Effects of Treatment by Laser-Assisted Uvuloplasty on Sleep Energy Expenditure in Obstructive Sleep Apnea Patients

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The purpose of this study was to evaluate the effect of successful laser-assisted uvulopalatoplasty (LAUP) on sleep energy expenditure (EE) in obstructive sleep apnea syndrome (OSAS) patients. Fifteen healthy subjects (group I) and 25 patients with moderately severe or severe OSAS (group II) proven by overnight sleep study and who wanted LAUP were enrolled. During the night of the sleep studies, EE was measured with a metabolic cart (indirect calorimetry with canopy), including basal metabolic rate (BMR), mean sleep EE, lowest sleep EE, ratios of mean sleep EE/BMR, and lowest sleep EE/BMR. For the OSAS patients, a second sleep study with EE measurement was performed 3 months after LAUP. Based on this assessment of their sleep architecture, they were divided into 2 groups: responders (group IIa) and nonresponders (group IIb). The mean sleep EE, the ratio of mean sleep EE/BMR and lowest EE/BMR were significantly higher in group II than group I. After LAUP in group II, 6 patients were found to be responders (group IIa) and 19 patients were nonresponders (group IIb). Group IIa had decreased mean sleep EE, ratios of mean sleep EE/BMR, and lowest sleeping EE/BMR after LAUP than before LAUP compared with no significant changes in group IIb after LAUP. In conclusion, there is increased sleep EE in moderately severe OSAS patients when compared with normal controls. LAUP, when effective in reversing the sleep abnormalities, also normalizes the sleep EE. If it does not adequately treat the OSAS, however, the sleep EE remains abnormal.

OBSTRUCTIVE SLEEP APNEA syndrome (OSAS) is commonly seen in obese persons, and obesity is considered to be a major risk factor for its development.[1] Body weight depends on the balance between energy intake and energy consumption. Energy consumption includes resting energy expenditure (EE), dietary thermogenesis (DT), the thermic effect of exercise, and facultative thermogenesis, which occurs in response to environmental stress. For all these functions, an intact hypothalamo-pituitary axis is necessary. Numerous studies have demonstrated that OSAS patients have abnormal function of the hypothalamo-pituitary axis, which improves with effective treatment.[2] There are several mechanisms by which OSAS may alter EE. DT is lower in obese than in lean subjects due to obesity-induced insulin resistance.[3] Sleep is believed to play an important role in thermoregulation and energy conservation. Abnormal hypothalamo-pituitary function may also affect facultative thermogenesis.[4]

Obesity is associated with morbidity and mortality.[5,6] OSAS is characterized by repetitive upper airway obstruction and increased upper airway resistance, leading to high negative intrathoracic pressures (-40 to -60 cm H_2O) with consequent increased work of breathing, alveolar hypoventilation with hypoxemia and increased sympathetic activity, frequent arousal, leg or body movement, sleep fragmentation, and derangement of sleep architecture.[7] All of these abnormalities may increase metabolic rate and EE during sleep.[8-13] Effective treatment of OSAS relieves upper airway obstruction and alveolar hypoventilation and may also decrease sleep EE.

Nasal continuous positive airway pressure (CPAP) is a very effective treatment for OSAS. Stenlof et al[11] showed that OSAS-induced increased mean sleep EE is normalized by treatment with nasal CPAP. However, not all patients are able to tolerate nasal CPAP. Uvulopalatopharyngoplasty (UPPP) has been recommended for patients with clinically symptomatic OSAS who have appropriate anatomic features and for whom other interventions, including nasal CPAP have been unsuccessful or intolerable. Laser-assisted uvulopalatoplasty (LAUP) causes less morbidity and postoperative pain than UPPP.[14] To our knowledge, there have been no studies published specifically evaluating metabolism and EE before and after treatment with LAUP. The purpose of this study was to evaluate whether OSAS patients who respond to LAUP have reduced sleep EE compared with those who fail to respond.

