Title: Health outcomes associated with improvement in mouth breathing in children with OSA

Running title: Health outcomes in children with mouth breathing and OSA

Authors: Anuja Bandyopadhyay[1], MD, James E. Slaven MS[2]

Affiliations: [1]Department of Pediatrics, Indiana University School of Medicine, Indianapolis, IN;

[2]Department of Biostatistics, Indiana University, Indianapolis, IN

Corresponding Author: Anuja Bandyopadhyay, MD

Riley Hospital for Children at Indiana University Health,

705 Riley Hospital Dr. ROC 4270,

Indianapolis, IN 46202-5225

Email: anubandy@iupui.edu

Phone: 317-944-6723

Fax: 317 944-5791

Key words: sleep apnea, obstructive; child; breathing, mouth; sleepiness; quality of life; polysomnography

Funding: None

Conflicts of interest/Competing interests: None

Acknowledgement: We would like to acknowledge Dr. Ronald Chervin for critically reviewing our work.

This is the author's manuscript of the article published in final edited form as:

Bandyopadhyay, A., & Slaven, J. E. (2021). Health outcomes associated with improvement in mouth breathing in children with OSA. Sleep and Breathing, 25(3), 1635–1639. https://doi.org/10.1007/s11325-020-02247-2

Abstract

Purpose: Children with mouth breathing (MB) report poor quality of life. It is unknown whether improvement in MB is associated with improvement in behavior or quality of life. We hypothesized, that in children with MB and obstructive sleep apnea (OSA), improvement in MB is associated with improvement in behavior and quality of life, independent of improvement in OSA.

Methods: This is a retrospective post-hoc analysis utilizing Childhood Adenotonsillectomy Trial (CHAT) dataset, a multicenter controlled study evaluating outcomes in children with OSA randomized into early adenotonsillectomy or watchful waiting. Children with OSA and MB at baseline (determined by reporting 2 or greater to OSA-18 questionnaire on mouth breathing) were divided into 2 groups: **improved mouth breathing (IMB**-determined by a lower score compared to baseline at follow up**)** and **persistent mouth breathing (PMB-** determined by an unchanged or higher score**).** Baseline characteristics, behavior (Conners GI score), sleepiness (Epworth sleepiness scale) and quality of life (Peds-QOL) were compared between the groups using appropriate statistical tests. ANCOVA models were used to analyze change in outcomes, adjusting for treatment arm and change in AHI.

Results: Of 273 children with OSA and MB at baseline, **IMB** (N=195) had significantly improved score between visits for Conner's GI Total T score, Epworth Sleepiness Scale and PedsQL compared to **PMB** (N=78), after adjusting for treatment arm and change in AHI.

Conclusion: Our study suggests an interesting association between mouth breathing and quality of life, independent of polysomnographic evidence. Future studies should explore the effect of mouth breathing on quality of life, in absence of OSA.

Main document

Mouth breathing affects more 55% of children aged 3-9 years[1]. Mouth breathing is described as a condition where the patient replaces correct nasal breathing pattern with a pattern of oral supplemental breathing or mixed breathing. Mouth breathing is associated with sleep disordered breathing including habitual snoring and obstructive sleep apnea (OSA)[2]. OSA is associated with comorbidities including learning disturbances, behavior changes and poor quality of life[3]. While the adverse effects of OSA are well described in literature, there is a paucity of data on the effect of mouth breathing in children. Mouth breathing leads to abnormal orofacial growth, a significant increase in upper airway resistance[4] and can independently increase risk for pulmonary hypertension[5]. Children with mouth breathing have reported a poorer quality of life compared to children with nasal breathing, assessed by Mouth breathing quality of life questionnaire amongst 9-10 year old children[6]. However, no study has been performed in children to see if improvement in mouth breathing is associated with improvement in behavior or quality of life, independent of the severity of OSA. With recent studies underscoring the limited utility of polysomnographic thresholds in the management of childhood OSA, it is important to identify other clinical parameters associated with improvement in health outcomes[7]. We hypothesized, that in children with mouth breathing and OSA, improvement in mouth breathing will be associated with improvement in behavior and quality of life.

The goal of this study was to identify the morbidity associated with mouth breathing utilizing data from Childhood Adenotonsillectomy Trial (CHAT). The CHAT study is a multicenter controlled study evaluating health and behavior outcomes in children with OSA randomized into early adenotonsillectomy or watchful waiting. The study design and initial findings have been published elsewhere[8]. The aim of this project was to compare change in behavior, sleepiness and quality of life between children with improvement in mouth breathing and children with persistent mouth breathing.

