



Published in final edited form as:

Int J Pediatr Otorhinolaryngol. 2018 August ; 111: 158–161. doi:10.1016/j.ijporl.2018.05.034.

Adenotonsillectomy in children with sickle cell disease and obstructive sleep apnea

Annie N. Farrell^{a,*}, Steven L. Goudy^{a,b}, Marianne E. Yee^{a,c,d}, Roberta M. Leu^{a,e}, and April M. Landry^{a,b}

^aEmory University School of Medicine, 1648 Pierce Drive NE, Atlanta, GA, 30307, USA

^bDepartment of Otolaryngology, Children's Hospital of Atlanta, Division of Pediatric Otolaryngology, 2015 Uppergate Drive, Atlanta, GA, 30322, USA

^cDepartment of Pediatrics, Children's Hospital of Atlanta, Division of Hematology/Oncology, 2015 Uppergate Drive, Atlanta, GA, 30322, USA

^dChildren's Hospital of Atlanta, Aflac Cancer and Blood Disorders Center, 1405 Clifton Road, Atlanta, GA, 30329, USA

^eDepartment of Pediatrics, Children's Hospital of Atlanta, Division of Pulmonary, Allergy/Immunology, Cystic Fibrosis, and Sleep, 1605 Chantilly Drive NE, Atlanta, GA, 30324, USA

Abstract

Introduction: Obstructive sleep apnea (OSA) is prevalent and may be more severe in children with Sickle Cell Disease (SCD) compared to the general pediatric population.

Objectives: The objective of this study was to describe the therapeutic effects and complications of tonsillectomy and adenoidectomy (T&A) for treatment of OSA in children with SCD.

Methods: A comprehensive database of pediatric SCD patients was reviewed to identify all patients who underwent T&A between 2010 and 2016. An IRB-approved, retrospective review of laboratory values, perioperative course, pre- and post-T&A hospital utilization, and polysomnography was conducted.

Results: There were 132 SCD children (108 HbSS) who underwent T&A. Mean age was 7.6 ± 4.6 years. The mean baseline hemoglobin of these patients was 9.3 ± 1.4 g/dL; 72.7% of patients had pre-operative transfusion, such that the mean Hb at time of T&A was 11.4 ± 1.0 g/dL. The average admission length surrounding T&A was 3.5 ± 1.2 days. Complications were documented in 11.4% of operative cases. Polysomnography was available in 104 pre-T&A and 45 post-T&A. The Apnea-Hypopnea Index decreased on post-T&A polysomnogram (7.6 ± 8.7 vs. 1.3 ± 1.9 , $p = 0.0001$). The O₂ nadir improved on post-T&A polysomnogram (81.2 ± 10.8 vs. 89.3 ± 7 , $p =$

*Corresponding author. Farrell.annie@gmail.com (A.N. Farrell).

Declarations of interest
None.

Appendix A. Supplementary data
Supplementary data related to this article can be found at <http://dx.doi.org/10.1016/j.ijporl.2018.05.034>.

0.0003). Emergency room visits (mean events per year) decreased post-operatively (2.6 ± 2.8 vs. 1.8 ± 2.2 , $p = 0.0002$).

Conclusions: T&A can be a safe and effective option to treat OSA in pediatric patients with SCD and was significantly associated with reduced AHI and fewer ER visits post-operatively.

1. Introduction

Sickle cell disease (SCD) is one of the most common hemoglobinopathies worldwide, with approximately 8% of the African-American population carrying the sickle B-globin gene, which produces Hemoglobin S [1]. SCD affects 1 in 400 African-Americans in the US alone [2]. The term SCD encompasses several subtypes of disease, including the homozygous subtype (HbSS), the hemoglobin C variant (HbSC), and sickle cell thalassemia (HbS Beta-Thal). Ear, Nose, and Throat (ENT) operations make up 20% of all surgical procedures performed in pediatric SCD patients [3]. A prior cross-sectional study evaluated adenotonsillar hypertrophy in 85 children and adolescents with SCD and estimated that 55.3% of these patients had adenotonsillar hypertrophy [3,4]. In contrast, obstructive sleep apnea (OSA), of which adenotonsillar hypertrophy is a common etiology, is estimated between 3 and 12% in the general pediatric population [5]. The increased prevalence of adenotonsillar hypertrophy in the pediatric SCD population is likely secondary to compensatory lymphoid enlargement from autosplenectomy, a result of chronic SCD [3].

