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Transitory increased blood pressure after upper airway surgery for snoring and sleep apnea correlates with the apnea-hypopnea respiratory disturbance index

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Abstract

A transitory increase in blood pressure (BP) is observed following upper airway surgery for obstructive sleep apnea syndrome but the mechanisms implicated are not yet well understood. The objective of the present study was to evaluate changes in BP and heart rate (HR) and putative factors after uvulopalatopharyngoplasty and septoplasty in normotensive snorers. Patients (N = 10) were instrumented for 24-h ambulatory BP monitoring, nocturnal respiratory monitoring and urinary catecholamine level evaluation one day before surgery and on the day of surgery. The influence of postsurgery pain was prevented by analgesic therapy as confirmed using a visual analog scale of pain. Compared with preoperative values, there was a significant ($P < 0.05$) increase in nighttime but not daytime systolic BP (119 ± 5 *vs* 107 ± 3 mmHg), diastolic BP (72 ± 4 *vs* 67 ± 2 mmHg), HR (67 ± 4 *vs* 57 ± 2 bpm), respiratory disturbance index (RDI) characterized by apnea-hypopnea (30 ± 10 *vs* 13 ± 4 events/h of sleep) and norepinephrine levels (22.0 ± 4.7 *vs* 11.0 ± 1.3 μg l^{-1} 12 h^{-1}) after surgery. A positive correlation was found between individual variations of BP and individual variations of RDI ($r = 0.81$, $P < 0.01$) but not between BP or RDI and catecholamines. The visual analog scale of pain showed similar stress levels on the day before and after surgery (6.0 ± 0.8 *vs* 5.0 ± 0.9 cm, respectively). These data strongly suggest that the cardiovascular changes observed in patients who underwent uvulopalatopharyngoplasty and septoplasty were due to the increased postoperative RDI.

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- Septoplasty
- Blood pressure
- Sympathetic activity

Introduction

Among the postoperative complications described in patients with obstructive sleep apnea syndrome (OSAS) undergoing upper airway surgical procedures, transient systemic hypertension has been reported (1-3). Recently, Riley et al. (1) reported that among 210 OSAS patients examined, 70% required postoperative antihypertensive medications during their hospital stay (1,4). This increase in blood pressure (BP) could in turn promote postoperative complications such as bleeding, stroke or myocardial ischemia in those patients with systemic hypertension and/or cardiovascular diseases (1). The mechanisms for transient elevation of BP in this critical situation are not understood. It is possible that increases in upper airway resistance due to postoperative airway edema or induced by oral breathing may decrease the upper airway area, thereby causing an increase in the frequency of the obstructive respiratory events during sleep (5-8). These repetitive episodes of apnea often coincide with marked hypoxia, hypercapnia, and arousals during sleep, all of which are known to increase sympathetic nervous outflow (9-11). These repetitive acute changes in sympathetic activity may be involved in the pathogenesis of cardiovascular disturbances, mainly BP elevation (12). Moreover, there is evidence that changes in sympathetic activity may be implicated in the development of sustained hypertension in these patients (13-16). Additionally, preoperative anxiety and fear and postoperative pain can induce a psychological stress that in turn can alter the homeostasis of BP, heart rate (HR) and neural activity (17-19). Severe pain has been frequently reported after upper airway surgery for OSAS, leading to the use of newer approaches for postoperative analgesia, such as the combination of a nonopioid analgesic with nonsteroidal anti-inflammatory drugs (20,21), but their efficacy after upper airway surgery has not been evaluated.

The main objective of the present study was to evaluate the changes in BP and in putative factors causing its elevation, particularly postoperative pain, in a group of snorers subjected to upper airway surgery.