MATERIALS AND METHODS

Selection of Subjects

Patients with moderately severe to severe OSAS who desired LAUP were selected along with a control group of healthy individuals. Both subjects and controls were required to be less than 50 years of age. To achieve a nearly matching mean weight for the 2 groups, the control subjects had to have a body mass index (BMI) greater than 26, while the OSAS subjects had a BMI less than 32. Group I consisted of 15 healthy individuals, while group II consisted of 25 patients with OSAS proven by overnight sleep study. All were otherwise healthy. Thyroid and cardiopulmonary dysfunction, diabetes mellitus, and other medical diseases, which might affect EE, were specifically ruled out by history, physical examination, chest x-ray, electrocardiogram, and blood tests (including free T_4, T_3 resin uptake, ante cibum [AC], and post cibum [PC] blood glucose). Subjects were excluded if there was any history or clinical evidence of primary central nervous system, systemic, or neuromuscular diseases or if they had evidence of acute infection within 1 month prior to the study. To avoid the effect of differing phases of the menstrual cycle, sleep studies and EE in women were measured on days 5 to 10 of the menstrual cycle, before ovulation. Alcohol or sedatives were avoided for at least 1 week prior to the overnight sleep study. Drugs or substances that alter metabolism (eg, caffeine, tea, nicotine, and theophylline) were avoided for at least 2 days.

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Sleep Studies

Overnight sleep studies were performed with standard polysomnography. The recordings included electroencephalography (EEG), electrooculography (EOG), submental electromyelography (EMG), bilateral tibial EMG, electrocardiography (ECG), nasal and oral airflow, arterial oxygen saturation (Sa_{O_2}), heart rate, and respiratory movement.[15,16] Sleep was staged by the method of Rechtschaffea and Kales[17] on the basis of 30-second epochs.

Apnea episodes were defined by the absence of ventilation for longer than 10 seconds as measured by calibrated inductive plethysmography.[18] Hypopnea was defined as a reduction in ventilation and a reduction in tidal volume to below 50%, without a major change in respiratory frequency. Oxygen desaturation was defined as a reduction in Sa_{O_2} of 4% or more from baseline by pulse oximeter. The respiratory disturbance index (RDI) was defined as the mean number of hypopneas and apneas per hour of sleep. Desaturation event frequency (DEF) was defined as the mean number of oxygen desaturation episodes per hour of sleep.[18] Sleep apnea syndrome was diagnosed as an RDI equal to or greater than 10 on overnight polysomnography. Obstructive apnea was defined as the absence of nasal and oral airflow despite continuing respiratory effort. Central apnea was defined as the cessation of nasal and oral airflow with the cessation of respiratory effort. Mixed apnea had both central and obstructive components. OSAS was diagnosed when obstructive and mixed apneas represented more than 80% of all apneic episodes. Mild OSAS was defined as an RDI equal to or greater than 10, but less than 20; severe OSAS as an RDI greater than 50 with the lowest Sa_{O_2} less than 50%; and moderately severe OSAS as falling between the criteria for mild and severe OSAS. The arousal index was defined as the mean number of arousals per hour of sleep.[16] Sleep efficiency was the percentage of total sleep time divided by total time in bed.

EE Measurement

Oxygen consumption ($\dot{V}O_2$, mL/min, standard temperature [0°C], and barometric pressure [760 mm HG] dry or STPD), CO_2 production ($\dot{V}CO_2$, mL/min, STPD), minute ventilation, respiratory equation (RQ), and EE were examined by the canopy dilution technique with an open circuit indirect calorimetry ventilated hood system (canopy) using the Vmax series/6200 autobox DL metabolic cart (Sensormedics, Yorba Linda, CA). It included an infrared CO_2 analyzer, fast response O_2 sensor, turbine volume transducer, temperature transducer, fully automated calibration system, and computerized data management system. It was programmed to provide 1-minute averages of tidal volume (VT, L/breath), $\dot{V}O_2$, $\dot{V}CO_2$, RQ, frequency (breaths/minute), and time. The transparent canopy was placed over the subject's head and secured around the neck. Air was drawn through the hood at a constant rate to maintain the CO_2 concentration of the outflow air between 0.8% and 1.0% (range, 25 to 35 L/min) according to the subject. If the RQ decreased below 0.70 or increased above 1.00 or if the VT decreased below 0.30 for a 3-minute output, the technician examined the mask and respiration circuit for possible leaks. The room temperature was kept constant at 25°C. Subjects were under constant supervision by laboratory staff while their heads were in the canopy. EE was calculated from $\dot{V}O_2$ and $\dot{V}CO_2$ using the following formula: $EE = 1.44 * (3.94 * \dot{V}O_2 + 1.1 * \dot{V}CO_2)$.