Methods:

Study samples for CHAT:

Details of the CHAT protocol are publicly available at https://sleepdata.org/datasets/chat. Children between 5.0 and 9.9 years of age with PSG-confirmed OSA(i.e. obstructive AHI⩾2 events·h−1or an obstructive apnea index (OAI)⩾1 events·h−1), a history of snoring and considered to be surgical candidates for Adenotonsillectomy were recruited from pediatric sleep centers/sleep laboratories, pediatric otolaryngology clinics, general pediatric clinics and the general community from six clinical centers. Exclusion criteria included comorbidities, medications for psychiatric or behavioral disorders, recurrent tonsillitis, extreme obesity and severe OSAS (AHI⩾30 events/hour,OAI⩾20 events/hour or oxyhemoglobin saturation <90% for >2% of total sleep time). The study was approved by the Institutional Review Board of each institution. The study was registered at Clinicaltrials.gov (#NCT00560859).

Chat interventions:

Children were randomly assigned to either early adenotonsillectomy (eAT-surgery within 4 weeks after randomization) or a strategy of Watchful waiting plus supportive care (WWSC) with reassessment of all the study variables at approximately 7 months. Complete bilateral tonsillectomy and removal of obstructing adenoid tissue was performed using standard surgical techniques.

Study sample for our analysis:

For the purpose of this study we identified children with mouth breathing at baseline (determined by reporting 2 or greater to the OSA-18 questionnaire on mouth breathing "in the past 4 weeks, how often has your child: mouth-breathed due to nasal obstruction?", with options-0 (none) 1 (almost none) 2 (few times) 3 (sometimes) 4 (many times) 5 (most of the time) and 6 (everytime))[9].

We divided this cohort into 2 groups-**improved mouth breathing (IMB)** (who reported improvement in mouth breathing at follow up) and **persistent mouth breathing (PMB)** (who did not report improvement in mouth breathing at follow up). This was determined according to their response to the same question at follow up: **IMB** (determined by a lower score compared to baseline to the OSA-18 questionnaire on mouth breathing) and **PMB** (determined by an unchanged or higher score compared to baseline to the OSA-18 questionnaire on mouth breathing).

Overnight polysomnography:

Each child underwent in-laboratory baseline and follow-up PSG carried out by study-certified technicians, following American Academy of Sleep Medicine pediatric guidelines for both acquisition and scoring. The

PSGs were centrally scored by registered sleep technicians. Overnight PSG was repeated approximately 7 months after randomization.

Quality of life, sleepiness and behavior:

Behavior measure included caregiver and teacher ratings of behavior (Conner's' Rating Scale Revised: Long Version Global Index, comprising Restless–Impulsive and Emotional Lability factor sets [caregiver-rated T scores range from 38 to 90, and teacher-rated T scores range from 40 to 90, with higher scores indicating worse functioning]). Sleepiness measure included Epworth Sleepiness Scale modified for children, in which scores range from 0 to 24, with higher scores indicating greater daytime sleepiness. Quality of life included global quality of life (caregiver-rated total score from the Pediatric Quality of Life Inventory [PedsQL], in which scores range from 0 to 100, with higher scores indicating better quality of life).

For the purpose of this study, based on literature review and clinical consensus, clinically accepted cut-off points reflecting clinically significant results were defined as follows: Epworth sleepiness scale score>10, Conner's GI Total T score>65, PedsQL total score<65. We also reported frequency of children with moderate OSA, defined as AHI>5/hr.

Statistical analysis:

Baseline general characteristics (race, age, BMI, rate of adenotonsillectomy, baseline sleepiness as measured by the Epworth Sleepiness Scale, and AHI, as well as AHI at follow-up) were compared between groups using Student's t-tests and Chi-Square tests for continuous and categorical variables, respectively. Frequency of children with abnormal test results were reported. Main outcomes at follow-up were assessed using Student's t-tests for unadjusted relationships and ANCOVA models were used to analyze change from baseline to follow-up in the main outcomes, adjusting for treatment arm and AHI at follow-up. All analytic assumptions were verified. Analyses were performed using SAS v9.4 (SAS Institute, Care, NC).

