Original Article

Passive Leg Movement as a Diagnostic Tool for Distinguishing Healthy Individuals from Those with Obstructive Sleep Apnea

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Abstract;

Background – Obstructive Sleep Apnea (OSA) is linked with endothelial dysfunction, posing a significant risk for cardiovascular diseases. The non-invasive assessment of endothelial function through passive leg movement (PLM) offers a novel diagnostic avenue. This study explores PLM's efficacy in differentiating between healthy individuals and those with OSA, alongside evaluating the impact of oral vitamin C on endothelial function within these groups.

Materials and Methods:

The study enrolled 26 male subjects, divided equally into healthy and OSA groups. PLM was performed using an isokinetic machine to assess femoral artery blood flow (FBF) and blood velocities (FBVs) via Doppler ultrasound. Subjects consumed 1000mg of oral vitamin C, with measurements repeated post-consumption. Data analysis involved repeated measures ANOVA to evaluate the diagnostic capability of PLM and the effect of vitamin C on FBF responses.

Results:

A significant difference in FBF was observed between OSA and healthy groups (healthy: 162.1 ml/min, OSA: 76.6 ml/min; $p < 0.05$), confirming PLM's diagnostic potential. However, vitamin C administration did not significantly alter FBF responses in OSA patients (pre-vitamin C: 76.6 ml/min, post-vitamin C: 79.9 ml/min; $p > 0.05$), challenging the anticipated benefits of oral vitamin C on endothelial function.

Conclusion:

PLM effectively distinguishes between healthy individuals and those with OSA, highlighting its diagnostic utility. Nonetheless, oral vitamin C did not improve endothelial dysfunction in OSA patients, suggesting the need for further research on alternative administration methods or dosages.

Key words: Passive Leg Movement (PLM), Obstructive Sleep Apnea (OSA), Endothelial Function, Femoral Artery Blood Flow (FBF), Vitamin C.

INTRODUCTION:

Obstructive Sleep Apnea (OSA) is a prevalent sleep disorder characterized by repetitive episodes of partial or complete obstruction of the upper airway during sleep, leading to disrupted sleep and hypoxemia. The condition

affects approximately 15 million adults in the United States, representing about 5% of the adult population, with a higher prevalence among males and obese individuals (1). OSA is not only a significant public health concern due to its impact on quality of life but also because of its association with an increased risk of cardiovascular diseases (CVD), including hypertension, atherosclerosis, and coronary artery disease (2, 3).

The pathophysiological mechanisms linking OSA to cardiovascular risk involve intermittent hypoxia, oxidative stress, systemic inflammation, and endothelial dysfunction (4). Endothelial dysfunction, characterized by a diminished capacity of the endothelium to regulate vascular tone, is an early marker of vascular pathology leading to CVD (5). The non-invasive assessment of endothelial function has become a critical aspect of cardiovascular research and clinical diagnostics. Traditionally, Flow-Mediated Dilation (FMD) has been utilized to assess endothelial function; however, Passive Leg Movement (PLM) has recently emerged as a simpler, reliable alternative (6).

PLM's potential as a diagnostic tool for distinguishing between healthy individuals and those with OSA is based on its ability to induce shear stress-mediated increases in femoral artery blood flow, thereby providing insights into endothelial function (7). This study focuses on exploring the diagnostic capability of PLM in differentiating individuals with OSA from healthy controls. Additionally, given the growing interest in antioxidants to attenuate endothelial dysfunction, the impact of oral vitamin C on endothelial function in OSA patients is also examined. Previous research suggests that vitamin C, a potent antioxidant, could mitigate endothelial dysfunction by improving nitric oxide bioavailability and reducing oxidative stress (8, 9).

Materials and Methods:

Study Design and Participants-

This study employed a cross-sectional design to investigate the utility of Passive Leg Movement (PLM) as a diagnostic tool for differentiating healthy individuals from those with Obstructive Sleep Apnea (OSA). Additionally, it examined the effects of oral vitamin C administration on endothelial function in these populations. A total of 26 male participants were recruited and divided into two groups: 13 healthy controls (HEAL) and 13 individuals diagnosed with OSA. Eligibility criteria included males aged 18-55 years, non-smokers, and no current diagnosis of cardiovascular or metabolic diseases. OSA patients were identified using the STOP-BANG questionnaire, a validated tool for OSA risk assessment. The study received approval from the Institutional Review Board of the University of Toledo, and all participants provided written informed consent.

Passive Leg Movement (PLM) Protocol-

PLM was conducted to assess endothelial function by measuring changes in femoral artery blood flow (FBF) and blood velocity (FBVs). Participants were seated in an isokinetic dynamometer (Biodex System 2, Biodex Medical Systems, Shirley, NY), which facilitated passive movement of the lower limb through a 90° range of motion at a frequency of 30 cycles/min. Doppler ultrasound (Model L8-2; Zonare Medical Systems, Mountain View, CA) was used to continuously measure FBF and FBVs before, during, and after PLM.

Vitamin C Administration-

Following baseline measurements, participants received an oral dose of 1000 mg of vitamin C. Post-vitamin C measurements were conducted 2 hours after ingestion to assess the impact of vitamin C on endothelial function.

Data Collection and Analysis-

Hemodynamic parameters, including heart rate, blood pressure, and femoral artery blood velocities, were recorded at baseline, during PLM, and post-vitamin C administration. The arterial diameter was measured at baseline to calculate FBF. Data analysis was performed using SPSS software (Version 25.0, IBM Corp., Armonk, NY). A repeated measures ANOVA was utilized to evaluate differences between groups (HEAL vs. OSA) and conditions (pre- vs. post-vitamin C). The level of significance was set at $p \leq 0.05$.

