

# Effect of UPPP on vascular reactivity of patients with OSAS

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## Abstract

**Objective:** The effect of uvulopalatopharyngoplasty (UPPP) on the endothelial function have not been evaluated in patients with obstructive sleep apnea syndrome (OSAS) in the literature. We investigated the vasoreactivity in patients with OSAS before and after UPPP via intravenous injection of the vitamin C comparing with healthy control group.

**Methods:** This prospective observational study included 39 patients who were admitted with the diagnosis of OSAS and 27 healthy controls. The patients were operated which is named UPPP. The anthropometric measures, routine blood tests, polysomnography (PSG) and flow mediated dilatation (FMD) were measured in all subjects. All measurements were repeated 8 weeks after UPPP in study group. Chi-square test and ANOVA tests were used for statistical analysis where appropriate.

**Results:** No statistically significant difference was observed between the two groups in the anthropometric features, blood pressure, PSG results (except apnea-hypopnea, oxygen desaturation index) and blood parameters. The preoperative baseline FMD was significantly lower in the study group when compared with the control group ( $p < 0.001$ ). After intravenous vitamin C, vasoreactivity unchanged in the control group ( $p = 0.912$ ). In the study group, vitamin C led to a statistically significant increase in preoperative FMD when compared with the preoperative baseline FMD ( $p < 0.001$ ). The preoperative baseline FMD was increased after UPPP ( $p < 0.001$ ). After UPPP in study group, vitamin C injection did not change the vasoreactivity ( $p = 0.610$ ).

**Conclusion:** It was concluded that UPPP could increase vascular reactivity in patients with OSAS.

## Introduction

Obstructive sleep apnea syndrome (OSAS) is a common pathologic condition qualified by apnea / hypopnea episodes during sleep. OSAS is associated with a significant increase in the risk for developing cardiovascular diseases [1-6]. Several mechanisms have been announced for the close relation between OSAS and cardiovascular diseases including circulating oxidative products, systemic inflammation, increase in sympathetic activity and blood pressure [5,7]. Abnormal oxygenation and pressures result in the disturbance of the vascular micromilieu, sympathetic nerve activity, disturbed endothelial function and haemodynamic instability [5,7-9]. Vitamins such as vitamin C or vitamin E have antioxidant effect [10]. And these vitamins can improve the endothelial function in patients with OSAS [11,12]. OSAS can be healed via continuous positive airway pressure (CPAP) treatment, oral appliances or surgical approach (such as uvulopalatopharyngoplasty (UPPP)) [13,14].

To our knowledge, there is no published study addressing the effect of UPPP surgery on the endothelial function in patients with OSAS. Therefore, we studied the vasoreactivity in patients with OSAS before and after UPPP via intravenous injection of the vitamin C comparing with healthy control group.

## Materials and methods

### Study population

Forty nonsmoking, otherwise healthy patients who were referred to Eskisehir Yunus Emre Government Hospital Sleep Laboratory, between June 2011 and July 2012 were included in this study. One

of them was excluded from the study; because he had a significant change in his body weight. So study completed with 39 patients (age range 31-50 years (mean  $\pm$  SD age,  $41.4 \pm 7.9$ )). Twenty-seven age and gender matched control subjects (age range 29-47 years (mean  $\pm$  SD age,  $38.8 \pm 7.6$ )) were picked from among healthy patients with normal polysomnography (PSG) results attending the same clinic during this study period.

At study entry, medical history was recorded and a physical examination was performed to all participants.

### Anthropometry

The anthropometric measures of all subjects were recorded (age, body-mass index (BMI), neck, waist and hip circumferences, waist-to-hip ratio (WHR)). Weight and height were measured to the kilogram and centimeter, respectively, and BMI was calculated ( $BMI = \text{weight (kg)} / \text{height}^2 \text{ (m}^2\text{)}$ ). Neck circumference was measured at the cricothyroid level, waist circumference in the middle between the 12th rib and the iliac crest, and hip circumference at the level of great trochanter by a tape, and WHR was calculated ( $WHR = \text{waist circumference (cm)} / \text{hip circumference (cm)}$ ).

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## Routine tests

Routine blood and urine analyses, cardiopulmonary graphs, and chest radiographs were performed to all subjects. In blood samples, total cholesterol, low-density lipoprotein, very low-density lipoprotein and high-density lipoprotein cholesterol, and HbA1c values specially were assessed in all subjects. .

## Overnight polysomnography

All subjects underwent an attended overnight polysomnography (PSG (Koninklijke Philips Electronics N.V./ Alice LE, Amsterdam, Netherlands)). PSGs were performed between 10:00pm - 06:00am. PSGs were assessed at baseline and repeated at the 8 weeks later than UPPP in the study group. PSGs were performed only one time (baseline) to the control subjects.

Apneas, hypopneas, and electroencephalography (EEG) recordings were automatically scored. Apnea was accepted as complete cessation of airflow more than 10 sec; hypopnea as a 50% reduction in airflow more than 10 sec, accompanied by more than 4% desaturation or by an EEG recorded arousal. Apnea-hypopnea index was calculated (AHI= total number of apneas and hypopneas /sleep time(hour)). In both groups, blood pressure values were taken from the right arm at the 4 hours intervals and averaged to compute the mean daytime blood pressure.