Patients and Methods

The protocol was approved by the Hospital Ethics Committee and informed consent was obtained from each patient. The study was performed on 10 normotensive (systolic BP: 125 ± 3 mmHg; diastolic BP: 81 ± 3 mmHg) patients with a mean age of 46 ± 1 years and a mean body mass index (BMI) of 23 ± 1 kg/m^2. All patients were snorers and most of them had mild OSAS. The mean respiratory disturbance index (RDI) of the group was 13 ± 4 events/h of recording (range: 2 to 30 events/h). We excluded from the study those patients who were: a) older than 60 years or younger than 18 years, b) had a body weight more than 1.6 times the ideal body weight (22) and/or had a BMI higher than 30 kg/m^2, c) had moderate to severe respiratory disease, and d) had cardiac arrhythmia and systolic BP ≥160 and/or diastolic BP ≥95 mmHg.

Nocturnal respiration monitoring

All studies were carried out at the Hôpital Saint-Antoine, Paris, France. Nocturnal respiration monitoring studies, including measurements of snoring and body movements, were carried out by a continuously recording technique (PolyMesam®, Taema, France) from 10:00 pm to 6:00 am on the preoperative day, on the day of surgery and one year after surgery. Nocturnal respiratory events were assessed by measuring naso-buccal airflow using a dual thermistor. Chest and abdominal wall respiratory movements were measured using noncalibrated inductive respiratory plethysmography, oxyhemoglobin saturation (SaO_2) was analyzed by finger oximetry in the PolyMesam® recorder, sound

intensity was measured using a microphone placed at the level of the neck, body position was monitored through a sensor positioned on the chest, and cardiac rhythm was monitored by electrocardiogram. Throughout the study, the movements of the subject were recorded with a wrist actigraph, which contained a motion detector and a system to record and store the number of wrist movements. Wrist movement intervals higher than 10 s were considered and computed every hour from 11:00 pm to 6:00 am. Every period without wrist activity was considered to be a period of sleep (23). RDI was indicated by the number of recognized apneic and hypopneic episodes recorded per hour of recording. It means that all respiratory disturbances during the evaluation period were added and divided by the number of hours of evaluation time. An event of obstructive apnea was defined as an 80% or greater decrease in airflow amplitude through the nose and mouth lasting more than 10 s in the presence of visible thoracic and abdominal respiratory efforts. An event of hypopnea was defined as a 10-s or longer decrease in oronasal airflow amplitude and the amplitude of thoracic and abdominal respiratory efforts to values less than 50% of those observed during normal breathing prior to the event. Desaturation events were recognized when oxygen saturation was 4% below baseline saturation, but desaturation was not a criterion for scoring either apnea or hypopnea.

Ambulatory blood pressure monitoring

Fully automatic systolic and diastolic BP and HR profiles were recorded continuously and noninvasively for 24 h using a system for ambulatory monitoring of BP (SpaceLabs 90207, SpaceLabs Inc., Redmond, Washington, DC, USA). Oscillometric units were used at 15-min sampling intervals throughout the recording period one day before surgery and on the day of surgery and the procedure was repeated again one year later. The readings were edited and averaged automatically by an interface (SpaceLabs ABP90209), set to discard systolic BP readings higher than 260 and lower than 70 mmHg, diastolic readings higher than 150 and lower than 40 mmHg, pulse pressure readings higher than 150 and lower than 20 mmHg, and readings with the diastolic BP higher than the systolic BP. The interface was also set to define the daytime and nighttime periods as the intervals between 7:00 am and 9:00 pm. On average, 95.8% BP readings per patient satisfied the editing criterion (range 91-100). At least two valid ambulatory BP readings per hour for the entire 24-h period were obtained for each patient. The presence of the "dip" in the BP recording observed during nocturnal sleep was investigated. A subject was considered a "nondipper" if his/her systolic and diastolic BP did not decrease by 10% during sleep compared to the mean values observed during the daytime.

Urinary catecholamines

Samples for determination of urinary norepinephrine and epinephrine were collected from 8:00 pm to 8:00 am during the three recording occasions (preoperative, postoperative and one year after surgery). Urine specimens for each sample were collected into polyethylene containers, acidified with 6 N HCl as preservative, kept at +4ºC overnight and stored at -20ºC until the time for assay. Urinary catecholamines were determined by high performance liquid chromatography with electrochemical detection (24,25).