Ethical Considerations-

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

This methodological approach aimed to rigorously evaluate PLM as a non-invasive diagnostic tool for OSA and explore the potential therapeutic effects of oral vitamin C on endothelial function in individuals with OSA.

Results:

Subject Characteristics-

The study involved two groups: one comprising healthy individuals (HEAL) and the other comprising individuals diagnosed with Obstructive Sleep Apnea (OSA). Both groups had similar demographic profiles in terms of age, height, and weight, with no significant differences between them, ensuring that any observed differences in the results could be attributed to the presence of OSA rather than to demographic variables.

Femoral Artery Blood Flow and Diameter Measurements-

The study focused on assessing the endothelial function through measurements of femoral artery blood flow (FBF) and femoral artery diameter (FAD) during passive leg movement (PLM). These measurements were crucial for understanding the vascular response in the context of OSA.

Experimental Findings-

Femoral Artery Blood Flow (FBF): The results indicated a significant difference in FBF response to PLM between the OSA and HEAL groups, highlighting PLM's potential as a diagnostic tool for endothelial dysfunction in OSA patients. Specifically, the HEAL group showed a more pronounced increase in FBF during PLM compared to the OSA group, suggesting impaired endothelial function in the latter.

Effect of Vitamin C on FBF: The administration of oral vitamin C did not significantly alter the FBF responses in OSA patients, indicating that a single dose of oral vitamin C might not be sufficient to improve endothelial function in this group.

Statistical Analysis-

Statistical analysis, including ANOVA and post hoc tests, confirmed the

significant differences in FBF response to PLM between the OSA and HEAL groups. However, no significant effect of vitamin C administration on FBF responses was observed within the OSA group.

The study's results demonstrate the efficacy of PLM as a non-invasive diagnostic tool for differentiating between healthy individuals and those with OSA based on endothelial function. Moreover, the findings suggest that further investigation is needed to explore the potential benefits of vitamin C or other interventions on endothelial function in OSA patients.

Tables of Results- Table 1:

Characteristics of Study Participants:

Variable	Healthy (HEAL) Group	OSA Group
Number of Participants	13	13
Age (years)	27.1 ± 3.6	Comparable to HEAL
Weight (kg)	77.6 ± 12.3	Comparable to HEAL
Height (cm)	178.8 ± 6.5	Comparable to HEAL

*Note: Values are mean ± SD.

Table 2: FBF Response to Passive Leg Movement (PLM):

Group	Pre-Vitamin C FBF (ml/min)	Post-Vitamin C FBF (ml/min)
Healthy	162.1	134.5
OSA	76.6	79.9

*Note: Values are mean; statistical significance noted between OSA and healthy groups ($p < 0.05$), but not between pre- and post-vitamin C within the OSA group.

Table 3: Statistical Analysis Outcomes:

Statistical Test	Result	P-Value
ANOVA (FBF Difference HEAL vs. OSA)	Significant	< 0.05
ANOVA (FBF Difference Pre- vs. Post-Vitamin C in OSA)	Not Significant	> 0.05

Discussion

The findings of this study underscore the utility of Passive Leg Movement (PLM) as a novel, non-invasive method for assessing endothelial function and differentiating between healthy individuals and those with Obstructive Sleep Apnea (OSA). Our results revealed a significant difference in femoral artery blood flow (FBF) response to PLM between healthy individuals and OSA patients, supporting the hypothesis that PLM can serve as a diagnostic tool for identifying endothelial dysfunction in OSA (1). These findings are consistent with previous research highlighting the association between OSA and impaired vascular function, attributed to factors such as intermittent hypoxia and oxidative stress (2, 3).

The lack of significant improvement in FBF response after oral vitamin C administration in OSA patients suggests that the bioavailability of nitric oxide (NO), a key regulator of endothelial function, might not be readily enhanced by a single dose of this antioxidant in the context of OSA-induced endothelial dysfunction (4). This is in contrast to studies that have shown improvements in

endothelial function with vitamin C administration in other populations (5, 6). The discrepancy could be due to the chronic nature of endothelial dysfunction in OSA, which might require more prolonged or targeted antioxidant therapy to reverse.

Furthermore, the absence of significant changes in endothelial function after vitamin C administration in our study aligns with findings from other studies, indicating that the pathophysiology of OSA-related vascular impairment may involve mechanisms beyond oxidative stress alone, such as inflammation and sympathetic nervous system activation (7, 8). This complexity underscores the need for multifaceted therapeutic approaches to address endothelial dysfunction in OSA.

Our study's findings also highlight the potential of PLM as a clinical tool for early detection of vascular impairment in asymptomatic or undiagnosed individuals at risk of OSA. Early identification and intervention could play a crucial role in preventing the progression of cardiovascular disease in this population (9). However, further research is needed to explore the long-term effects of interventions aimed at improving endothelial function in OSA patients, including lifestyle modifications, CPAP therapy, and pharmacological treatments (10).

Conclusion

In conclusion, while PLM emerges as a promising diagnostic tool for endothelial dysfunction in OSA, the challenge of effectively improving vascular health in this condition remains. Future studies should aim to elucidate the underlying mechanisms of OSA-induced vascular impairment and explore combination therapies that target these pathways to restore endothelial function and reduce cardiovascular risk in this population.

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