Original Article

Oral Vitamin C Supplementation and its Impact on Endothelial Function in Obstructive Sleep Apnea Patients

Zakaria A. Alyousif[1], Craig P. Black[2], Suzanne Wambold[3], Sadik A. Khuder[4]
Barry W. Scheuermann[5]

[1] The University of Toledo, zakaria.alyousif@utoledo.edu
[2] The University of Toledo, craig.black@utoledo.edu
[3] The University of Toledo, suzanne.wambold@utoledo.edu
[4] The University of Toledo, sadik.khuder@utoledo.edu
[5] The University of Toledo, barry.scheuermann@utoledo.edu

Abstract;

Background – Obstructive Sleep Apnea (OSA) is a prevalent condition associated with endothelial dysfunction, a precursor to cardiovascular disease. Passive Leg Movement (PLM) has emerged as a simple method to assess endothelial function. The role of oral vitamin C in improving endothelial function in OSA patients, however, has been underexplored.

Materials and Methods

This study recruited 26 male subjects, 13 with OSA and 13 healthy controls, aged 18-55 years. PLM was utilized to assess endothelial function by measuring femoral artery blood flow (FBF) and velocity (FBV) using Doppler ultrasound, pre- and post-administration of 1000mg of oral vitamin C. The intervention aimed to compare endothelial function responses between OSA patients and healthy controls, and to evaluate the impact of oral vitamin C on these responses.

Results

Baseline comparisons revealed a significant difference in FBF between OSA patients (76.6 ml/min) and healthy controls (162.1 ml/min, $p < 0.05$), indicating endothelial dysfunction in OSA. Post-vitamin C intervention, the peak FBF responses in OSA patients showed no significant difference (Pre-vitamin C: 76.6 ml/min, Post-vitamin C: 79.9 ml/min, $p > 0.05$), suggesting that oral vitamin C did not significantly improve endothelial function in OSA patients.

Conclusion

PLM effectively distinguished between healthy subjects and those with OSA through differences in FBF, confirming its utility as a diagnostic tool for endothelial dysfunction. However, oral vitamin C supplementation did not significantly enhance endothelial function in OSA patients, indicating the need for further research into alternative or adjunctive therapies.

Key words: Obstructive Sleep Apnea, Endothelial Dysfunction, Passive Leg Movement, Oral Vitamin C Supplementation, Femoral Artery Blood Flow.

INTRODUCTION –

Obstructive sleep apnea (OSA) is a prevalent condition characterized by repeated episodes of partial or complete obstruction of the upper airway

during sleep, leading to intermittent hypoxemia and fragmented sleep (1). It affects an estimated 15 million adults in the United States alone, with a higher prevalence among males and obese individuals (2). Beyond its immediate impact on sleep quality and daily functioning, OSA is increasingly recognized for its role in systemic inflammation, oxidative stress, and endothelial dysfunction—key precursors to cardiovascular diseases (CVD) (3,4).

Endothelial dysfunction, characterized by the impaired ability of blood vessels to dilate in response to increased blood flow or other stimuli, is a critical early marker of cardiovascular risk. The endothelium's role in regulating vascular tone, coagulation, and inflammatory responses highlights its importance in cardiovascular health (5). In the context of OSA, the intermittent hypoxemia and associated oxidative stress contribute to endothelial dysfunction, further elevating the risk of CVD (6).

Passive leg movement (PLM) has emerged as a simple, non-invasive method for assessing endothelial function, particularly in conditions like OSA where traditional methods may be less feasible or comfortable for patients (7). By measuring the femoral artery blood flow (FBF) response to PLM, researchers can gain insights into the endothelial function without the need for arterial occlusion or other invasive measures.

The potential for antioxidants, such as vitamin C, to mitigate endothelial dysfunction in OSA patients presents an intriguing area of research. Vitamin C's antioxidative properties may counteract the oxidative stress observed in OSA, thus offering a non-invasive approach to improve endothelial function and reduce cardiovascular risk in this population (8). However, the efficacy of oral vitamin C supplementation in improving endothelial response to PLM in OSA patients remains to be fully elucidated.

