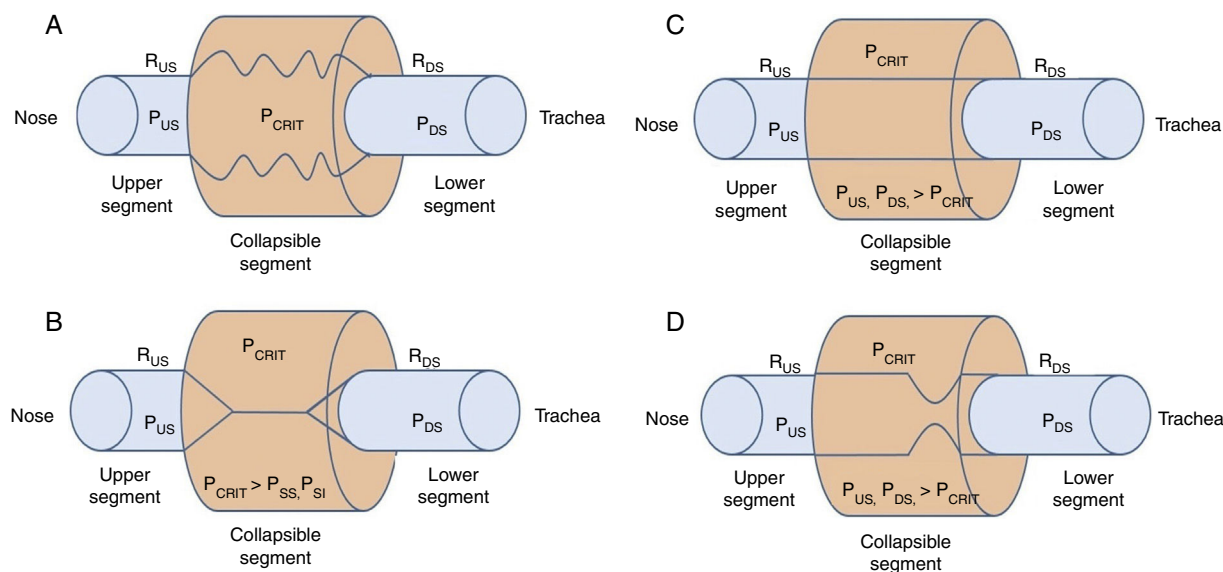


Figure 1 Starling's upper airway resistance model. A. A flexible segment is connected to an upstream rigid segment (nasal fossa) and a downstream rigid segment (trachea). These rigid segments are characterized by the intraluminal pressures in the upstream and downstream segments (P_{US} and P_{DS}), respectively, and airflow resistance in the upstream and downstream segments (R_{US} and R_{DS}), respectively. B. When the $P_{CRIT} > P_{US}, P_{DS}$, the airway is closed. C. When both, P_{US} and P_{DS} are maintained above the P_{CRIT} , the airway is permeable. D. When the P_{US} is greater than the P_{CRIT} , but the P_{DS} is lower than the P_{CRIT} , the airway presents a limited flow during inspiration and it can rapidly change between an open and closed state^{9,10}.

In this model, a decrease of the P_{DS} does not generate an occlusion of the upper airway and cannot be a factor for the development of sleep obstructive apneas.

It is important to point out that inspiratory airflow limitation has two implications in the respiratory system. First, upper airway resistance increases notably when flow is limited in comparison with a normal state. In the absence of upper airway obstruction, the combined resistances of the upstream and downstream segment fluctuate between 1 and 2 $\text{cmH}_2\text{O}/\text{l/s}$, which represent approximately half the total resistance of the system during normal breathing. In contrast, during periods of limited inspiratory flow, airflow resistance of the upstream segment can increase up to 20 and 40 $\text{cmH}_2\text{O}/\text{l/s}$. Second, an additional burden to the respiratory system during periods of flow limitation given the fact that patients continue to exert a greater inspiratory effort without increasing airflow. Essentially, a great part of the pressure generated by the inspiratory muscles is wasted by not increasing respiration due to the dynamic collapse of the upper airway. Therefore, the increase in the upper airway resistance and the dynamic collapse of the upper airway lead to an overexertion that will not overcome airflow obstruction. Several studies have demonstrated a directly proportional relationship between pharyngeal collapsibility and the severity of the respiratory obstruction^{11,12} (Fig. 2). As the P_{CRIT} elevates, an increasing level of upper airway obstruction during sleep is clinically observed. Minimal elevations of the P_{CRIT} have been associated with snoring, meanwhile, moderate elevations (levels of -5 and 0 cmH_2O) have been associated with hypopnea and the upper airway resistance syndrome (UARS). With more pronounced increases of the P_{CRIT} , it becomes positive, leading to obstructive sleep apnea. Therefore, the quantitative differences of the P_{CRIT} have been associated with gradual