OSA is not only more prevalent in the pediatric SCD population, but also more severe when compared to the non-SCD pediatric population [6]. OSA leads to oxygen desaturation secondary to upper airway obstruction, which disrupts ventilation and can predispose to repeat red blood cell sickling events [7]. Specifically, oxygen saturation has been shown to be a predictor of abnormal transcranial doppler velocities, which are known to be a risk factor for stroke in this patient population [8]. As such, sleep disorders have been shown to negatively affect long term disease outcome in patients with SCD [7].

Though tonsillectomy and adenoidectomy (T&A) is a common surgical treatment for OSA in the general pediatric population, surgical treatment for OSA in the pediatric SCD population has not been studied in a large patient cohort. Specifically, it remains unknown whether the benefits of OSA symptom alleviation outweigh the potential complications surrounding operating on patients with SCD. Several retrospective analyses have suggested clinical symptom improvement of OSA after T & A in this patient population [1,7,9]. However, these studies are limited by sample size and have called for larger studies to further explore optimal management and clinical impact of T&A in pediatric SCD patients with OSA. To further assess the therapeutic benefit of T&A for OSA in this population, we conducted a retrospective analysis of patient characteristics, polysomnography (PSG) studies, and hospital utilization in pediatric SCD patients with OSA treated with T&A.

2. Methods

A database of the SCD patients followed by the AFLAC Blood and Cancer Center at Children's Hospital of Atlanta from 2010 to 2016 was reviewed. Patients who met study criteria were included in this retrospective review. To meet inclusion criteria, patients were

required to have: a SCD diagnosis of any genotype (HbSS, HbSC, or HbS Beta-Thal), a diagnosis of OSA by PSG, and be aged 0–18 years at time of T&A for treatment of OSA.

Patient demographics (including body mass index (BMI) percentiles per age), medical history, and pre- and post-transfusion hemoglobin levels were collected at time of T&A. Pre-T&A and Post-T&A PSG parameters including the Apnea-Hypopnea Index (AHI), O₂ Nadir, Mean SpO₂, and Periodic Leg Movement (PLM) Index were collected.

Complications, per study definitions, were recorded in the immediate post-operative period. For this study, we noted the following to be operative complications if occurring before patient discharge from the hospital: acute chest episode, pain crisis, intubation, hypotension, and stroke. We noted an upper-airway bleed to be an operative complication if occurring within two weeks post-operatively [10]. In addition, vaso-occlusive crises, acute chest episodes, and emergency department visits were recorded for the 12 months pre-T&A and post-T&A.

This study was IRB approved with a waiver of consent from patients included in the study. Descriptive statistics were used to describe patient demographics, sickle cell severity, hospital utilization, and PSG parameters. Paired differences of sleep study parameters and hospital utilization were evaluated pre- and post-operatively using paired two sample *t*-test analyses. Missing data was analyzed using complete case analysis. All analyses were conducted using IBM SPSS Statistics, version 24.

3. Results

132 patients (108 HbSS, 16 HbSC, 8 other) from the AFLAC Blood and Cancer Center sickle cell database met study criteria for the period of interest and were included in this retrospective study. Demographic information from our patient population is represented in Table 1. Mean age at T&A was 7.6 ± 4.6 years (range 1–19). There was an approximately even split between male and female patients (48.5% vs. 51.5%). The mean BMI percentile (per age) was 49.8 ± 30.6 , with 9.2% of patients having a BMI percentile in the overweight range and 6.1% of patients having a BMI percentile in the obese range. 38.6% were on Hydroxyurea therapy and 12.9% were on chronic transfusion therapy at time of T&A.

