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Original Article

Impact of Obstructive Sleep Apnea on Cardiac Troponin I: Comparisons of the Effects of Nasal O_2 and Positive Airway Pressure on this Biomarker

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ABSTRACT

Background: Sleep apnea is a common disorder and is known to impact myocardial stress and increase morbidity and mortality. The concentrations of cardiac highly sensitive troponin I (hs-TnI) are currently in clinical use as markers of myocardial injury.

That obstructive sleep apnea (OSA) may lead to myocardial injury and elevated cardiac troponin levels suggests that the treatment of sleep apnea with positive airway pressure (PAP) should decrease myocardial injury.

Methods: We studied 114 patients with a diagnosis of moderate-to-severe OSA who were referred to our cardiovascular department. None of the patients had a history of cardiovascular problems and diabetes. The mean age was 30.65±3.96 years. The patients were divided into 2 groups: the first group (the O_2 group) received nasal O_2 for 2 weeks, and the second group (the PAP group) received PAP for about 2 weeks. The concentrations of hs-TnI were measured in evening blood samples in selected patients. After 2 weeks of treatment with O_2 or PAP, the serum hs-TnI level was rechecked and compared with the baseline and between the 2 groups.

Results: The level of hs-TnI did not differ significantly between the 2 groups. No patients in either O_2 or PAP group showed elevated troponin levels before the treatment. The cardiac biomarker, hs-TnI, was detectable (≥1 ng/L) in none of the patients in the O_2 group before and after the treatment and only in 2 (3%) patients in the PAP group after treatment.

There was no significant difference in the hs-TnI level before and after the treatment with nasal O_2 (P=0.4).

Conclusions: Although OSA is well known to impact myocardial stress, we did not find increased amounts of cardiac hs-TnI as a biomarker of myocardial damage even in the severe form of OSA. PAP did not cause any myocardial damage detectable with the hs-TnI level and it was somewhat more effective than was O_2 in decreasing the baseline level of troponin. ***(Iranian Heart Journal 2019; 20(2): 75-80)***

KEYWORDS: Obstructive sleep apnea, Positive airway pressure, Troponin I

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Sleep apnea is a disorder characterized by a reduction or a pause in breathing during sleep. It is a relatively common sleep disorder and leads to increased morbidity and mortality.

The risk factors for sleep apnea in the adult population are the male gender, obesity, increased neck circumference, diabetes, and the anomaly of the upper respiratory tract.[1] The symptoms are insidious and are present from a few years before the diagnosis.

Some surveys have assessed peri-apneic hemodynamic alterations, the heart rate, blood pressure, the cardiac output, and peripheral resistance and shown that the heart rate is elevated significantly 10 beats immediately after apnea.

Both hypoxemia and sympathetic arousals cause rapid hemodynamic changes that may escape autoregulatory mechanisms and make patients suffering from OSA vulnerable to acute cardiovascular events.[2]

Previous investigations have demonstrated that obstructive sleep apnea (OSA) is associated with a rise in the incidence of coronary heart disease, heart failure, stroke, and atrial fibrillation. Additionally, treatment with continuous positive airway pressure (PAP) improves not only daytime sleepiness, the quality of life, and mood but also intermediate cardiovascular end points such as high blood pressure, the cardiac ejection fraction, vascular parameters, and arrhythmias. However, data from a large-scale randomized trial did not support a role for PAP therapies to reduce cardiovascular mortality.[3]

Using a highly sensitive troponin I (hs-TnI) assay, some researchers have shown that the severity of OSA is associated with myocardial injury, independent of comorbidities, and have suggested that frequent apneas or hypoxemia in OSA may cause low-grade myocardial injury.[4,5] Nonetheless, some other researchers have not observed such higher proportions of detectable hs-TNT in this group of patients and concluded that this association is caused by a larger amount of cardiovascular risk factors among this population.[6,7,8]

It is known that hs-TnI has superior low-range sensitivity in comparison with the hs-TnT assay and assays. In addition, the quantification of the concentrations of cardiac troponin hs-TnI—as markers of myocardial injury—is currently in clinical use.

The fact that obstructive sleep apnea may lead to myocardial injury and elevated cardiac troponin levels leads to the thought that the treatment of OSA with PAP should decrease myocardial injury; the current evidence, however, fails to confirm this notion.

