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Developmental delay in young children with sleep-disordered breathing before and after tonsil and adenoid surgery☆

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ABSTRACT

Objective: Our objective was to determine the developmental status of young children with sleep-disordered breathing (SDB) as measured by the Ages and Stages Questionnaire (ASQ-3) and to evaluate improvement after treatment.
Methods: The ASQ-3 was completed at entry, 3 months and 6 months after adenotonsillectomy or adenoidectomy. The questionnaire consists of 30 items that assess five domains: communication, gross motor, fine motor, problem solving and personal-social. Domain scores were compared with normative values: abnormal ≥2 SDs and borderline ≥1 but <2 SDs below the mean.
Results: 80 children, mean (SD) age 3.0 (0.94) years, 62.5% male, 77.5% African American, were enrolled. Median (range) apnea–hypopnea index (AHI) was 12.6 (1.4–178.5). At entry, 22 (27.5%) children scored in the abnormal range in at least one developmental area and an additional 23 (28.8%) had at least one borderline score. A generalized linear model including gender, AHI, maternal education and prematurity showed that only prematurity was an independent predictor of at least one abnormal or borderline entry score (likelihood ratio test $p < 0.001$). Adjusting for covariates and excluding children with a history of prematurity, the prevalence of at least one abnormal or borderline score (based on 112 observations of 70 children) was estimated at 49% (95% CI [37, 62]) at baseline; 34% (95% CI [17, 56]) at 3 months; and 22% (95% CI [10, 41]) at 6 months. Post-hoc pairwise comparison of time points showed the baseline versus 6-month difference to be statistically significant ($p = 0.015$).
Conclusions: The 27.5% baseline prevalence of abnormal ASQ scores in children with SDB indicates it is a risk factor for developmental delay. Significant improvements in score classifications were found 6 months after surgery.

1. Introduction

Pediatric sleep-disordered breathing (SDB) is viewed as a continuum of severity based on the degree of upper airway narrowing, arousal, and gas exchange abnormality ranging from snoring to upper airway resistance syndrome to obstructive sleep apnea (OSA) [1]. The mechanisms underlying the development of SDB are unknown. A combination of structural abnormalities including adenotonsillar hypertrophy, craniofacial anomalies, or obesity, and neuromotor abnormalities affecting the upper airway dilator muscles must be present for OSA to occur [2]. SDB is an important cause of morbidity in children and may lead to growth failure, neurocognitive and behavioral abnormalities, metabolic abnormalities and cardiovascular effects. Overnight polysomnography (PSG) is the current gold standard for definitive diagnosis.

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In children, adenotonsillectomy (T&A) is usually the first line of treatment although residual mild OSA has been reported in 40–50% of children and moderate-to-severe OSA in 20–25% [3]. SDB affects 1–4% of children of school-aged children and is underdiagnosed as most of the symptoms are apparent only when the child is asleep [4].

Behavioral and neurocognitive difficulties are common in children with SDB, having been reported in 8.5–63% of affected children [5,6]. Children with primary snoring but otherwise normal sleep study indices have also been shown to have lower scores using a battery of neurobehavioral tests as compared to control children, although the mean scores for both groups were still in the normal range [7]. Studies using standardized behavioral and neurocognitive assessments have documented significant improvements in test scores after T&A suggesting that the neurocognitive deficits are potentially reversible [8–12]. Most of the prior studies have focused on school-aged children, and little is known about younger children who comprise a large proportion of children with SDB and may be particularly vulnerable to its neurocognitive effects. Prior studies in pre-school children using a variety of cognitive tests have yielded conflicting results, with some reporting deficits and others not demonstrating any difficulties [13–18].

Our objective was to determine the developmental status of young children with SDB as measured by the Ages and Stages Questionnaire, 3rd edition (ASQ-3). We also measured improvement in ASQ-3 scores at 3 and 6 months after T&A or adenoidectomy. The ASQ-3 is a parent-completed developmental screening tool that is a valid and reliable instrument for the identification of infants and young children at risk for developmental delay and for determining the need for referral [19].