Sleep EE and sleep RQ were defined for mean EE and RQ during the period from 11:00 PM to 7:00 AM, excluding all periods of wakefulness from 11:00 PM until sleep onset or from morning awakening until 7:00

Table 1. Patient Demographics and Baseline Measurements

	Group I (n = 15)	Group II (n = 25)
Age	38 ± 5	41 ± 6
Sex (male/female)	13/2	23/2
BMI (kg/m^2)	28.4 ± 2.2	29.8 ± 2.5
FEV1 (% predicted)	91.6 ± 4.2	90.5 ± 3.6
FVC (% predicted)	88.3 ± 3.9	86.2 ± 3.5
FEV1/FVC	87.1 ± 3.8	86.8 ± 3.5
Hematocrit	42.5 ± 0.4	42.7 ± 0.5
Baseline PaO_2 (mm Hg)	95.7 ± 0.8	94.6 ± 0.6
Mean sleep EE (kcal/kg/h)	0.69 ± 0.04	0.84 ± 0.09*
Presleep RQ	0.82 ± 0.04	0.84 ± 0.05
Sleep RQ	0.82 ± 0.04	0.85 ± 0.05
BMR (kcal/kg/h)	0.78 ± 0.05	0.81 ± 0.06
Mean sleep EE/BMR	0.88 ± 0.05	1.02 ± 0.06*
Lowest sleep EE (kcal/kg/h)	0.64 ± 0.04	0.81 ± 0.08*
Lowest sleep EE/BMR	0.82 ± 0.06	1.00 ± 0.06*

NOTE. Data are presented as mean ± SD. Student's *t* test was used.
Abbreviation: BMI, body mass index.
*$P < .05$ comparison between groups I and II.

Table 2. Baseline Sleep Study Results

	Group I (n = 15)	Group II (n = 25)
RDI (times/h)	4.6 ± 2.8	40.2 ± 7.3*
DEF (times/h)	2.3 ± 2.2	35.2 ± 5.3*
Mean Sa_{O_2} (%)	97.0 ± 0.4	92.4 ± 0.5*
Baseline Sa_{O_2} (%)	98.4 ± 0.4	97.8 ± 0.8
Lowest Sa_{O_2} (%)	92.0 ± 0.7	70.8 ± 5.3*
Sleep architecture		
Stage 1 (%)	15.1 ± 2.3	29.7 ± 4.7*
Stage 2 (%)	55.8 ± 3.4	49.2 ± 3.2*
Stage 3 + 4 (%)	6.8 ± 1.7	3.8 ± 0.7*
REM (%)	22.3 ± 2.8	17.3 ± 2.4*
AI (times/h)	4.3 ± 2.1	33.1 ± 4.5*

NOTE. Data are presented as mean ± SD. Student's *t* test was used.
Abbreviations: RDI, respiratory disturbance index; DEF, desaturation event frequency; REM, rapid eye movement; AI, arousal index.
*$P < .05$ comparison between group I and group II.