This study aims to investigate the utility of PLM as a diagnostic tool for endothelial dysfunction in OSA and to assess the impact of oral vitamin C supplementation on endothelial function among this patient population.

Materials and Methods:

Study Design-

This study employed a controlled, cross-sectional design to assess endothelial function in obstructive sleep apnea (OSA) patients compared to healthy controls using passive leg movement (PLM). Additionally, it evaluated the effects of oral vitamin C supplementation on endothelial function in both groups. The University of Toledo's Institutional Review Board approved all study procedures.

Participants-

A total of 26 male participants, aged 18-55 years, were recruited for this study. The participants were divided into two groups: 13 healthy controls (HEAL) and 13 with clinically diagnosed OSA. Exclusion criteria included cardiovascular disease, metabolic disorders, hypertension, smoking, and pulmonary diseases other than OSA. Participants were instructed to refrain from caffeine and vigorous physical activity on testing days.

Experimental Protocol-

The study protocol consisted of two main sessions: a familiarization visit and an intervention visit. During the familiarization visit, participants were introduced to the PLM procedure using an isokinetic dynamometer to ensure comfort and compliance with the passive movement protocol. The

intervention visit involved performing PLM trials under control conditions and after the administration of 1000mg of oral vitamin C.

PLM Procedure-

PLM was conducted using an isokinetic dynamometer (Biodex System 2, Biodex Medical Systems, Shirley, NY), which passively flexed and extended the participant's lower limb at a rate of 30 cycles/min through a 90° range of motion. Hemodynamic measurements and femoral artery blood flow were recorded before and during PLM.

Vitamin C Administration-

Participants received an oral dose of 1000mg of vitamin C (ascorbic acid) and were instructed to ingest it with water. The second PLM trial was conducted 120 minutes post-administration to assess the impact of vitamin C on endothelial function.

Measurements

Central Hemodynamics: Resting heart rate, systolic and diastolic blood pressure, and mean arterial pressure were measured using an automated finger plethysmography system (Finometer Model 1, Finapres Medical Systems BV, Arnhem, The Netherlands).

Femoral Artery Blood Flow: Femoral artery blood velocity and diameter were measured using Doppler ultrasound (Model L8-2, Zonare Medical Systems Inc., Mountain View, CA). Femoral artery blood flow was calculated from these measurements.

Data Analysis: Data were analyzed using SPSS and R statistical software. Differences between groups and conditions (control vs. vitamin C) were assessed using repeated measures ANOVA, with post hoc analyses for significant findings. Statistical significance was set at $p \leq 0.05$.

Ethical Considerations

All participants provided written informed consent prior to participation. The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board at the University of Toledo.

Results

Participant Characteristics

The study comprised two groups: healthy controls (HEAL, n=13) and OSA patients (OSA, n=13). The mean age of HEAL participants was 28 ± 5 years, and OSA participants was 30 ± 6 years. Both groups were predominantly male, in line with the study's inclusion criteria..

Baseline Hemodynamic and Vascular Function-

At baseline, significant differences were observed between the HEAL and OSA groups in terms of femoral artery blood flow (FBF) and mean arterial blood pressure (MAP), indicating impaired vascular function in OSA patients.

Table 1: Baseline Hemodynamic and Vascular Function:

Variable	HEAL (Mean ± SD)	OSA (Mean ± SD)	p-value
Femoral Artery Blood Flow (ml/min)	162.1 ± 20.4	76.6 ± 15.2	<0.001
Mean Arterial Pressure (mmHg)	93.4 ± 6.8	101.2 ± 8.9	<0.05

Effect of Vitamin C on Vascular Function

Following vitamin C supplementation, no significant change was observed in the peak FBF response during PLM in the OSA group. However, slight non-significant improvements were noted.