Results:

395 children responded to the OSA-18 question on mouth breathing at baseline and at follow up. Of these, 273 children reported mouth breathing at baseline (score of 2 or more to the mouth breathing question) were included in our analysis (**Figure 1**). Based on our definition of mouth breathing responders, 195 children reported improvement in mouth breathing at the end of the 7 months (**IMB**) compared to 78

children who did not report any improvement (persistent mouth breathing-**PMB**). Frequency of adenotonsillectomy was higher in the children with IMB compared to children with PMB. **IMB** had a significantly lower AHI at follow up and had a higher rate of adenotonsillectomy(**Table 1**). **IMB** had a significantly decreased score between visits for Conner's GI Total T score, Epworth Sleepiness Scale, PedsQL for child, and PedsQL for parent compared to **PMB** (**Table 1**). Based on clinically accepted cut-offs, IMB had lower prevalence of abnormal ESS, Conners GI Total T score and Peds QL total score at follow up compared tp PMB. While both groups had a decrease in prevalence of moderate OSA at follow up, IMB showed a greater decrease.

IMB showed a greater improvement in behavior, sleepiness and quality of life compared to **PMB** after adjusting for follow up AHI and treatment arm (adenotonsillectomy, WWSC) (**Table 2**).

Discussion:

Our retrospective post-hoc analysis showed that children with OSA and improved mouth breathing, have improved behavior, decreased sleepiness and a increase in quality of life. Previous studies have shown greater quality of life improvement in children with increased severity of OSA[10]. However, after adjusting for change in severity of OSA (measured by AHI) and treatment effect (adenotonsillectomy, WWWSC), the improvement was sustained in children with improved mouth breathing. The quality of life improvement was perceived by parents. While there was a similar trend noted in quality of life reported by children, it failed to achieve statistical significance.

Mouth breathing has been associated with abnormal craniofacial growth including cranio-cervical hyperextension. This can result in differences in airway dimensions. Furthermore, in mouth breathers, nasal mucosa is hypertrophied, pale and decreased passage of air can lead to hypoplasia of maxillary sinuses and narrowing of nasal fossae[11]. Abnormal craniofacial development can lead to increased upper airway obstruction and resistance, speech alterations and learning difficulties. Treatment options for mouth breathing include adenoidectomy, myofunctional therapy and orthodontic appliances. Due to its modifiable nature, mouth breathing in children with OSA is a potential target for therapy.

Our study had several limitations due to the post-hoc and retrospective nature of the analysis. CHAT study was not designed to study health outcomes of mouth breathing, in absence of OSA. We did not have data on intranasal steroid use in the 2 groups. Our study was unable to measure other impairments associated with mouth breathing including speech delays or measure craniofacial changes. There can be parental recall bias while reporting quality of life after surgery, in order to justify the surgery. However, the differences between the 2 groups were sustained after adjusting for treatment arm and severity of OSA. Mouth breathing was reassessed 7 months after the initial assessment. 7 months may not be sufficient duration to see improvement in the WWSC group. Finally, we did not have objective measurements for mouth breathing and had to rely on subjective improvement reported by the family.

Despite the post-hoc nature of the analysis, our study suggests an interesting association between mouth breathing and quality of life, independent of polysomnographic evidence. We conclude that in children with OSA and mouth breathing, those with improvement in mouth breathing report improved behavior, sleepiness and quality of life compared to those children without improvement in mouth breathing. Future studies should explore the effect of mouth breathing on quality of life, in absence of OSA.

	Improved mouth breathing/**IMB** (N=195)	Persistent Mouth Breathing/**PMB** (N=78)	P value
Race (black) (%)	106 (54.4)	40 (51.3)	.855
Age at baseline (years SD)	6.67 (1.47)	6.45 (1.19)	.204
BMI z score	0.88 (1.31)	0.88 (1.31)	.996
Treatment arm (eAT)	121 (62.1)	20(25.6)	**<.001**
WWWSC	74 (38.0)	58 (74.4)	
Baseline Epworth sleepiness scale (ESS)	8.29 (5.27)	8.05 (6.33)	.767
Frequency of children with elevated ESS (ESS>10) at baseline	60 (30.8)	23 (29.5)	.835
Follow up ESS	6.31 (5.30)	8.31 (6.38)	**.016**
Frequency of children with elevated ESS (ESS>10) at follow up	38 (19.5)	29 (37.2)	**.002**
Baseline AHI	5.89 (5.80)	5.80 (5.44)	.901
Frequency of children with moderate OSA at baseline	74 (38.0)	32 (41.0)	.638
Follow up AHI	2.15 (4.51)	5.76 (9.99)	**.003**
Frequency of children with moderate OSA at follow up	23 (11.9)	23 (29.5)	**.001**
Baseline mouth breathing score	4.16 (1.47)	3.90 (1.43)	.174
Follow up mouth breathing score	1.22 (1.43)	4.65 (1.37)	**<.001**
Conner's GI Total T score at baseline	-3.42 (8.22)	-0.29 (12.03)	**.038**
Frequency of children with elevated Conner's GI Total score (>65) at baseline	28 (14.4)	15 (19.2)	.318
Conner's GI Total T score teacher	-5.63 (13.52)	-1.12 (10.48)	**.042**
Frequency of children with elevated Conner's GI Total T score teacher (>65) at baseline	38 (28.4)	14 (23.0)	.429
Conner's GI Total T score teacher at follow up	52.41 (11.56)	53.46 (12.94)	.582
Frequency of children with elevated Conner's GI Total T score teacher (>65) at follow up	19 (15.1)	11 (18.6)	.540
Peds qol total score at baseline	77.14 (15.22)	75.58 (17.39)	.463
Frequency of children with low peds qol total score (<65) at baseline	41 (21.0)	23 (29.5)	.136
Peds qol total score parent at follow up	82.87 (14.00)	74.67 (16.49)	**<.001**
Frequency of children with low Peds qol total score (parent) (<65) at follow up	30 (15.4)	20 (25.6)	**.048**
Change in ESS	-1.98 (4.94)	0.26 (4.85)	**.001**
Change in Peds qol total score	3.92 (17.26)	1.68 (15.87)	.325
Change in Peds qol total score (parent)	5.72 (14.75)	-0.91 (13.12)	**.001**