changes in the severity of the airway obstruction during sleep.

3. Anatomical considerations

Given the functional importance of the nose in the process of breathing, the presence of a permeable nasal valve, a midline positioned nasal septum (both bone and cartilaginous), inferior and middle turbinates of adequate volumes, and a lymphoid tissue that is not hypertrophic, could facilitate said function without altering the development of the midface.

Different researchers have identified a variety of anatomical factors that contribute an increase in the collapsibility of the upper airways. Several craniofacial characteristics related to the morphology of the facial skeleton or the pharyngeal soft tissues can predispose to the collapse of the upper airways. The size of the mandible, the height of the upper maxillary bone and the position of the hyoid bone have been associated with a risk of obstructive sleep apnea-hypopnea syndrome (OSAHS)^{13,14}. The decrease of the soft palate zone and both adenoid and tonsil hypertrophy are characteristics of the soft tissues that have been associated with an increase upper airway collapsibility¹⁵. In general, it is believed that these anatomical variants will increase the P_{CRIT} by restricting the size of the bony enclosure around the pharynx and by increasing the amount of soft tissue contained in this area¹⁶. Obesity is also an anatomical risk factor of special importance for the upper airways and their obstruction during sleep. The upper airways of obese individuals are more susceptible to collapse¹⁷ because the P_{CRIT} increases 1.0 and 1.7 cmH_2O for every 10 kg/m^2 increase in body mass index (BMI) in women and men, respectively. The increase in the fatty deposits around the pharynx and

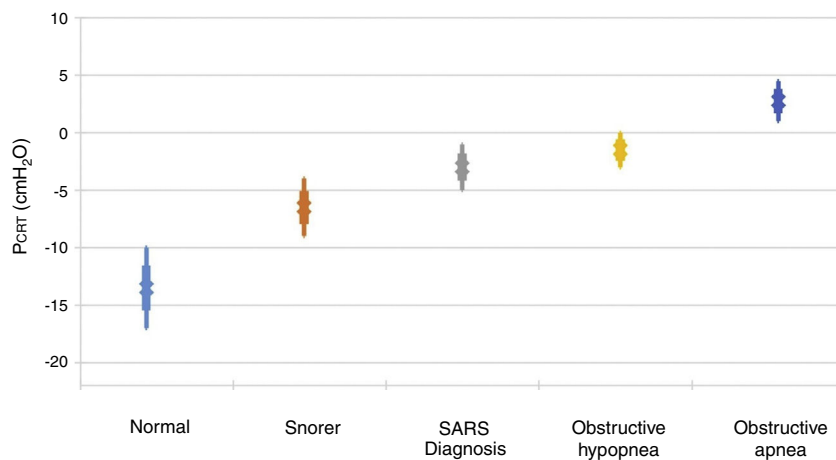


Figure 2 Relationship between the critical pressure (P_{CRIT}) and clinical disorders characterized by upper airway obstruction during sleep. As the P_{CRIT} increases, the severity of the upper airway obstruction increases progressively, which suggests a directly proportional relationship between the collapsibility of the upper airway and worsening of the obstruction in asymptomatic snorers, patients with upper airway resistance syndrome (UARS), obstructive hypopnea and obstructive apnea^{10,12}.

the upper airways¹⁶ can increase the pressure exerted by the extraluminal tissue and, therefore, the collapsibility of the upper airway¹⁸. Moreover, lung volume decrease in the obese, which leads to a decrease in the flow in the upper airway through a positivization of the P_{CRIT} ¹⁹. These flow reductions are more pronounced in patients with adipose abdomen, in which lung volumes can decrease up to nearly the residual volume²⁰. Inversely, improvement in OSAHS by weight loss are due probably to a reduction in the pressure of the surrounding tissues and the increase in air flow by generating a negativization of the P_{CRIT} ¹⁷.