Anesthetic and surgical procedures

All patients received 100 mg hydroxyzine dihydrochloride (orally) one hour prior to surgery. General anesthesia was induced with propofol (Diprivan®), the trachea was intubated and anesthesia was maintained with

isoflurane and atracurium dibesylate (Tracurium®). Injections of sufentanil were performed as decided by the anesthesiologist responsible for the patient. Uvulopalatopharyngoplasty (UPPP) was performed as originally described by Fujita et al. (26). Bilateral tonsillectomy was then performed followed by septoplasty in all patients. Patients were monitored in the recovery room postoperatively. Antibiotics were used and postoperative pain was controlled with a combination of ketoprofen (Profenid, 50 mg, *iv*; Specia Laboratory, Paris, France) and propacetamol hydrochloride (Prodafalgan, 2 g, *iv*; UPSA Laboratory, Rueil Malmaison, France), an acetaminophen pro-drug, diluted in 100 ml dextrose.

Evaluation of postoperative pain

The first pain medication with ketoprofen (50 mg, *iv*) plus propacetamol (2 g, *iv*) was administered at the time of extubation in the operating room and the second was administered 4 h later. After this period, the drug was administered every 6 h for 28 h.

A subjective criterion was used to evaluate the postoperative pain scores and the efficacy of the analgesic combination. A 10-cm long ruler with endpoints marked as "no pain" to "severe pain" was used as a visual analog scale (VAS) to assess the pain intensity described by the patient (27-29). After the patient had pointed at the pain classification on the VAS the corresponding score was measured by the investigator. The first pain evaluation was carried out in the recovery room, when the patient was able to perform VAS evaluation before returning to his room (control period). The other measurements were made 30 min before and 3 h after the administration of the analgesic combination over a period of 28 h. The location and kind of pain reported by the patient were also recorded using a validated French version of the McGill Pain Questionnaire (Questionnaire Douleur de Saint-Antoine, QDSA; 30).

The psychological stress, especially anxiety, was also evaluated using a VAS that permitted the patient to self-report the level of anxiety, which ranged from "no anxiety" to "severe anxiety". This evaluation was performed in the recovery room concomitantly with pain evaluation. In addition, the development of sensory and affective components of the anxiety state was assessed using the QDSA. We also wanted to determine the subjective impression of sleep since there is no objective sleep, and for this purpose we used the VAS changing the endpoints of the long ruler from "no sleep" to "good sleep" to assess the sleep score described by the patient.

Statistical analysis

Results are reported as means ± SEM. One-way analysis of variance (ANOVA) for repeated measures followed by a protected *post hoc* test (Fisher least significant difference procedure) was used for comparisons of the mean values of the parameters recorded on the three different occasions (31). Linear regression analysis was employed to obtain the correlation between changes in BP and RDI and between changes in BP and catecholamines. The level of significance was set at $P < 0.05$ for all comparisons.

Results

Wrist activity and disordered sleep breathing

No differences in mean wrist motion duration were observed between the preoperative night (5.2 ± 3.1 movements/h) and the night following surgery (5.4 ± 3.0 movements/h), suggesting that there were similar sleep times. No significant changes were observed between the two nights in terms of subjective sleep quality evaluation measured by the VAS (6.0 ± 0.8 and 5.0 ± 0.9 cm, respectively).

A significant increase in RDI was ob-

served during the night following surgery when compared with the preoperative night (30 ± 10 *vs* 13 ± 4 events/h, respectively; $P < 0.05$). One year later the values were similar to those observed on the preoperative day. These results were accompanied by a tendency ($P > 0.05$) for the mean nocturnal SaO_2 to decrease during the night after surgery (7.0 ± 5.0% below baseline saturation) compared to the preoperative values (4.3 ± 3.3% below the baseline saturation), and to those observed one year later (4.9 ± 4.2% below the baseline saturation).