Table 1: Characteristics of children with OSA and mouth breathing
Values are means (standard deviations) for continuous variables and frequencies (percentages) for categorical variables.

	Improved mouth breathing/**IMB** (N=216)	Persistent Mouth Breathing/**PMB** (N=102)	P value
Change in Conner's GI Total T score	-3.42 (0.70)	-0.29 (1.12)	**.022**
Change in Conner's GI Total T score teacher	-5.10 (1.32)	-1.84 (1.83)	.164
Change in ESS	-1.78 (0.36)	-0.16 (0.57)	**.020**
Change in Peds qol total score	4.16 (1.25)	1.23 (1.97)	.223
Change in Peds qol total score (parent)	5.23 (1.04)	0.09 (1.67)	**.011**

Table 2: Change in health outcomes, adjusted for AHI and treatment arm(eAT/WWSC), in children with OSA and mouth breathing
values are least square means (standard errors)

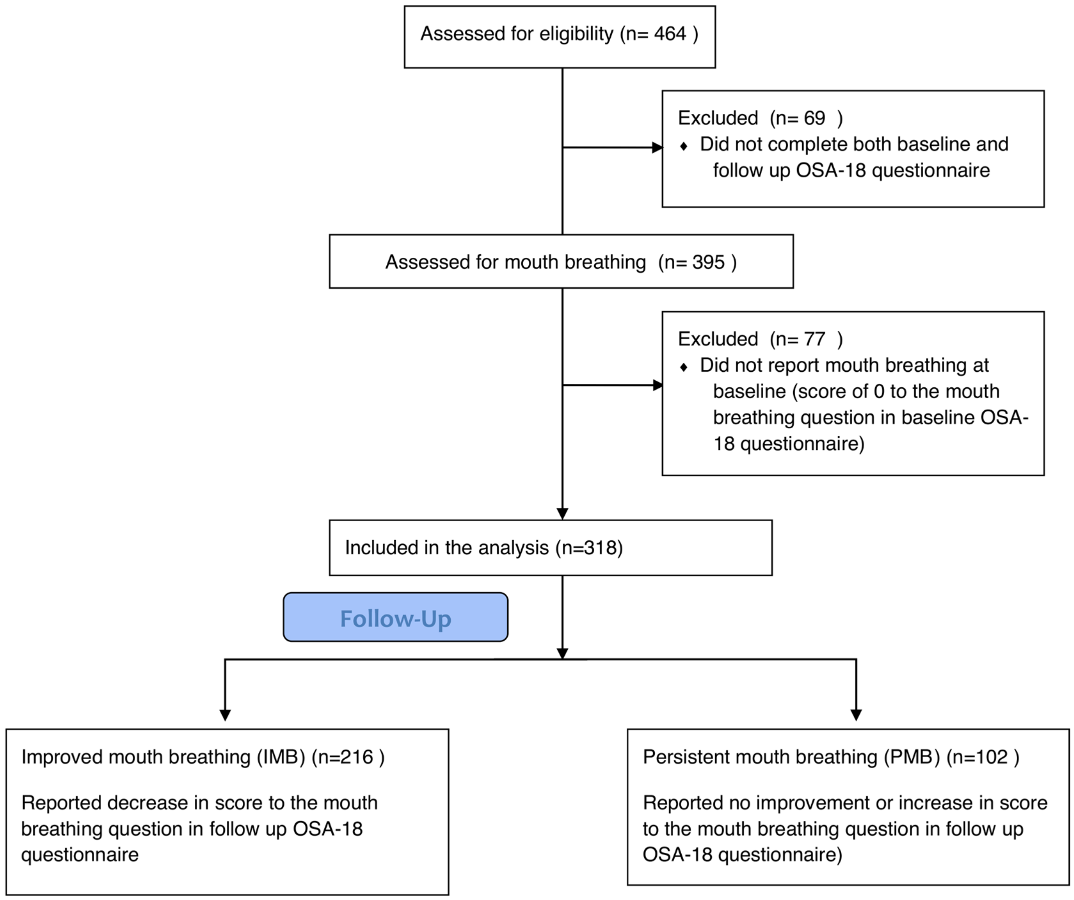

Figure 1: Post hoc analysis of CHAT cohort for children with OSA and mouth breathing

REFERENCE:

1. Abreu RR, Rocha RL, Lamounier JA, Guerra AF (2008) Prevalence of mouth breathing among children. J Pediatr (Rio J) 84 (5):467-470. doi:10.2223/jped.1806
2. Zhao G, Li Y, Wang X, Ding X, Wang C, Xu W, Han D (2018) The predictive value of polysomnography combined with quality of life for treatment decision of children with habitual snoring related to adenotonsillar hypertrophy. Eur Arch Otorhinolaryngol 275 (6):1579-1586. doi:10.1007/s00405-018-4984-6
3. da Silva Gusmao Cardoso T, Pompeia S, Miranda MC (2018) Cognitive and behavioral effects of obstructive sleep apnea syndrome in children: a systematic literature review. Sleep Med 46:46-55. doi:10.1016/j.sleep.2017.12.020
4. Chambi-Rocha A, Cabrera-Domínguez ME, Domínguez-Reyes A (2018) Breathing mode influence on craniofacial development and head posture. J Pediatr (Rio J) 94 (2):123-130. doi:https://doi.org/10.1016/j.jped.2017.05.007