4. Pathophysiology associated with the development of the midface

Nasal breathing is healthy because the air is treated in many ways in the different structures of the nose, paranasal sinuses and the nasal mucosa. Nasal physiological functions, such as heating and humidification, are essential to the functionality of the airway. It is estimated that an adult inhales an average of 10,000 liters of air in about 30,000 breaths a day²¹.

- Filtration. The first filter of particles from the ambient is the nasal cavity. The nasal mucous and nose hair, or vibrissae, oversee trapping of the entering particles
- Humidification. Humidification is another important process of nasal physiology. The abundant vascularization of the nasal mucosa and the turbinates moisten the entering air, increasing its humidity up to 80% before it reaches the nasopharynx²¹
- Heating. Inhaled air must have a temperature of at least 33-35 °C for it not to originate pathological reactions to the alveoli. Once again, due to the turbulence, cold air is forced to be in contact with water vapor that emanates from the mucosa and submucosa of the turbinates, increasing its temperature up to 10 °C. A series of neurovascular reflexes are also produced so that, if

necessary, capillaries are dilated and warm the overlying mucosa providing more heat to the air²¹

- Smell. Nasal aerodynamics also contributes to the olfactory system by letting ambient particles reach the olfactory striae located at the base of the skull²¹
- The nasal cavity as a resonance chamber. The nose and paranasal sinuses act as factors that contribute to modifying voice intensity

According to the previously stated, any disorder that generates permanent difficulties to nasal airflow during breathing will cause alterations that are secondary to the absence of the described functions as well as underdevelopment of the required amplitude of the nasal airway, since it will diminish the stimulation of growth of the sinus cavities and alter the development of the midface¹. The different clinical characteristics (Table 1) are dependent on the affected region of the airway as well as the moment of diagnosis since children have growth spurts of the midface. Sixty percent of this growth occurs during the first four years of life. Therefore, an adequate clinical history by intentionally interrogating about associated signs will allow for an early suspicion of this disorder (Table 2).

The fundamental condition for respiratory sleep disorders to exist resides in the obstruction of the airway; flow decrease through its upstream segment, which is the nose, is the definitive factor. If the obstruction is prolonged until the end of the second childhood, this segment will be permanently insufficient in adolescence and adulthood, triggering

Table 1 Most common diseases altering nasal airflow.

- Nasal valve obstruction
- Deviated septum
- Turbinate hypertrophy
- Adenoid hypertrophy
- Tonsil hypertrophy
- Lingual tonsil hypertrophy

Table 2 Clinical characteristics commonly associated with nasal obstruction.

- Mouth breathing syndrome
- Disorders of phonation
- Disorders of the secondary dentition
- Masticatory and swallowing disorders
- Difficulty initiating sleep
- Frequent nocturnal awakening
- Daytime sleepiness
- Difficulty concentrating
- Irritability
- Hyperactivity and aggressiveness syndrome
- Headache
- Enuresis

the factors that generate a positive P_{CRIT} and leading to the obstruction of the flexible segment of the airway during sleep, which could be denominated as obstructive syndrome in pediatrics. The proposed hypothesis establishes that if there is a moment when the definitive narrowing of the upstream segment can be prevented, it is during the development of the midface, which is fundamental, finite, and unrepeatable. Up to 60% of this development occurs in the first four years of life; thus, an early diagnosis and definitive unblocking is required to achieve an adequate development that will allow free transit of the necessary airflow to favor the negativization of the P_{CRIT} , and avert the possibility of developing any respiratory disorder of sleep, particularly the development of OSAHS.

Funding

Authors' own resources.

Conflict of interest

The authors declare no conflict of interest of any nature.

Acknowledgements

To the medical and directive personnel of the Hospital Médicas de la Salud and the Hospital Lomas de San Luis for their support to the care of our patients.