Cardiovascular changes

Figure 1 shows average BP and HR values continuously recorded over a period of 24 h. Data showed a significant ($P < 0.05$) increase in nighttime values of mean systolic (119 ± 5 *vs* 107 ± 3 mmHg) and diastolic BP (72 ± 4 *vs* 67 ± 2 mmHg), mean BP (88 ± 4 *vs* 81 ± 3 mmHg), and HR (67 ± 4 *vs* 57 ± 2 bpm) compared to preoperative control values. One year later, when the patients were monitored again, these values were normalized (104 ± 3, 64 ± 2, 78 ± 3 mmHg and 56 ± 1 bpm, respectively). Nocturnal dipping in BP was observed in 9 of the 10 patients on the preoperative day and one year later but only in one patient on the day of surgery.

Pre- and postoperative correlation analysis was performed to obtain a first assessment of the degree of relationship between BP values and other dependent variables. Figure 2 shows that both systolic and diastolic BP were significantly correlated with RDI ($r = 0.81$ and $r = 0.74$, respectively; $P < 0.01$).

Urinary catecholamines

The 12-h catecholamine urinary excretion rates showed a significant ($P < 0.05$) increase of norepinephrine during the night immediately following surgery (22.0 ± 4.7

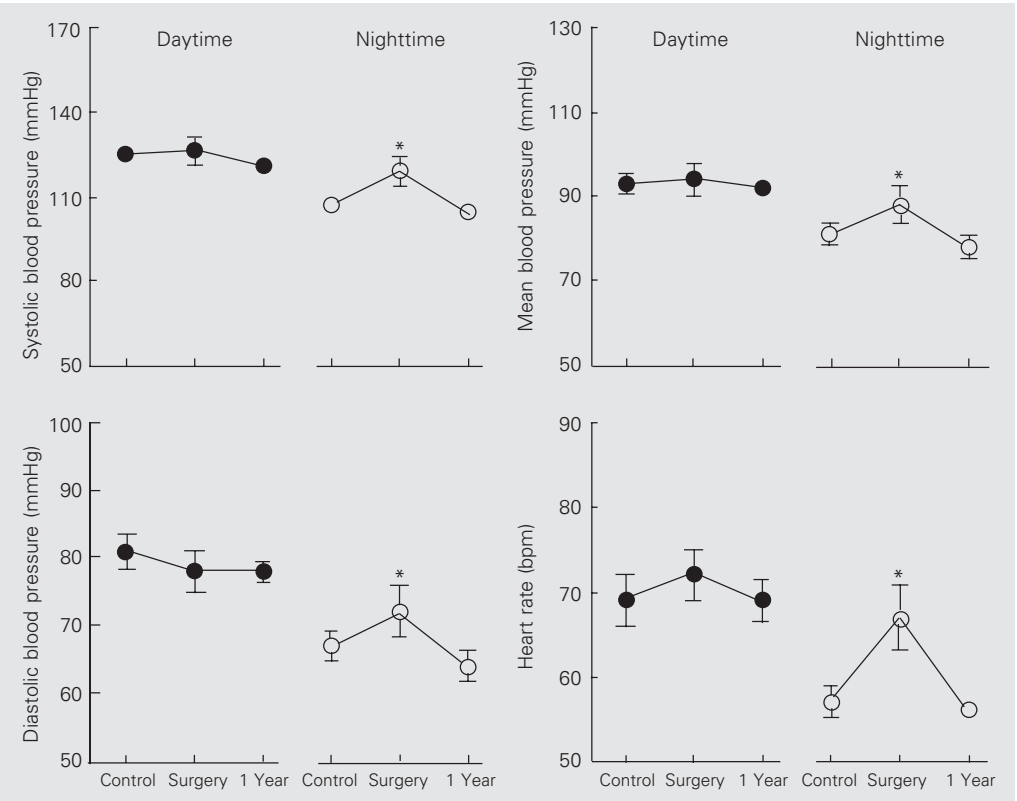

Figure 1. Systolic, diastolic and mean blood pressure and heart rate measured for 24 h in normotensive snorers one day before surgery (control), on the day of uvulopalatoplasty surgery and one year later. Data are reported as means ± SEM. Asterisks indicate significantly higher values on the night of the day of surgery compared to control ($P < 0.05$, one-way ANOVA).