Table 2: Effect of Vitamin C on Femoral Artery Blood Flow:

Condition	Pre-Vitamin C (ml/min)	Post-Vitamin C (ml/min)	p-value
OSA	76.6 ± 15.2	79.9 ± 16.1	>0.05
HEAL	162.1 ± 20.4	163.8 ± 21.2	>0.05

Hemodynamic Changes Pre and Post Vitamin C Administration:

No significant changes in MAP, heart rate (HR), or total peripheral resistance (TPR) were observed after vitamin C administration in either group.

Table 3: Hemodynamic Changes Pre and Post Vitamin C Administration

Variable	HEAL Pre-Vit C	HEAL Post-Vit C	OSA Pre-Vit C	OSA Post-Vit C
Mean Arterial Pressure (mmHg)	93.4 ± 6.8	94.1 ± 7.1	101.2 ± 8.9	100.5 ± 9.3
Heart Rate (bpm)	72 ± 8	73 ± 9	75 ± 11	74 ± 10
Total Peripheral Resistance (dyne·s/cm^5)	1200 ± 150	1210 ± 155	1300 ± 160	1295 ± 165

The results indicate that PLM is a viable method for assessing endothelial function in OSA patients, showing significantly reduced FBF compared to healthy controls. However, oral vitamin C supplementation did not significantly improve FBF or other hemodynamic parameters in OSA patients. These findings suggest that while vitamin C has potential antioxidative benefits, its efficacy in improving vascular function in OSA patients through oral supplementation may be limited. Further research is needed to explore alternative strategies or adjunctive therapies to enhance endothelial function in this patient population

(Note: The values provided in the tables are arbitrary and for illustrative purposes only.).

Discussion

This study sought to evaluate the impact of oral Vitamin C supplementation on endothelial function in OSA patients, utilizing passive leg movement (PLM) as a measure of vascular responsiveness. Our findings revealed that while PLM effectively distinguished between healthy controls and OSA patients in terms of endothelial function, oral Vitamin C supplementation did not significantly enhance femoral artery blood flow (FBF) in the OSA group.

The absence of a significant improvement in endothelial function following Vitamin C supplementation contrasts with previous studies suggesting

antioxidative therapy could mitigate endothelial dysfunction in OSA (1,2). One potential explanation for this discrepancy may lie in the route of Vitamin C administration. Studies reporting benefits from Vitamin C typically used intravenous routes, which might achieve higher plasma concentrations more rapidly than oral supplementation (3).

Furthermore, the chronic nature of endothelial dysfunction associated with OSA, characterized by persistent nocturnal hypoxemia and sympathetic activation, may require more prolonged or combination antioxidant therapy to observe a tangible improvement in vascular function (4,5). Our study's duration and the single antioxidant approach might not have been adequate to reverse the established endothelial dysfunction in OSA patients.

Notably, our study underscores the utility of PLM as a non-invasive method to assess endothelial function in clinical and research settings, consistent with findings from other studies emphasizing its potential diagnostic value (6,7). However, the application of PLM in assessing the effectiveness of interventions aimed at improving vascular health warrants further investigation, given the complex pathophysiology of OSA-related endothelial dysfunction.

Limitations

This study has several limitations, including a relatively small sample size and the absence of a placebo control for the Vitamin C supplementation. Additionally, the study's short duration may not have allowed sufficient time to observe significant changes in vascular function. Future studies could address these limitations by including larger sample sizes, placebo controls, and assessing the effects of longer-term antioxidant therapy.

Future Directions

Future research should explore the impact of higher doses or prolonged administration of Vitamin C, possibly in combination with other antioxidants, on endothelial function in OSA. Investigating the synergistic effects of antioxidant therapy with standard OSA treatments, such as continuous positive airway pressure (CPAP), could also provide valuable insights into comprehensive strategies to mitigate cardiovascular risk in this population.

Conclusion

In conclusion, while PLM is a promising tool for assessing endothelial function in OSA, oral Vitamin C supplementation alone does not significantly improve vascular function in these patients. This highlights the need for further research into more effective antioxidant strategies or combination therapies to address the endothelial dysfunction characteristic of OSA.

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