References

1. Moss ML, Bromberg BE, Song IC, Eisenman G. The passive role of nasal septal cartilage in mid-facial growth. *Plast Reconstruct Surg.* 1968;41:536–42.
2. Faria PT, de Oliveira Ruellas AC, Matsumoto MA, Anselmo-Lima WT, Pereira FC. Dentofacial morphology of mouth breathing children. *Braz Dent J.* 2002;13:129–32.
3. Vig PS, Sarver DM, Hall DJ, Warren DW. Quantitative evaluation of nasal airflow in relation to facial morphology. *Am J Orthod.* 1981;79:263–72.
4. Permutt S, Howell JB, Proctor DF, Riley RL. Effect of lung inflation on static pressure-volume characteristics of pulmonary vessels. *J Appl Physiol.* 1961;16:64–70.
5. Pride NB, Permutt S, Riley RL, Bromberger-Barnea B. Determinants of maximal expiratory flow from the lungs. *J Appl Physiol.* 1967;23:646–62.
6. Guyton AC, Granger HJ, Coleman TG. Autoregulation of the total systemic circulation and its relation to control of cardiac output and arterial pressure. *Circ Res.* 1971;28 Suppl 1:93–7.
7. Claridge M, Shuttleworth KE. The dynamics of obstructed micturition. *Invest Urol.* 1964;2:188–99.
8. West JB, Dollery CT, Naimark A. Distribution of blood flow in isolated lung; relation to vascular and alveolar pressures. *J Appl Physiol.* 1964;19:713–24.
9. Gleadhill IC, Schwartz AR, Schubert N, Wise RA, Permutt S, Smith PL. Upper airway collapsibility in snorers and in patients with obstructive hypopnea and apnea. *Am Rev Respir Dis.* 1991;143:1300–3.
10. King ED, O'Donnell CP, Smith PL, Schwartz AR. A model of obstructive sleep apnea in normal humans. Role of the upper airway. *Am J Respir Crit Care Med.* 2000;161:1979–84.
11. Pham LV, Schwartz AR. The pathogenesis of obstructive sleep apnea. *J Thorac Dis.* 2015;7:1358–72.
12. Schwartz AR, Smith PL, Wise RA, Gold AR, Permutt S. Induction of upper airway occlusion in sleeping individuals with subatmospheric nasal pressure. *J Appl Physiol (1985).* 1988;64:535–42.
13. Sforza E, Bacon W, Weiss T, Thibault A, Petiau C, Krieger J. Upper airway collapsibility and cephalometric variables in patients with obstructive sleep apnea. *Am J Respir Crit Care Med.* 2000;161 2 Pt 1:347–52.
14. Clark RW, Schmidt HS, Schuller DE. Sleep-induced ventilatory dysfunction in Down's syndrome. *Arch Intern Med.* 1980;140:45–50.
15. Marcus CL, McColley SA, Carroll JL, Loughlin GM, Smith PL, Schwartz AR. Upper airway collapsibility in children with obstructive sleep apnea syndrome. *J Appl Physiol (1985).* 1994;77:918–24.
16. Schwab RJ, Gupta KB, Gefter WB, Metzger LJ, Hoffman EA, Pack AI. Upper airway and soft tissue anatomy in normal subjects and patients with sleep-disordered breathing. Significance of the lateral pharyngeal walls. *Am J Respir Crit Care Med.* 1995;152 5 Pt 1:1673–89.
17. Schwartz AR, Gold AR, Schubert N, Stryzak A, Wise RA, Permutt S, et al. Effect of weight loss on upper airway collapsibility in obstructive sleep apnea. *Am Rev Respir Dis.* 1991;144 3 Pt 1:494–8.
18. Davies RJ, Stradling JR. The relationship between neck circumference, radiographic pharyngeal anatomy, and the obstructive sleep apnoea syndrome. *Eur Respir J.* 1990;3:509–14.
19. Squier SB, Patil SP, Schneider H, Kirkness JP, Smith PL, Schwartz AR. Effect of end-expiratory lung volume on upper airway collapsibility in sleeping men and women. *J Appl Physiol (1985).* 2010;109:977–85.
20. Isono S. Obesity and obstructive sleep apnoea: mechanisms for increased collapsibility of the passive pharyngeal airway. *Respirology.* 2012;17:32–42.
21. Mackay IS, Bell TR, editors. *Rhinology.* In: Kerr, A., editor. *Scott-Brown's otolaryngology.* Oxford: Butterworth-Heinemann; 1997.