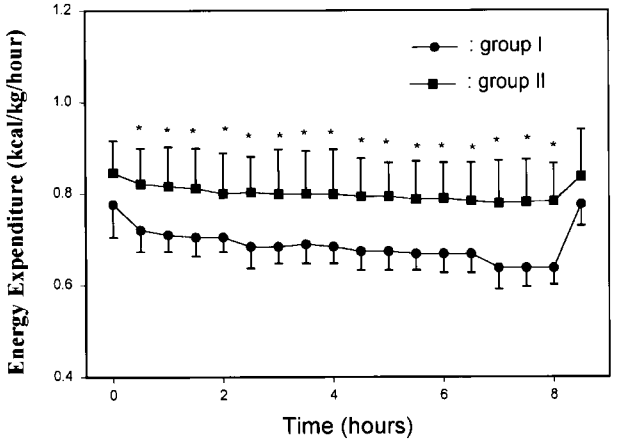

Fig 1. Comparison of sleep EE between groups I and II throughout the night. In group I, there was a clearly decreased EE, followed by a relatively constant overnight EE until being awakened for the BMR measurement. In contrast, there is an absence of decreased mean sleep EE in group II subjects ($P < .05$). Statistical analysis was performed using the ANOVA test and Scheffe test. The EE was higher in group II than group I during the sleep period. *$P < .05$ comparison between the mean EE of groups I and II throughout the night. Statistical analysis was performed using the paired Student's *t* test.

Table 3. Effect of LAUP on Nocturnal Oxygenation and Sleep Architecture in Groups IIa and IIb

	Group IIa (n = 6)		Group IIb (n = 19)	
	Before	After	Before	After
RDI (times/h)	38.7 ± 7.5*	9.8 ± 5.2	40.7 ± 7.2	38.9 ± 6.4
DEF (times/h)	34.1 ± 5.0*	7.7 ± 4.3	35.6 ± 5.3	32.7 ± 5.5
Mean Sao_2 (%)	92.6 ± 0.5*	95.3 ± 0.4	92.3 ± 0.5	92.5 ± 0.5
Baseline Sao_2 (%)	97.7 ± 0.7	97.8 ± 0.4	97.9 ± 0.8	97.8 ± 0.5
Lowest Sao_2 (%)	73.1 ± 5.7*	89.3 ± 3.3	70.1 ± 5.2	71.5 ± 5.3
Sleep architecture				
Stage 1 (%)	29.5 ± 4.9*	19.4 ± 2.4	29.8 ± 4.6	29.2 ± 4.1
Stage 2 (%)	48.7 ± 3.3*	54.5 ± 2.6	49.3 ± 3.1	49.3 ± 3.2
Stage 3+4 (%)	4.3 ± 0.6*	5.3 ± 0.4	3.6 ± 0.7	3.8 ± 0.8
REM (%)	17.5 ± 2.3*	20.8 ± 1.8	17.3 ± 2.6	17.7 ± 1.9
AI (times/h)	31.6 ± 4.1*	8.8 ± 2.3	33.6 ± 4.8	31.3 ± 4.4

NOTE. Student's *t* test was used.
Abbreviations: RDI, respiratory disturbance index; DEF, desaturation event frequency; REM, rapid eye movement; AI, arousal index.
*$P < .05$ comparison between before and after LAUP in Group IIa.

AM. Periods of awakening related to toileting were also excluded between 11:00 PM and 7:00 AM. However, the period during which sleep EE was measured could contain brief periods of wakefulness, with less than 5 minutes of arousal. The EE values from each hour of the 8-hour recording period were averaged to obtain a value for each hour of the night, for each night, for each subject. The lowest sleeping EE (lowest SEE) was defined as the lowest continuous 30-minute period recorded during this time. Presleep EE and presleep RQ were defined as the EE and RQ measurement for each subject during the resting awake metabolic observation period 10 minutes before sleep onset each night. Baseline observations containing sleep or body movement greater than 3 seconds were deleted before averaging.

LAUP Technique

LAUP was performed under general anesthesia with nasotracheal intubation. A hand held CO_2 laser was used to resect a wedge or crescent of soft palate on either side of the uvula and then to ablate the uvula itself. Laser settings were 14 to 18 W, using the Sharplan Swiftlase system (Lumenis Ltd, Yokneam, Israel). When the size of the faucial tonsil was enlarged and crossed the plane of the anterior and posterior pillars, the tonsil was also removed. Responders to LAUP therapy were defined as those who had a more than 50% decrease in RDI and RDI less than 20 after LAUP and were designated as group IIa, with nonresponders designated as group IIb.[14]

Study Protocol

Both control and OSAS patients underwent baseline sleep studies with EE measurement. Subjects in group II had a second study before LAUP and then a second study 3 months after LAUP.