μg l^{-1} 12 h^{-1}) as compared to values observed during the preoperative night (11.0 ± 1.3 μg l^{-1} 12 h^{-1}) and were normalized one year later (12.0 ± 2.3 μg l^{-1} 12 h^{-1}). Similar results were observed for epinephrine excretion rates (3.1 ± 0.9, 2.0 ± 0.2, 1.7 ± 0.4 μg l^{-1} 12 h^{-1}, respectively). Data analysis of absolute values showed that urinary catecholamine excretion rates did not correlate with BP (systolic: r = 0.33 and diastolic: r = 0.19) nor with RDI desaturation index (r = 0.29) and similar negative correlations were observed when values were determined as changes (Δ values).

Stress and pain evaluation

No differences in anxiety scores quantified by the VAS were observed among the five postoperative periods (4, 10, 16, 22 and 28 h) compared to the same periods of time on the preoperative day. In addition, all scores were below the limit values of the test (5 cm), which means that these patients were not abnormally anxious during the preoperative period. The evaluation of time course of VAS pain intensity scores for patients receiving the analgesic combination showed no significant differences among the mean values measured in the five postoperative periods in the recovery room (4 h: 5.0 ± 0.7, 10 h: 3.7 ± 0.7, 16 h: 4.0 ± 0.5, 22 h: 3.8 ± 0.5 and 28 h: 2.2 ± 0.4 cm) when compared to the preoperative control values (5.1 ± 0.7 cm).

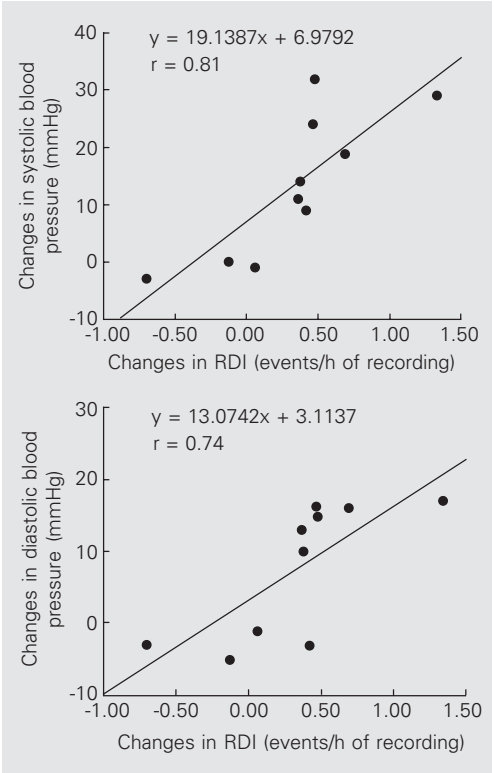

Figure 2. Regression analysis showing the positive relationship between changes in systolic or diastolic blood pressure and changes of recording in respiratory disturbance index (RDI) in normotensive snorers (P < 0.01, one-way ANOVA)

Discussion

The present study confirms that upper airway surgery (UPPP) associated with septoplasty is followed by a significant elevation of RDI. This phenomenon was accompanied by an elevation of systemic BP and HR in normotensive snorers or mild OSAS patients during the first night postsurgery. Since postoperative pain was controlled by an analgesic, the elevation of BP and HR seems to be a direct consequence of surgically induced disordered breathing.

An increase in RDI and oxyhemoglobin desaturation (5-9) has been reported frequently after upper airway surgery in OSAS patients. As expected, in our study the mean RDI value increased significantly during the night after UPPP plus septoplasty surgery both in snorers and mild OSAS patients compared to the values observed on the preoperative day. We speculate that postoperative airway edema associated with upper airway occlusion and the mouth breathing due to nasal packing after septoplasty could worsen the unstable respiratory status in these patients (8).