## Operation

UPPP is a procedure designed to enlarge the potential airspace in the oropharynx. The uvula and part of the free edge of the soft palate were removed under general anesthesia.

## Endothelial function testing protocol

The test was started at 15:00 in all cases. All subjects were scrutinized in the supine position after a resting period of 10 min. Flow mediated dilatation (FMD) was measured by high-resolution ultrasonography (Acuson ; Siemens, Philadelphia/ USA) of the right brachial artery (BA). The vessel diameter was evaluated under resting baseline resting conditions. Later on, forearm blood ischemia was created for 5 min by inflating a cuff to suprasystolic pressures. The cuff was deflated, causing a dilation of the BA, and arterial diameter was continuously monitored over a period of 3 min. The rise in vessel diameter sighted 60 seconds after cuff liberation was determined and expressed in relative percent values as compared with baseline conditions. FMD in response to intravenous injection of vitamin C (totally 5 ml) (Vitabiol C; ascorbic acid (500 mg/5 ml)) and sublingual application of nitroglycerine spray (totally 0.8mg)(Nitrolingual; glyceryl trinitrate (0.4 mg/puff)) was measured.

## Exclusion criterias

Study patients and control subjects with any clinical or laboratory evidence of vascular and metabolic diseases, those who had received vitamin therapy in the one month prior to the study, or those who were taking any drugs that might affect vascular reactivity (antihypertensive drugs, anticholesterol and endocrine agents), subject had a significant change in his body weight were also excluded from the study.

All subjects had given written informed consent to participate and the aim of the study and possible risks were fully explained. This study was acknowledged by the Ethical Committee of Eskisehir Osmangazi University Hospital.

## Statistics

SPSS® software package, version 17.0 (SPSS Inc., Chicago, IL, USA) for Windows® was used for the statistical analyses.

Continuous variables were presented as mean  $\pm$  SD and categorical variables were presented as percentage. Continuous variables, which were the characteristics of the groups were compared by one-way ANOVA. Categorical variables were analyzed using the chi-square test.

Within the study group, univariate analysis was performed to relate FMD to parameters of OSAS severity, such as AHI and other variables, such as BMI.

Data continuous variables were analyzed statistically using nonparametric tests, using the Friedman two-way ANOVA to establish the differences in arterial diameter occurring in response to reactive hyperemia and after vitamin C/nitroglycerine.

A value of  $P < 0.05$  was considered to be statistically significant.

## Results

Thirty-nine (25 male, 14 female) patients were completed the study. Postoperative velopharyngeal insufficiency as a complication of UPPP occurred in one patient (2.6%). He received u-shaped flap palatoplasty to cure the complication.

Anthropometric features of all subjects are shown in table 1. The two groups were matched in age, gender and anthropometric properties. There was no statistical difference between groups.

Sleep properties of all subjects are shown in table 2. Blood pressure were within the normal range and there was not statistical significant difference. AHI, oxygen desaturation index (ODI) results were higher in study group and they were decreased after UPPP.

As shown in table 3; there were no statistically difference in blood parameters between groups.

The preoperative baseline FMD was significantly lower in the study group when compared with the control group ( $6.1 \pm 0.7\%$ ;  $8.9 \pm 1.1\%$  ( $p < 0.001$ )). After intravenous injection of 0.5 g vitamin

**Table 1.** Comparison of anthropometric characteristics between the two groups.

	Study Group (n=39) (mean $\pm$ SD)	Control Group (n=27) (mean $\pm$ SD)	P
Age (years)	41.4 $\pm$ 7.9	38.8 $\pm$ 7.6	0.378
Sex (male/female)	25/14	16/11	0.466
BMI (kg/m <sup>2</sup> )	36.6 $\pm$ 7.5	34.7 $\pm$ 6.3	0.169
Neck circumference (cm)	45.7 $\pm$ 3.9	44.8 $\pm$ 3.5	0.232
Waist circumference (cm)	123.1 $\pm$ 15.3	120.6 $\pm$ 17.2	0.187
Hip circumference (cm)	128.8 $\pm$ 23.7	125.3 $\pm$ 25.7	0.121
WHR	0.96 $\pm$ 0.07	0.96 $\pm$ 0.07	0.909

BMI: body mass index; WHR: waist to hip ratio.

**Table 2.** Characteristics of sleep properties between the control group and preoperative-postoperative result of study group.

