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Original article

Early improvement in obstructive sleep apnea and increase in orexin levels after bariatric surgery in adolescents and young adults

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Abstract

Background: Obstructive sleep apnea (OSA) associated with obesity is known to improve after bariatric surgery, but little is known about early changes in this condition after surgery.
Objectives: To study the clinical course of OSA after bariatric surgery
Setting: Children's hospital in the United States
Methods: Adolescents and young adults with obstructive sleep apnea undergoing vertical sleeve gastrectomy (n = 6) or gastric bypass (n = 1) were enrolled in this prospective study. Participants underwent formal polysomnography before and at 3 and 5 weeks after bariatric surgery. Anthropometric measurements and assay for orexin and leptin were also performed at study visits. Thirty-one adolescents who underwent 2 polysomnography studies that were 4 weeks apart served as control patients.
Results: Baseline mean (range) age of participants was 17.8 (15.4–20.7) years, 71% were male, with body mass index of 55.2 (41.3–61.6) kg/m^2 and had a median apnea hypopnea index (AHI) of 15.8 (7.1–23.8) events/hour. Differences in least-square means from longitudinal analysis did not show significant differences in AHI in the control group but showed significant postoperative decline in AHI relative to baseline. AHI declined postoperatively from baseline by 9.2 events/hour (95% confidence interval: 3.8 to 14.5) at 3 weeks ($P = .002$) and 9.1 events/hour (95% confidence interval: 3.8 to 14.5) at 5 weeks ($P = .002$); there was no significant change from 3 to 5 weeks in AHI. Leptin decreased and orexin levels increased significantly by 3 weeks postoperatively.
Conclusions: These observations suggest that OSA responds early and out of proportion to weight loss after metabolic and or bariatric surgery, thus weight independent factors may at least in part be responsible for early improvement in OSA postoperatively. (Surg Obes Relat Dis 2017;13:95–100.)

Keywords: Sleeve gastrectomy; Sleep apnea; Orexin; Leptin; Polysomnography

In severely obese adults with body mass index (BMI) ≥40 kg/m^2, the prevalence of obstructive sleep apnea (OSA) ranges from 64% to 98% [1,2]. OSA is also a major problem for younger age groups. In a large series of severely obese adolescents undergoing bariatric surgery in the Teen Longitudinal Assessment of Bariatric Surgery (Teen-LABS) consortium [3], OSA was the second most prevalent co-morbidity at baseline, with 57% diagnosed with OSA at baseline [4]. Prior studies have documented

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OSA improvement in the majority of adults and even resolution in adolescents when assessed at 3-12 months after bariatric surgery [5], and the majority of evidence for improvement in OSA comes from studies of Roux-en-Y gastric bypass patients. Little is known about specific diagnostic characteristics of OSA after vertical sleeve gastrectomy. In addition, the factors that contribute to the resolution of OSA after bariatric surgery besides weight loss are yet to be defined. Testing for change in OSA severity *after* major bariatric weight loss has occurred does not permit the examination of possible early, weight independent neurohormonal effects of surgery that might contribute to OSA resolution.

The objectives of this study were to describe changes in OSA at 3 and 5 weeks after bariatric surgery, and explore links to physiologic changes occurring postoperatively. We hypothesized that in adolescents with documented OSA, the severity of OSA would decrease within as early as 2 weeks after surgery. We further hypothesized that change in OSA status is associated with a decrease in serum leptin and an increase in plasma orexin, a hormone that is known to regulate wakefulness, and respiratory control, and a decrease in leptin.