PSG was available in 79.5% of patients pre-T&A and 20.5% of patients post-T&A. Post-T&A, there was a significant improvement in mean PSG parameters, including AHI (7.6 ± 8.7 vs. 1.3 ± 1.9 , $p = 0.0001$), O₂ Nadir (81.2 ± 10.8 vs. 89.3 ± 7.0 , $p = 0.0003$), and Mean SpO₂ (95.7 ± 2.7 , 97.0 ± 3.0 , $p = 0.016$; Table 2). Prior to T&A, 72.7% of patients received a packed red blood cell transfusion to lessen the possibility of intra- or post-operative red blood cell sickling. Transfusion shifted the baseline hemoglobin from 9.3 ± 1.4 g/dL to 11.4 ± 1 g/dL at time of T&A (Table 3). Mean admission surrounding T&A was 3.5 ± 1.2 (1–13) days, and complications were observed in 11.4% of patients (Table 4), with 4 (26.6%) of these complications occurring in patients with a BMI percentile in the overweight or obese range. The most common complication observed was development of acute chest in the post-operative period, which occurred in 6% of cases. Review of the post-operative course of these patients showed a significant decrease in mean emergency department visits per year in the 12 months following T&A (2.6 ± 2.8 vs. 1.8 ± 2.2 , $p =$

0.0002; Table 5). However, frequency of pain crises and acute chest episodes were not significantly different prior to and post-T&A (Table 5).

4. Discussion

Sleep related disorders are becoming increasingly recognized as a potential contributor to SCD severity [11]. Oxygen desaturation is one of the strongest triggers for vaso-occlusion, due to polymerization and consequent sickling of red blood cells, which can lead to increased patient pain, neurovascular complications (including stroke), cardiovascular complications, hemolytic anemia, and recurrent infections [12,13]. Nearly 50% of children with SCD experience oxygen desaturation during sleep [7,11]. Nightly oxygen desaturations to a mean level less than 96% has been identified as a risk factor for cerebral insults in SCD patients [14]. Our data demonstrate that surgical treatment of OSA with T&A in pediatric SCD patients improves PSG measurements, including AHI, O₂ Nadir, and Mean SpO₂. The clinical significance associated with these findings is far reaching and could potentially lead to a decreased risk of stroke and neuro-cognitive complications, in addition to improving sleep quality and restfulness in pediatric SCD patients.

Our investigation is the largest review to date investigating the effects and complications of T&A in the pediatric SCD population. Although T&A is a standard treatment for OSA in the general pediatric population, previous studies have not fully described the symptomatic and health status improvement following T&A in this specific patient population [7]. Our results support prior published data showing improvement of PSG measurements and post-T&A complications (Table 6) [6,7,9]. Specifically, the improvement in AHI post-T&A shifted severity of OSA from moderate to mild in our patient population, though OSA was not completely resolved in all patients.¹⁵A significant reduction in AHI, as seen in our study data, can decrease likelihood of OSA-related morbidities in pediatric SCD patients, including lowering the risk of cardiovascular morbidity, neurocognitive impairment, metabolic imbalances, poor school performance and behavior [15].

Treatment with T&A in this patient population also showed a decrease in emergency room visits in the 12 months following T&A. This suggests that improvement in overnight oxygen saturation can lessen clinical complications associated with OSA, as previously listed [15]. In addition, the decrease in annual emergency room visits can be associated with a reduced economic burden of SCD in these patients [16,17]. We did not identify a significant decrease in acute chest episodes and pain crises as were reported in other studies. However further investigation with longer follow up may be needed to determine the effects of improved PSG parameters from T&A on these clinical outcomes. Complications observed from T&A in our patients (11.4%) was similarly reported in other studies, ranging from 7 to 32% [3].

The limitations of this study include its retrospective nature. As data was reviewed retrospectively, there were significantly less post-T&A PSG studies available compared to pre-T&A studies. Of the 17 pre-operative PSG studies with AHI >10, only 11 received post-operative sleep studies, yielding a 64.7% compliance with standard procedure for obtaining a post-operative sleep study. In addition, the observational period for clinical data was

limited to 12 months prior to and post T&A, which may not have been a sufficient amount of time to observe a trend in sickle cell complications.