During the night of the sleep study with EE measurement, all subjects finished dinner before 6:30 PM and then received nothing by mouth except water. The patient entered the sleep laboratory before 9:00 PM. After the sleep monitoring equipment was set up, the subject rested for 30 minutes. At about 10:40 PM, with the subject lying motionless with eyes open and an EEG demonstrating an awake state, minute ventilation (VE), $\dot{V}O_2$ and $\dot{V}CO_2$ were measured by indirect calorimetry with the canopy. This monitoring continued until a steady state was established, as determined by variations in VE and $\dot{V}O_2$ of 10%, and an RQ of 5%. The steady state occurred within 5 to 10 minutes in all subjects. At least 10 measurements at 1-minute intervals during the steady state were obtained, and the mean of the 10 lowest values was taken to represent presleep REE. If the eyes closed, but the EEG still demonstrated an awake state, the investigator asked the patients to open their eyes by saying quietly, "Please open your eyes." Such occasional communication did not lead to loss of the steady state. The light was turned off at 11:00 PM, the subject was allowed to fall asleep, and the overnight sleep study was performed. The light was switched on at 7:00 AM, 10 minutes after which the basal metabolic rate (BMR) was measured for 10 minutes, similar to the procedure for presleep EE measurement. The EEG was monitored closely to ensure wakefulness.

Data Analysis

The Student's *t* test and analysis of variance (ANOVA) test were used for statistical analysis where appropriate. If the ANOVA test showed statistical significance, the Scheffe test was also performed. All values were expressed as the mean ± SD, with significance accepted when *P* was less .05.

Table 4. EE and BMR Measurements

	Group IIa		Group IIb	
	Before	After	Before	After
Presleep EE (kcal/kg/h)	0.88 ± 0.08	0.84 ± 0.07	0.88 ± 0.09	0.84 ± 0.08
Presleep RQ	0.85 ± 0.05	0.84 ± 0.05	0.84 ± 0.05	0.85 ± 0.06
Mean sleep EE (kcal/kg/h)	0.85 ± 0.09*	0.72 ± 0.05	0.83 ± 0.09	0.78 ± 0.10
Mean sleep RQ	0.86 ± 0.05	0.84 ± 0.04	0.85 ± 0.05	0.85 ± 0.05
BMR (kcal/kg/h)	0.82 ± 0.06	0.82 ± 0.05	0.81 ± 0.05	0.78 ± 0.07
Lowest sleep EE (kcal/kg/h)	0.83 ± 0.08*	0.68 ± 0.04	0.81 ± 0.08	0.75 ± 0.08
Mean sleep EE/BMR	1.03 ± 0.06*	0.88 ± 0.05	1.02 ± 0.06	1.01 ± 0.06
Lowest sleep EE/BMR	1.01 ± 0.06*	0.83 ± 0.05	1.00 ± 0.06	0.96 ± 0.06

NOTE. Student's *t* test was used.
*$P < .05$ comparison between before and after LAUP in Group IIa.

RESULTS

Demographic Data and Sleep Measurements

There were no significant differences in age, sex, BMI, forced expiratory volume in 1 second (FEV1), forced vital capacity (FVC), FEV1/FVC, hematocrit, or baseline Pao_2 between groups I and II (Table 1).

There was no significant difference in baseline Sao_2 between groups I and II, but all patients in group II had a greater RDI and DEF, a greater decrease in the mean Sao_2, and a lower "lowest Sao_2" compared with group I. Group II had a more abnormal sleep architecture characterized by a higher percentage of stage I sleep, but a lower percentage of stages 2, 3 + 4, and REM stage sleep, and a higher arousal index than group I (Table 2). These results were all consistent with the diagnosis of OSAS in group II.

Metabolic Rate and EE During Sleep

Figure 1 demonstrates the mean EE of groups I and II (prior to LAUP) throughout the night. In group I, there was a clear decrease in EE, followed by a relatively constant overnight metabolic rate until being awakened for the BMR measurement. In contrast, mean sleep EE did not decrease significantly in group II subjects, with the mean and lowest sleep EE being higher in group II than group I. There was no significant difference in BMR, presleep RQ, or mean sleep RQ between the 2 groups. The ratio of mean sleep EE/BMR and lowest sleep EE/BMR were significantly higher in group II than group I (Table 1).