Materials and methods

Adolescents and young adults undergoing bariatric surgery were enrolled in this prospective observational study. Patients who were 18 years of age or older underwent written informed consent for the study whereas those <18 years of age provided verbal assent and their parent or legally authorized representative gave written permission for their participation. After enrollment, patients underwent anthropometric assessments, and a formal overnight polysomnogram in the sleep laboratory at visit 1. These assessments were repeated at visit 2 (range: 2–35 d, median 20 days postoperatively), and visit 3 (range: 30–44 d, median 39 days postoperatively). Polysomnography was performed using a computerized system and the following parameters were recorded during the study: electroencephalogram, right and left electro-oculogram, submental, tibial and intercostal electromyogram, electrocardiography, nasal and oral airflow through nasal pressure sensor, end-tidal CO_2 measured at the nose by infrared capnometry, oxygen saturation by pulse oximeter, oximeter pulse waveform, and video monitoring using an infrared video camera and recorded on a videotape. Rib cage and abdominal volume changes were recorded with a computer-assisted respiratory inductance plethysmograph. OSA severity was measured by apnea hypopnea index (AHI). Phlebotomy was also performed at baseline, and visits 2 and 3; and plasma orexin and leptin were measured. BMI was measured by weighing participants in light clothing on a digital scale and height by stationary stadiometer. To minimize confounding, the first postoperative evaluation was performed after discontinuation of narcotic medication usage. Patients' dietary intake during the first 3 months was approximately 500–700 Cal per day. The diet is composed of 40% carbohydrate, 30% protein, and 30% fat.

To determine the night-to-night variability in adolescents with obstructive sleep apnea, we enrolled 31 patients who underwent 2 polysomnograms that were 4 weeks apart.

Linear mixed effects models for repeated measures were used to assess changes from baseline for each follow-up time and also postoperatively between weeks 3 and 5, with respect to each outcome of interest in the OSA group. Differences over time were estimated using least-square means; the 95% confidence interval (CI) is reported for each estimated difference. Tukey adjustment for multiple comparisons was used to obtain *P*-values, which were considered statistically significant if $P < .05$. Analyses were implemented using SAS 9.3 (SAS Institute, Cary, NC). The intraclass correlation coefficient was obtained to estimate the night-to-night variability in the control group.

Results

Seven adolescents with OSAS (71% males) with mean (range) age of 17.8 (15.4–20.7) years participated in the study (Table 1). Additional baseline co-morbid conditions are shown in Table 1. Six patients underwent sleeve gastrectomy and 1 underwent Roux-en-Y gastric bypass. Mean BMI at the first visit (baseline) was 55.2 (range, 41.3–61.6) kg/m^2 (weight 164.6 [126.5–198]). There were no statistically significant longitudinal changes in BMI, which decreased by 3.2 (95% CI: −10.9 to 4.6) kg/m^2 by week 3; from week 3 to week 5, the decrease was 2.4 (95% CI: −10.1 to −5.4) kg/m^2. Similarly, weight loss over the postoperative period occurred but changes did not meet statistical significance in this sample (decrease from baseline to week 3: 9.5 kg, 95% CI: −36.7 to 17.7; decrease from week 3 to week 5: 7.2 kg, 95% CI: −34.4 to 20.0).

The AHI at baseline in the surgical group was 15.8 (median) or 14.6 (mean) events/hour with a range of 7.1 to 23.8. There was a significant decrease in AHI postoperatively (Table 2; Fig. 1). From baseline to week 3, AHI decreased by 9.2 events/hr (95% CI: 3.8 to 14.5). Although the mean decrease in AHI was not significant from week 3 to week 5 (decrease: −0.01, 95% CI: −5.4 to 5.3), the AHI at week 5 was significantly lower than the preoperative (baseline) level (decrease: 9.1 events/hr; 95% CI: 3.8 to 14.5).

In addition to changes in severity of OSAS, a significant decrease in systolic but not diastolic blood pressure was measured between the baseline and the third visit (Fig. 1; median decrease 9%). Finally, compared with baseline levels, serum leptin decreased and orexin increased from baseline to both postoperatively time points in the 5 participants with biochemical data available (Fig. 2).

The control group consisted of 31 patients (58% males) with a mean (range) age of 15 (13–17) years and mean BMI of 36.90 ± 9.09. The night-to night variability in AHI and