5. Ramos VM, Nader CM, Meira ZM, Capanema FD, Franco LP, Tinano MM, Anjos CP, Nunes FB, Oliveira IS, Guimaraes RE, Becker HMG (2019) Impact of adenotonsilectomy on nasal airflow and pulmonary blood pressure in mouth breathing children. Int J Pediatr Otorhinolaryngol 125:82-86. doi:10.1016/j.ijporl.2019.06.025
6. Leal RB, Gomes MC, Granville-Garcia AF, Goes PS, de Menezes VA (2016) Impact of breathing patterns on the quality of life of 9- to 10-year-old schoolchildren. Am J Rhinol Allergy 30 (5):147-152. doi:10.2500/ajra.2016.30.4363
7. Isaiah A, Pereira KD, Das G (2019) Polysomnography and Treatment-Related Outcomes of Childhood Sleep Apnea. Pediatrics 144 (4). doi:10.1542/peds.2019-1097
8. Marcus CL, Moore RH, Rosen CL, Giordani B, Garetz SL, Taylor HG, Mitchell RB, Amin R, Katz ES, Arens R, Paruthi S, Muzumdar H, Gozal D, Thomas NH, Ware J, Beebe D, Snyder K, Elden L, Sprecher RC, Willging P, Jones D, Bent JP, Hoban T, Chervin RD, Ellenberg SS, Redline S (2013) A randomized trial of adenotonsillectomy for childhood sleep apnea. N Engl J Med 368 (25):2366-2376. doi:10.1056/NEJMoa1215881
9. Franco RA, Jr., Rosenfeld RM, Rao M (2000) First place--resident clinical science award 1999. Quality of life for children with obstructive sleep apnea. Otolaryngol Head Neck Surg 123 (1 Pt 1):9-16. doi:10.1067/mhn.2000.105254
10. Lee C-H, Kang K-T, Weng W-C, Lee P-L, Hsu W-C (2014) Quality of life after adenotonsillectomy for children with sleep-disordered breathing: a linear mixed model analysis. International Journal of Pediatric Otorhinolaryngology 78 (8):1374-1380
11. Pereira FC, Motonaga SM, Faria PM, Matsumoto M, Trawitzki L, Lima SA, Lima WTA (2001) Myofunctional and cephalometric evaluation of mouth breathers. Rev Bras Otorrinolaringol 67:43-49