Effect of LAUP on Presleep EE and BMR

Only 6 of the 25 OSAS patients responded to LAUP (group IIa). There was no significant difference in sleep architecture (percentage of stages 1, 2, 3 + 4, and REM stage sleep), arousal index, RDI, DEF, baseline Sao_2, mean Sao_2, and lowest Sao_2 between group IIa and group IIb before LAUP. However, all of these parameters except for baseline Sao_2 improved in the 6 group IIa subjects after surgery, while they remained unchanged in group IIb (Table 3).

The mean sleep EE, lowest sleep EE, ratio of mean sleep EE/BMR, and lowest sleep EE/BMR were significantly decreased in group IIa, but not group IIb before and after LAUP (Table 4). There was no significant difference in presleep RQ, mean sleep RQ, BMR, and presleep EE before and after LAUP in either group IIa or group IIb (Table 4). Figures 2, 3, and 4 demonstrate the differences graphically.

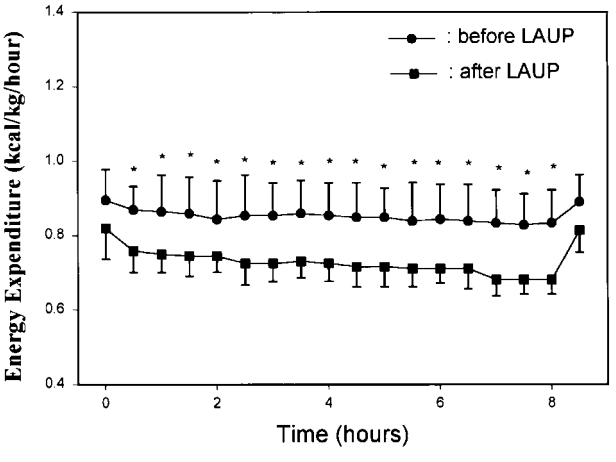

Fig 2. Comparison of the mean sleep EE throughout the night in group IIa before and after LAUP. There was a clearly decreased sleep EE followed by a relatively constant overnight sleep EE until being awakened for the BMR measurement after LAUP. In contrast, there was an absence of decreased sleep EE before LAUP ($P < .05$). Statistical analysis was performed using the ANOVA test and Scheffe test. The EE was higher in group IIa before LAUP than after LAUP. *$P < .05$ comparison between the mean EE of group IIa before and after LAUP. Statistical analysis was performed using the paired Student's *t* test.

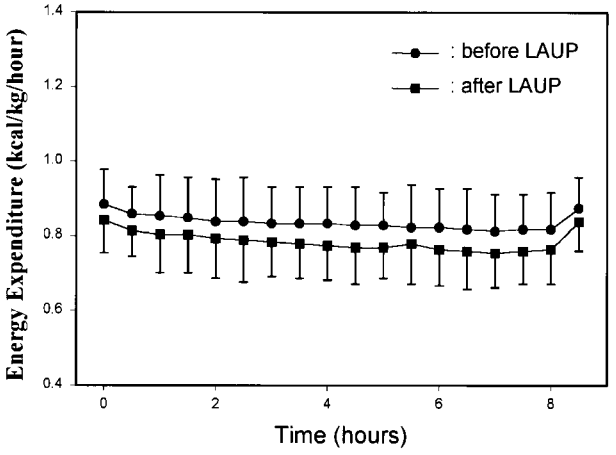

Fig 3. Comparison of the nocturnal mean EE throughout the night in group IIb before and after LAUP. There was an absence of decreased sleep EE during the overnight sleep study both before and after LAUP. Statistical analysis was performed using the ANOVA test and Scheffe test and paired Student's *t* test.

DISCUSSION

Many factors have been reported to affect sleep EE, including age, diet, weight, phase of the menstrual cycle, and exercise.[19-24] We tried to control for these factors in our study. Therefore, we are confident that the differences we found are related primarily to the sleep disturbance found in OSAS.