In conclusion, T&A can safely improve sleep quality in the pediatric SCD population and decrease emergency room visits post-operatively. Other possible benefits warrant further investigation with more extensive follow up. Prospective cohort studies should be conducted to further investigate T&A management, efficacy, and complications in the pediatric SCD population.

References

- [1]. Halvorson DJ, McKie V, McKie K, Ashmore PE, Porubsky ES, Sickle cell disease and tonsillectomy. Preoperative management and postoperative complications, *Arch. Otolaryngol. Head Neck Surg.* 123 (1997) 689–692. [PubMed: 9236586]
- [2]. Al Okbi MH, Alkindi S, Al Abri RK, Mathew J, Nagwa AA, Pathare AV, Sensorineural hearing loss in sickle cell disease—a prospective study from Oman, *Laryngoscope* 121 (2011) 392–396. [PubMed: 21271595]
- [3]. Abou-Elhamd KE, Otorhinolaryngological manifestations of sickle cell disease, *Int. J. Pediatr. Otorhinolaryngol.* 76 (2012) 1–4. [PubMed: 22018730]
- [4]. Salles C, Ramos RT, Daltro C, Nascimento VM, Matos MA, Association between adenotonsillar hypertrophy, tonsillitis and painful crises in sickle cell disease, *J. Pediatr.* 85 (2009) 249–253.
- [5]. Chan J, Edman JC, Koltai PJ, Obstructive sleep apnea in children, *Am. Fam. Phys.* 69 (2004) 1147–1154.
- [6]. Warriar R, Chauhan A, Athale U, Tonsillectomy and adenoidectomy for obstructive sleep apnea in sickle cell anemia, *Indian J. Pediatr.* 77 (2010) 669–672. [PubMed: 20532682]
- [7]. Finch P, Stocks RM, Smeltzer MP, Kimble A, Schoumacher R, Hankins JS, Effects of adenotonsillectomy on polysomnographic parameters in children with sickle cell disease, *Pediatr. Blood Canc.* 60 (2013) E26–E28.
- [8]. Quinn CT, Variste J, Dowling MM, Haemoglobin oxygen saturation is a determinant of cerebral artery blood flow velocity in children with sickle cell anaemia, *Br. J. Haematol.* 145 (2009) 500–505. [PubMed: 19344400]
- [9]. Rogers VE, Lewin DS, Winnie GB, Geiger-Brown J, Polysomnographic characteristics of a referred sample of children with sickle cell disease, *J. Clin. Sleep. Med.* 6 (2010) 374–381. [PubMed: 20726287]
- [10]. Oron Y, Marom T, Russo E, Ezri T, Roth Y, Don't overlook the complications of tonsillectomy, *J. Fam. Pract.* 59 (2010) E4–E9. [PubMed: 20922173]
- [11]. Rogers VE, Marcus CL, Jawad AF, et al., Periodic limb movements and disrupted sleep in children with sickle cell disease, *Sleep* 34 (2011) 899–908. [PubMed: 21731140]
- [12]. Rosen CL, Debaun MR, Strunk RC, et al., Obstructive sleep apnea and sickle cell anemia, *Pediatrics* 134 (2014) 273–281. [PubMed: 25022740]
- [13]. Katz T, Schatz J, Roberts CW, Comorbid obstructive sleep apnea and increased risk for sickle cell disease morbidity, *Sleep Breath.* (2018) 1–8. [PubMed: 29372382]
- [14]. Kirkham FJ, Hewes DK, Prengler M, Wade A, Lane R, Evans JP, Nocturnal hypoxaemia and central-nervous-system events in sickle-cell disease, *Lancet* 357 (2001) 1656–1659. [PubMed: 11425370]
- [15]. Dehlink E, Tan HL, Update on paediatric obstructive sleep apnoea, *J. Thorac. Dis.* 8 (2016) 224–235. [PubMed: 26904263]
- [16]. Hollocks MJ, Kok TB, Kirkham FJ, et al., Nocturnal oxygen desaturation and disordered sleep as a potential factor in executive dysfunction in sickle cell anemia, *J. Int. Neuropsychol. Soc.* 18 (2012) 168–173. [PubMed: 22114954]