Esclamado et al. (2) retrospectively reviewed 135 patients with OSAS undergoing UPPP and associated procedures and noted that 13% showed complications such as airway obstruction after extubation or hemorrhage. On the other hand, Riley et al. (1) reported that among 210 patients analyzed after a surgical procedure performed for the

correction of OSAS, 53% required intraoperative and 70% postoperative antihypertensive medications. Among these patients, only 31% had a history of hypertension. The surgical procedure included an UPPP for the majority of these patients (77%), but it was generally associated with a mandibular osteotomy with genioglossus advancement and/or hyoid myotomy and suspension (68%). In our study the surgical procedure always consisted of UPPP and septoplasty. The nasal surgery was required to correct a significant nasal septum deformity in all patients and was conducted at the same time of the UPPP to limit the number of procedures requiring general anesthesia. There was an acute significant increase of BP in 80% of these normotensive patients during the night immediately following UPPP surgery as compared to the preoperative night. Even a moderate acute elevation in BP involves a higher risk of complications, especially postoperative bleeding, for any given value even if these pressures have been long-standing (2,3). This increase in BP could in turn promote another kind of postoperative complications such as stroke or myocardial ischemia in patients with ischemic cardiovascular disease.

It is interesting to observe that in our study the normotensive patients undergoing surgical UPPP plus septoplasty had only nocturnal BP increases, e.g., during the night after surgery they presented no nocturnal "dipping". Perhaps the most critical aspect of the transient postoperative hypertension occurring after UPPP surgery is to evaluate their consequences during a period while the patients are sleeping. We chose to study only normotensive subjects in order to obtain an uncomplicated effect on BP caused by surgery and sleep disordered breathing in simple snorers or in patients with very mild sleep apnea. We speculate that the immediate consequences of surgery for BP could be more severe and require treatment in borderline or hypertensive patients, as reported by Riley et al. (1). The acute and paradoxical creation of repetitive upper airway occlusions due to the surgical procedure allowed us to obtain data that permitted the understanding of the vascular consequences of apnea for normotensive snorers.

Several studies have suggested that a possible mechanism producing transient BP elevation is increased sympathetic activity during sleep in patients with OSAS, as indicated by high urinary catecholamine levels (13,14). Our results are in general agreement with these data. It appears that an average cumulative value, such as that generated by an overnight urine collection, would better reflect the difference between apnea and nonapnea periods. It has been clearly established in chronic OSAS patients that sleep disordered breathing results in acute elevation of systemic BP, presumably mediated by the sympathetic nervous system (7-11). However, the present results showed that even in snorers or mild OSAS patients the values of systolic and diastolic BP on the day before and after surgery were significantly related to the severity of OSAS as indexed by RDI. Although urinary norepinephrine excretion rates increased significantly during the night after surgery compared to the preoperative night, we did not find a significant correlation between changes in BP and changes in catecholamine levels. In contrast, several studies have reported that during the episodes of sleep apnea the asphyxia results in marked hypoxia and hypercapnia and vigorous inspiratory efforts, which eventually lead to arousal when ventilation is reestablished (9-12). The neurocirculatory responses to hypoxia and hypercapnia could be mediated by chemoreflex mechanisms leading to increases in sympathetic nervous system activity and thereby increasing BP (32). In addition, there is electroencephalographic evidence that arousal increases sympathetic nervous system activity and contributes to BP elevation in response to hypoxia and the hemodynamic effects of negative intratho-

racic pressures generated by the obstructed inspiratory efforts (9,33).

Although other investigators have proposed pain as a cause for postoperative hypertension associated with increased circulating catecholamines, our results show that the combination of propacetamol and ketoprofen was effective for pre- and postoperative analgesia, reducing peripheral nociception and hence reducing the pain and inflammatory response to surgical trauma (20,21). In addition, because this analgesic combination does not cause adverse effects such as those produced by opioids (respiratory depression, sedation, urinary retention, nausea and vomiting) it did not contribute to the repetitive surgically induced disordered breathing (20).

The transient BP elevation observed immediately after a common upper airway surgery in normotensive snorers with or without mild OSAS seems to be associated with repetitive increases of sleep disordered breathing created by the surgical procedure that could also increase the sympathetic activity and the observed changes in BP. Future experiments should test the hypothesis that the transient elevation of BP and HR following surgery could be prevented using a continuous positive airway pressure associated with a face mask (34).

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