We found no significant differences in presleep EE and BMR between groups I and II. This is consistent with the results of Ryan et al,[4] who corrected REE for lean body mass and demonstrated that REE and DT were not reduced in moderate to severely obese OSAS patients compared with healthy individuals. They suggested that patients with OSAS have a pattern of obesity characterized by energy homeostasis at an elevated weight set-point.[4] Severe OSAS is commonly seen in obese patients. Their mean sleep EE is increased even though their weight remains stable or increases. Possibly, a sedentary lifestyle and daytime hypersomnolence, which may decrease daytime activity, plus exercise-induced thermogenesis may counterbalance the increased sleep EE in OSAS patients. In addition, OSAS patients have higher energy intake than those without OSAS.

In the group I control subjects, mean sleep EE was only 88%

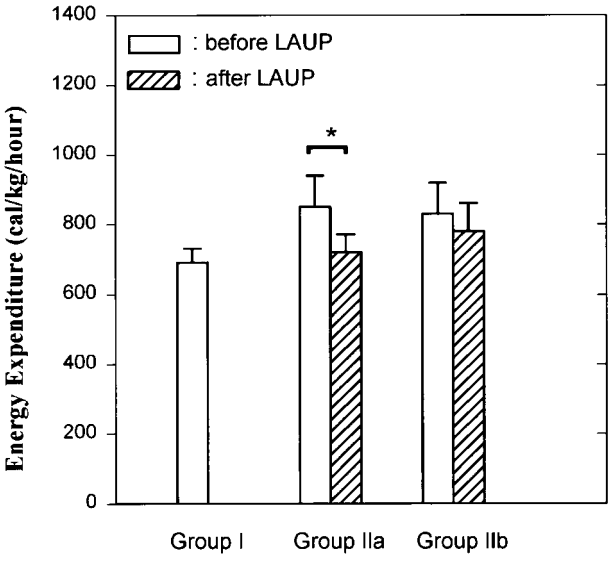

Fig 4. Mean sleep EE of group I and of groups IIa and IIb before and after LAUP. There was a clear decrease in mean sleep EE in group IIa after LAUP. In contrast, there was an absence of decreased mean sleep EE in group IIb subjects after LAUP. *$P < .05$ comparison between before and after LAUP. Statistical analysis was performed using Student's *t* test.

of the BMR, and lowest sleep EE was only 82% of the BMR, a result consistent with a previous report.[25] In contrast, our patients with moderate or severe OSAS did not have a corresponding decrease in sleep EE, a finding consistent with that of Bonnet et al,[12] who demonstrated that both brief and extended arousal during sleep are accompanied by increases in $\dot{V}O_2$ and $\dot{V}CO_2$. The increase in metabolism is related to the length of arousal, and the metabolic effect may continue for 90 minutes after a 30-second wakening. The time course of metabolic changes after arousal is related to the fragmentation required to decrease the restorative function of sleep. The sleep RQ did not change from the presleep value because increased sleep $\dot{V}O_2$ is associated with increased sleep $\dot{V}CO_2$.

There are many methods for evaluating EE, including a canopy, body chamber, and tight mask.[11] Our subjects tolerated the measurements performed in a canopy well. Our concomitant use of sleep monitoring equipment ensured that measurements of EE and BMR were performed under appropriate conditions of sleep or quiet wakefulness.

Sher et al[26] reported an overall 40.7% success rate of UPPP for OSAS when success was defined as a greater than 50% decrease in apnea index or RDI and a postoperative RDI of less than 20. The high failure rate may be explained by the likelihood of upper airway collapse at sites other than the palate. LAUP is not a traditional palatopharyngoplasty; instead, LAUP excises only part of the uvula and associated soft palate tissues and does not remove lateral pharyngeal wall tissues. Therefore, LAUP has a lower success rate when compared with classic UPPP. Reported success rates have varied from 0% to 90%.[27] In this study, only 6 of 25 patients responded to LAUP. The normalization of sleep EE following successful LAUP in group IIa is consistent with the findings of Stenlof et al[11] after treatment with nasal CPAP.

In conclusion, there is increased sleep EE in moderately severe or severe OSAS patients when compared with normal controls. This can be corrected by effective LAUP, but in those whose OSAS does not resolve after LAUP, normalization of EE does not occur.

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