- [17]. Tripathi A, Jerrell JM, Stallworth JR, Cost-effectiveness of adenotonsillectomy in reducing obstructive sleep apnea, cerebrovascular ischemia, vaso-occlusive pain, and ACS episodes in pediatric sickle cell disease, *Ann. Hematol.* 90 (2011) 145–150. [PubMed: 20714723]

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Table 1

Demographics and clinical characteristics of children with sickle cell disease (at time of T&A).

Parameter	Number of Patients (%)	Mean \pm SD
Age (years)	132	7.6 \pm 4.6
SCD Genotype: HbSS	108 (81.8%)	
SCD Genotype: HbSC	16 (12.1%)	
SCD Genotype: HbSS HPHF	3 (2.3%)	
SCD Genotype: HbS Beta Thalassemia	5 (3.8%)	
Sex (male)	64 (48.5%)	
Sex (female)	68 (51.5%)	
BMI (kg/m ²)	131	17.0 \pm 3.0
BMI percentile for age (%)	131	49.8 \pm 30.6
Patients (overweight) ^a	12 (9.2%)	
Patients (obese) ^a	8 (6.1%)	
Patients (underweight) ^a	9 (6.9%)	
Systolic Blood Pressure	130	106.6 \pm 11.5
Diastolic Blood Pressure	130	61.4 \pm 9.2
Baseline Hemoglobin (g/dL)	131	9.3 \pm 1.4
Hydroxyurea Therapy (yes)	51 (38.6%)	
History of Asthma	29 (22%)	
Chronic Transfusion Therapy	17 (12.9%)	

^aWeight classifications of overweight, obese, and underweight were based on BMI percentiles per age.

– Overweight: 85% BMI percentile < 95%.

– Obese: 95% BMI percentile.

– Underweight: BMI percentile \leq 5%.

Table 2

Pre and Post T&A polysomnography parameters in children with sickle cell disease.

	Pre-op (N = 104)	Post-op (N = 45)	Paired difference^b	P-value^b
Apnea-Hypopnea Index ^a	7.6 ± 8.7 (0–43)	1.3 ± 1.9 (0–11)	-6.3 ± 8.7	0.0001
O2 Nadir (%)	81.2 ± 10.8 (50–97)	89.3 ± 7.0 (62.7–96)	8.2 ± 12	0.0003
Mean SpO2 (%)	95.7 ± 2.7 (73–100)	97.0 ± 3.0 (85–100)	1.4 ± 3.3	0.016
O2 initiated during sleep study	N = 10 (9.6%)	N = 3 (6.7%)		

Results are presented as mean ± standard deviation (range).

^aThere were 17 Sleep studies with AHI > 10. Of these 17, 11 received post-operative sleep studies, yielding a 64.7% compliance with standard procedure for obtaining a post-operative sleep study.

^bUsing complete case analysis.

Table 3

Peri-operative transfusion data in children with sickle cell disease at time of T& A.

Parameter	N (%)	Mean \pm SD	Range
Baseline Hemoglobin (g/dL)	131	9.3 \pm 1.4	
Pre-operative transfusion performed (yes)	96 (72.7%)		
Pre-operative prbc transfusion amount (mL)	95 (72.0%)	277.6 \pm 128.7	80–900
Post-transfusion hemoglobin (g/dL)	95 (72.0%)	11.4 \pm 1.0	9–14.6

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Table 4

Admission length and post-T&A complications in children with sickle cell disease.