	Study Group (n=39)		Control Group (n=27)	P
	Preoperative	Postoperative		
Systolic BP (mmHg)	133.9 $\pm$ 7.8	132.7 $\pm$ 7.7	132.2 $\pm$ 7.4	0.468
Diastolic BP (mmHg)	82.7 $\pm$ 7.3	81.9 $\pm$ 7.5	80.9 $\pm$ 7.6	0.969
AHI (/hour)	29.6 $\pm$ 6.3	18.9 $\pm$ 5.8	8.1 $\pm$ 3.7	<0.001
FEV1 (% pred.)	90.1 $\pm$ 8.9	90.7 $\pm$ 8.1	92.2 $\pm$ 7.8	0.626
FVC (% pred.)	90.2 $\pm$ 9.8	89.9 $\pm$ 9.5	89.3 $\pm$ 9.3	0.528
pH	7.42 $\pm$ 0.02	7.41 $\pm$ 0.01	7.41 $\pm$ 0.01	0.839
PaO <sub>2</sub> (mm Hg)	82.6 $\pm$ 6.2	82.9 $\pm$ 6.2	83.1 $\pm$ 5.9	0.126
PaCO <sub>2</sub> (mm Hg)	38.1 $\pm$ 2.8	38.2 $\pm$ 2.5	38.9 $\pm$ 1.6	0.814
ODI (times/hour)	47.1 $\pm$ 18.8	19.3 $\pm$ 5.3	8.2 $\pm$ 3.9	<0.001

BP: blood pressure; AHI: apnea hypopnea index; FEV1: forced expiratory volume (1st second); FVC: forced vital capacity; ODI: oxygen desaturation index.

**Table 3.** Crosscheck of blood parameters between the control group and preoperative-postoperative result of study group.

	Study Group (n=39)		Control Group (n=27)	P
	Preoperative	Postoperative		
Total cholesterol (mg/dl)	103.4 ± 14.3	98.7 ± 11.9	94.1 ± 10.2	0.412
LDL (mg/dl)	88.5 ± 9.2	79.6 ± 8.8	81.7 ± 8.9	0.571
HDL (mg/dl)	47.3 ± 6.1	51.1 ± 6.2	50.2 ± 5.7	0.933
TG (mg/dl)	107.7 ± 11.9	105.8 ± 10.7	98.4 ± 9.1	0.762
HbA1c (%)	5.4 ± 0.1	5.3 ± 0.1	4.9 ± 0.1	0.187

HDL: high-density lipoprotein; LDL: low-density lipoprotein; TG: triglycerit; HbA1c: hemoglobinA1c.

**Table 4.** Flow-mediated dilation (FMD) of the brachial artery at baseline and after intravenous administration of vitamin C in the study (pre-post operative) and control groups.

	Study Group (n=39)		Control Group (n=27)
	Preoperative	Postoperative	
Baseline FMD (%)	6.1 ± 0.7	7.6 ± 0.8	8.9 ± 1.1
FMD after intravenous Vitamin C (%)	7.4 ± 0.7	7.7 ± 0.9	8.8 ± 1.1

FMD: Flow mediated dilatation.

C, vasoreactivity remained unchanged in the control group (8.9 ± 1.1%; 8.8 ± 1.1% (p=0.912)). In the study group, vitamin C led to a statistically significant increase in preoperative FMD when compared with the preoperative baseline FMD (6.1 ± 0.7%; 7.4 ± 0.7% (p<0.001)). The preoperative baseline FMD was increased after UPPP (6.1 ± 0.7%; 7.4 ± 0.7% (p<0.001)). After UPPP in study group, vitamin C injection did not change the vasoreactivity (7.6 ± 0.8%; 7.7 ± 0.9% (p=0.610)). Also there was no difference between postoperative baseline FMD of study group and baseline FMD of control group (7.6 ± 0.8%; 8.9 ± 1.1% (p=0.107)).

## Discussion

The present study demonstrates that endothelial dysfunction in patients with OSAS like as the literature [15,16]. And the endothelial dysfunction was reversed by intravenous injection of vitamin C in patients with OSAS. The possible factors that could effect the vasoreactivity were excluded in the subjects. We found that treating OSAS patients via UPPP can improve the endothelial function in OSAS patients without any changes in BMI. This is the sorter property of our study. In the published literature, there was shown that FMD in OSAS has been found to improve after several weeks of continuous positive airway pressure therapy [15,17]. But this is the first study about the changes of endothelial function before and UPPP in patients with OSAS comparing with healthy controls.

Our study differs from the previous works in two ways. First, our groups were similar in all anthropometric characteristics, blood pressures, serum cholesterol and HbA1c levels which can effect the FMD [15,18,19]. But the published studies have many limitations such as, investigators applied the PSG only to patients, and their groups include any female subjects. Also they did not say anything about the anthropometric measurement of their subjects [4,15,17].

Secondly, we assessed study group before and after UPPP operation. So this is the first published study which assesses the impact of UPPP on endothelial function in patients with OSAS.

The limitation of our study is that we did not investigate the long-term effects of UPPP on vascular reactivity in OSAS. The second limitation is that all subjects received the same dose of vitamin C. This study can not clarify the dose-response relationship between the amount of vitamin C and FMD in patients with OSAS.

## Conclusion

Accumulating evidence suggest that OSAS has a role in the endothelial dysfunction associated with vascular disease and UPPP have comperable increase on FMD like antioxidant agent vitamin C. So, we need further investigation about the relation between the oxidative mechanisms, vascular reactivity and cardiovascular problems and the effect of UPPP on these issues in patients with OSAS.

## Conflicts of interest

None declared.

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