In this study, we sought to determine whether OSA can cause elevated troponin levels and whether hypoxemia by itself can be the cause of such a rise in the level of cardiac troponin. We also compared the troponin level after treatment with supplement nasal oxygen alone or with PAP in 2 different groups of nasal O_2 and PAP and then compared the level of CTn-I between the 2 groups.

METHODS

The present study was approved by the Ethics Committee of Tehran University of Medical Sciences, Iran. Informed consent was obtained from all the patients.

Study Population

We studied 200 patients with a diagnosis of moderate-to-severe OSA who were referred to our cardiovascular department. None of the patients had a history of cardiovascular problems and diabetes.

After adjustments were made for age and gender, the patients with high levels of estimated creatinine clearance, a history of known coronary artery disease and diabetes mellitus, a history of anginal chest pain, a history of other cardiac diseases, and mild sleep apnea were excluded. Ultimately, 114 Patients with a moderate and high apnea-hypopnea index (AHI) were enrolled. Electrocardiography

(ECG) and echocardiography were done for all the patients, and those with abnormal echocardiography and ECG were excluded.

Polysomnography

The severity of OSA, expressed as the AHI, was assessed with in-hospital polysomnography.

All the participants underwent in-hospital polysomnography (sleep length=6.2±1.2 h [mean ± SD]). The registrations were thereafter analyzed by trained sleep technologists manually, revised by a sleep medicine specialist (RPSGT), and scored according to the 2017 manual of the American Academy of Sleep Medicine (AASM). The severity of OSA was expressed as the AHI. Apnea was defined as the absence of the airflow for more than 10 seconds. Hypopnea was defined as >30% reduction in the airflow followed by a decrease in SPO_2 of >3%. The AHI was calculated as the mean number of apneas and hypopneas as per hour of sleep according to the recommendations of the AASM.[9]

Ultimately, 114 patients with an AHI ≥15 were defined as having moderate-to-severe OSA and were enrolled in this study.

Measurement of Cardiac Troponin I

The concentrations of hs-TnI were measured in evening blood samples in selected patients. The quantitative measurement of hs-TnI was achieved via an immunoassay for the quantitative determination of cardiac hs-TnI in plasma, with the upper limit of normal of 1 ng/mL representing the 99th percentile in a normal reference population and a coefficient of variation of <10%. The values of hs-TnI below the limit of blank are reported as 0.005 ng/L. After 2 weeks of treatment with O_2 or PAP, the serum troponin level was rechecked and compared with the baseline and between the 2 groups.

Statistical Analysis

The statistical analyses were conducted using the SPSS, version 16. The continuous variables are presented as the mean (SD) or the median (interquartile range for data with skewed distributions). The patients' characteristics were compared using the Student *t*-test and the analysis of variance. A *P* value<0.05 was considered statistically significant.

RESULTS

Totally, 114 patients with a diagnosis of moderate-to-severe OSA were enrolled in this study.

The mean age was 30.65± 3.96 years. The patients were divided into 2 groups: the O_2 group received nasal O_2 for 2 weeks and the PAP group received PAP for about 2 weeks.

The demographic characteristics of the 2 groups are summarized in Table 1. No significant differences were observed between the PAP and O_2 groups regarding age, sex, a history of smoking, and hypertension.

Table 1. Patient characteristics

Variable	PAP	O_2 Therapy	*P* value
Number	**58**	**56**	
Age (y)	49.89±12.76	46.11±9.65	0.22
Body mass index (kg/m^2)	32.04±4.39	29.27±3.53	0.24
Gender (number of men)	38	28	0.71
Smoker (number, percent)	11(19.8%)	14(25%)	0.26
History of hypertension (number)	8(13.7%)	6(10.7%)	0.71
Systolic blood pressure, mm Hg (range, median)	122-147(132)	127(117-137)	0.18
Diastolic blood pressure, mm Hg (range, median)	70-83.2(75.2)	65-85(78)	0.66

The levels of the cardiac marker, hs-TnI, did not differ significantly between the 2 groups. None of the patients in either O_2 or PAP group showed elevated troponin levels before the treatment. The level of hs-TnI was detectable (≥1 ng/L) in none of the patients in the O_2

group before and after the treatment and only in 2 (3%) patients in the PAP group after the treatment (Table 2). The hs-TnI level before and after the treatment was compared using the Wilcoxon signed-rank test. The median of the hs-TnI level before the treatment with O_2 at the range of 0.005–0.08 was 0.02 and after 2 weeks of treatment at the range of 0.005–0.09 was 0.007. There was no significant difference in the troponin level before and after the treatment with nasal O_2 (P=0.4). Figures 1 and 2 show the box plot diagram of the hs-TnI level before and after the treatment in both groups. The changes in the troponin level are depicted in Table 2.