Parameter	N (%)	Mean ± SD	Range
Total admission length (days)	132 (100%)	3.5 ± 1.2	1–13
Other surgical procedure performed with T&A (yes)	25 (18.9%)		
Post-operative complications			
Total number of complications	15 (11.4% of cases)		
Post-operative acute chest episode	8 (6% of cases)		
Upper airway bleed	2 (1.5% of cases)		
Post-operative pain crisis	1 (0.8%)		
Intubation	1 (0.8%)		
Hypotension without pressor requirement	1 (0.8%)		
Hypotension with pressor requirement	2 (1.5%)		
Post-operative stroke	0 (0% of cases)		
Total number of complications among patients with elevated BMI percentile ^a	4 (3% of cases)		

^a A BMI percentile > 85%.

Table 5
Pre and Post T&A hospital utilization in pediatric patients with sickle cell disease.

	Pre-op (N = 132)	Post-op (N = 126)	Paired difference**	P-value
Pain crises (mean events per year)	1.3 ± 2.3 (0–18)	1.0 ± 1.8 (0–8)	0.17 ± 1.7	0.274
Acute chest syndrome (mean events per year)	0.27 ± 0.6 (0–5)	0.2 ± 0.4 (0–2)	0.8 ± 0.7	0.213
ED visits (mean events per year)	2.6 ± 2.8 (0–19)	1.8 ± 2.2 (0–10)	0.8 ± 2.2	0.0002

Results are presented as mean ± standard deviation (range).

** Using complete case analysis.

Table 6
A comparison of different investigations into T&A as a method to treat OSA in the SCD pediatric population.

Parameter	Warrier et al. [1]	Finch et al. [2]	Rogers et al. [3]	Our Investigation
<i>Demographics</i>				
Year of publication	2010	2013	2010	
Number of patients	8	13	55	132
Age at T&A	10.3 (5–15yo)	7.0	10.6 ± 4.6	7.6 ± 4.6
HbSS Genotype	6	8	41	111
HbSC Genotype	2	4	16	16
Beta-Thal Genotype	0	1	0	5
Sex – Male	5	7	24	64
Sex – Female	3	6	31	68
On Hydroxyurea therapy at T&A		1	16	51
Baseline Hgb:		8.8 ± 1.7	HbSS: 8.4 ± 1.3 HbSC: 9.3 ± 1.9	9.3 ± 1.4
<i>T&A Polysomnogram Parameters</i>				
AHI		6.3 ± 5.8	HbSS: 6.2 ± 11.7 HbSC: 3.1 ± 2.1	7.6 ± 8.7
Post T&A		2.0 ± 2.1		1.3 ± 1.9
P value		0.003		0.0001
O2 Nadir		79.6 ± 11	HbSS: 85.6 ± 10.5 HbSC: 90.8 ± 5.1	81.2 ± 10.8
Post T&A		88.2 ± 8.5		89.3 ± 7.0
P value				0.0003
Mean SpO2		97 (93–99)		95.7 ± 2.7
Post T&A	94 (91–99)			97.0 ± 3.0
P value				0.016
<i>Acute Clinical Events</i>				
Pain requiring admission (mean events per year)		0.3 ± 0.6		1.3 ± 2.3
Post T&A		0.2 ± 0.4		1.0 ± 1.8
P value		0.75		0.274
Acute chest syndrome (mean events per year)		0.2 ± 0.4		0.8 ± 0.7
Post T&A				

Parameter	Warrier et al. [¹]	Finch et al. [²]	Rogers et al. [³]	Our Investigation
Post T&A		0.2 ± 0.4		0.27 ± 0.6
P value		1		0.213

Results are presented as mean ± standard deviation (range).

¹Warrier R, Athale U. Tonsillectomy and Adenoidectomy for Obstructive Sleep Apnea in Sickle Cell Anemia. *Indian Journal of Pediatrics* (2010); 77: 669–672.

²Finch P, Stocks RM, Smeltzer M, Kimble A, Schoumacher R, Hankins J. Effects of Adenotonsillectomy on Polysomnographic Parameters in Children with Sickle Cell Disease. *Pediatric Blood and Cancer* 2013; 60: E26-E28.

³Rogers V, Lewin DS, Winnie, GB, Geiger-Brown J. Polysomnographic Characteristics of a Referred Sample of Children with Sickle Cell Disease. *J Clin Sleep Med* 2010; 6(4): 374–381.