2. Materials and methods

2.1. Study design/patient selection

This is a before-after study of 80 children ages 18 to 60 months with SDB as documented by positive PSG. Children were recruited from those referred to the Pediatric Otolaryngology private offices and clinics of the University Hospital of Brooklyn for treatment of SDB. PSG was obtained as part of routine clinical care. Those with positive PSG as determined by an apnea–hypopnea index (AHI) $\geq$ 2, apnea index (AI) $\geq$ 1, oxygen saturation $<$92% or $>$10% of the night spent with oxygen saturation $<$90% were eligible for the study. Children with known developmental delay secondary to major congenital abnormalities, craniofacial syndromes, cerebral palsy, and neuromuscular disease were excluded. Children who had prior treatment for SDB were also excluded. The ASQ-3 is validated in English and Spanish, so parents of children speaking other languages were excluded [19]. The study was approved by the Institutional Review Board of the State University of New York Downstate Medical Center, informed consent was obtained from the parents or caretakers and a convenience sample was recruited.

Children were evaluated by a standardized clinical assessment including history and physical examination and the clinical assessment score-15 (CAS-15) was obtained. The CAS-15 has been previously validated by the principal investigator as a useful tool to predict positive PSG in an office-setting [20]. A score $\geq$32 was optimal for predicting a positive PSG. For children aged 2 and above, the body mass index (BMI) was calculated by dividing the child's weight in kilograms by the square of the height in meters, and was compared to standard percentiles for age and sex (BMI Calculator for Child and Teen, Center for Disease Control and Prevention). Weight for length percentiles were calculated for children under 2 years of age (Center for Disease Control and Prevention/National Center for Health Statistics Infant Weight for Length Percentiles [$<$36 months]). Children underwent T&A or adenoidectomy based on decisions made in the course of routine clinical care. Repeat CAS-15 was performed 4 to 6 weeks after surgery. Parents of children completed the ASQ-3 preoperatively in the office or in the pre-operative suite on the day of surgery and three months and six months after surgery by mail. Parents received one telephone call reminder if forms were not received within one month.

2.2. Ages and Stages Questionnaire-3 (ASQ-3)

The ASQ-3 consists of 21 age-specific questionnaires that allow screening of infants and children aged 1 to 66 months. For children born more than 3 weeks premature and under 2 years of age, the child's age is adjusted for prematurity to select the correct age interval questionnaire. The questionnaire consists of 30 developmental items to assess five domains of child development: communication, gross motor, fine motor, problem solving and personal-social. For each item, the parent indicates "yes" (10 points), "sometimes" (5 points) or "not yet" (0 points) to describe a child's ability to perform a task. Each domain score is obtained by the sum of the items. Domain scores are compared with normative values and a score is considered abnormal if it is $\geq$2 SD below the mean. A score $\geq$1 but $<$2 SDs below the mean falls within a monitoring zone. The global score is considered abnormal if one domain is in the abnormal range [19].

2.3. Sample size estimation

There are no data on developmental status in children with SDB. Using the senior author's previous data on behavioral and emotional problems in children with SDB, 25% of children with SDB had abnormal scores on the Child Behavior Checklist and only 8% had abnormal scores after T&A [10]. Assuming that 25% of subjects would have abnormal ASQ-3 scores at enrollment, 8% would have abnormal scores after surgery, 2% would have normal scores at enrollment but abnormal scores after surgery, a significance level of 0.05, and a power of 90%, using a 2-sided exact binomial test, 70 subjects were required. Assuming a drop-out rate of 20% (14), 84 would need to be enrolled.

2.4. Biostatistical design and analysis

For each ASQ-3 domain, scores were dichotomized as normal versus borderline (monitoring zone) or abnormal. As few abnormal scores were obtained, scores in the monitoring zone were grouped with the abnormal scores to better delineate differences at each time point. Any abnormality (borderline or abnormal) on any domain at study entry was predicted in a generalized linear model by gender, AHI, maternal education (high school or less vs. beyond high school), and prematurity ($<$37 weeks vs. $\geq$37 weeks).

A generalized mixed linear model was constructed with the dependent variable defined as an abnormality (borderline or abnormal) on any subscale at each time point. This Bernoulli-distributed outcome was predicted by time, AHI, gender, and mother's education level. Patient identification was introduced as a random factor. Subsequent analyses examined abnormalities on individual subscales. As all 9 children with a history of prematurity had abnormal scores, the children with prematurity were excluded from the model to prevent prematurity from driving the model with our limited number of observations. Comparisons between patients who completed at least one post-operative ASQ-3 and patients who did not were compared by a 2-tailed Mann–Whitney test for continuous variables and Fisher exact test for categorical variables. Change in CAS-15 over time