Table 2. Changes in the troponin level before and after the treatment

Variable	Baseline hs-TnI	hs-TnI After Treatment	*P* value
O_2 group	0.005-0.08 (Median=0.02)	0.005-0.09 (median=0.007)	0.4
PAP group	0.05-0.08 (median=0.06)	0.05-5.00 (median=0.06)	0.02

hs-TnI, Highly sensitive troponin I; PAP, Positive air pressure

Although there was a significant rise in the cardiac troponin after the treatment with PAP, the amount of the increase in only 2 patients was above the cutoff point of 1 ng/L and showed myocardial injury.

The level of changes in cardiac troponin was compared between the O_2 and PAP groups, and the results are summarized in Table 3.

Table 3. Comparison of the troponin level between the 2 groups

Treatment	Mean ±SD	*P* value
PAP	0.036±0.032	0.03
O_2	0.78±0.81	

PAP, Positive air pressure

None of the participants (100%) had hs-TnI concentrations above the limit of detection (1 ng/L). Furthermore, the concentration of cardiac troponin was even lower in the PAP group than in the O_2 group.

DISCUSSION

Sleep apnea is a reduction or pause in breathing during sleep. This disorder not only leads to daytime sleepiness and reduces the quality of life but also causes several other significant problems such as myocardial injury and cerebrovascular accident. Researchers have shown that treatment with PAP can reduce the incidence of these problems and promote the quality of life. Sleep apnea can lead to myocardial injury by several mechanisms. Intermittent apneas lead to nocturnal hypoxemia and sympathetic arousal, which results in pulmonary and systemic hypertension, increased myocardial load, wall stress, and ultimately myocardial injury.[10,11,12]

Troponin I is a highly sensitive and specific marker of myocardial injury. Troponin T is another marker for myocardial injury but is not as specific as troponin I. The specificity and correlation with angiographic findings are higher in hs-TnI than in hs-TnT.[13] Accordingly, we used hs-TnI as a marker of myocardial injury.

Our main objective was to determine whether hypoxemia alone can lead to myocardial injury and whether the amount of the increase in cardiac troponin I can be reversed by the use of nasal O_2 without PAP.

The existing literature abounds with discrepancies in the results of previous studies on the effects of OSA on cardiac troponin.

Some researchers have reported high hs-TnT levels in patients with OSA,[4,14,15] whereas others have demonstrated that even patients suffering from OSA with coexisting coronary artery disease have no episodes of myocardial injury detectable by cardiac TnT assays.[6-16] In the current study, we did not find high troponin I levels in our patients with OSA, all of whom had normal baseline troponin levels, which was increased by the use of neither O_2 nor PAP.

Although the baseline troponin level was not high in both groups, after the treatment, the

total average of this level was lower in the patients who received PAP than in those who received O_2. Some previous investigations have compared treatment with PAP and O_2 from different aspects. Phillips et al[17] showed that PAP was more effective than O_2 in reducing apnea, whereas nasal O_2 improved oxygenation more optimally. Some other researchers have concluded that PAP is more effective than is supplemental nocturnal O_2 in controlling daytime and nighttime blood pressure[18,19] and on heart rate variability, which is a predictor of cardiovascular mortality.[20]

Our finding is in stark contrast to some previous studies that have demonstrated increased troponin levels after treatment with PAP.[21] Nonetheless, some other investigations have shown that PAP has no effect on troponin and cardiac remodeling.[14,15,22,23] This discrepancy between the results may be due to the assessment of parameters such as the AHI, as a marker of OSA. A previous study reported that the effects of PAP on cardiac troponin had no association with the AHI but were mostly dependent on the severity of hypoxia.[24]

In summary, although OSA is well known to impact myocardial stress, we did not find increased amounts of cardiac troponin as a biomarker of myocardial damage even in the severe form of OSA. PAP did not cause any myocardial damage detectable by high troponin levels and it was somewhat more effective than was O2 in decreasing the baseline level of troponin.

The major limitation of our study is its small sample size; our results should, therefore, be viewed with caution. Further studies with large samples are needed.

Conflict of Interest None declared.

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