Cardiovascular Research Institute Basel

University Hospital Basel

Plasma endothelin-1 and risk of obstructive sleep apnea among young and healthy adults

Tobias Schoen[1,2], Stephanie van der Lely[1,2], Stefanie Aeschbacher[1,2], Joel Estis[3], John Todd[3], Martin Risch[4], Lorenz Risch[4], David Conen[1,2]

[1] Department of Medicine, University Hospital Basel, Basel, Switzerland; [2] Cardiovascular Research Institute Basel, Basel, Switzerland; [3]Singulex, Inc., CA, USA ; [4]Labormedizinisches Zentrum Dr Risch, Schaan, Principality of Liechtenstein

Purpose

Recently, obstructive sleep apnea (OSA) has been linked to endothelial dysfunction, a major precursor of cardiovascular disease. The aim of this study was to assess the relationship between plasma levels of endothelin-1 (ET-1) and OSA among young and healthy adults.

Methods

We performed a population-based study among 1409 healthy adults aged between 25 and 41 years in the Principality of Liechtenstein. Individuals with prevalent cardiovascular disease, diabetes or a body mass index >35 kg/m^2 were excluded. ET-1 was measured from fasting plasma samples. All individuals underwent nighttime pulsoximetry with nasal flow measurement. OSA was defined as apnea-hypopnea index (AHI) ≥5 (n=152). Multivariable logistic regression analyses with elevated AHI as outcome variable were used to assess the relationship between ET-1 and OSA.

Table 1 Baseline characteristics

n=1409	AHI ≥5 (10.8%)	AHI < 5 (89.2%)	p-value
Age, years	37 (33; 40)	35. (30; 39)	0.0002
Female sex, %	30 (20)	711 (57)	<0.0001
BMI, kg/m^2	27.2 (24.3; 30.7)	23.9 (21.7; 26.5)	<0.0001
Current smokers, %	44 (29)	272 (22)	0.04
Endothelin-1, pg/ml	2.9 (2.4; 3.6)	2.5 (2.1; 3.0)	<0.0001
systolic BP, mmHg	128 (120; 133)	119 (111; 127)	<0.0001

Data are medians (interquartile range). BMI= body mass index; BP= blood pressure

Table 2 Relationship between endothelin-1 and obstructive sleep apnea (Multivariable logistic regression analysis)

n= 1409	Odds Ratio (95% CI)	p-Value
Crude	4.7 (2.8; 7.9)	<0.0001
Age- and sex adjusted model	3.6 (2.1; 6.3)	<0.0001
Multivariable model	3.5 (1.9; 6.3)	<0.0001

Endothelin-1 was log-transformed. Multivariable model adjusted for age, sex, body mass index, estimate
d glomerular filtration rate, smoking, systolic and diastolic blood pressure, low- and high density lipoprotein, HbA1c, and high-sensitive C-reactive protein.

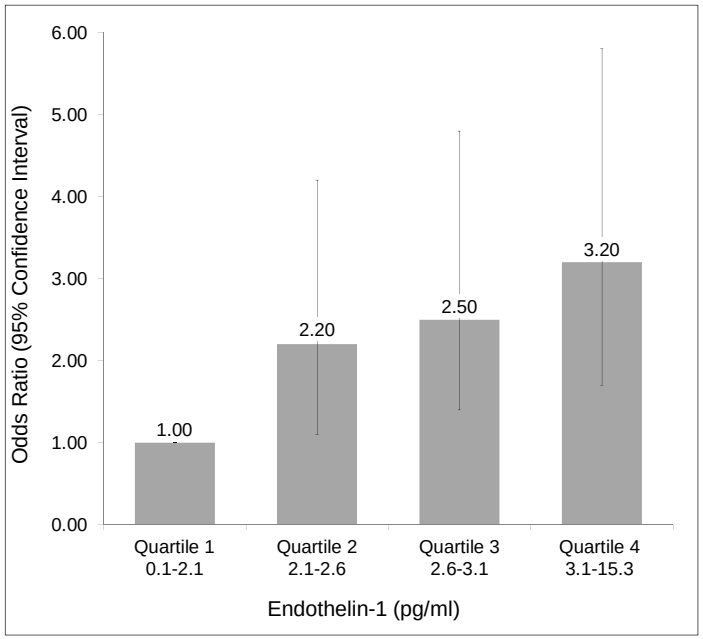

Figure 1 Endothelin-1 quartiles and risk of obstructive sleep apnea (Multivariable logistic regression analyses)
Multivariable model adjusted for age, sex, body mass index, estimated glomerular filtration rate, smoking, systolic and diastolic blood pressure, low- and high density lipoprotein, HbA1c, and high-sensitive C-reactive protein.

Results

Baseline characteristics stratified by AHI are presented in **Table 1**. 10.8% of participants met criteria for OSA. Median ET-1 levels in subjects with and without OSA were 2.9 pg/ml (interquartile range [IQR]: 2.4, 3.6) and 2.5 pg/ml (IQR: 2.1, 3.0; p<.0001), respectively.

In multivariable logistic regression models, log-transformed ET-1 was significantly associated with an increased risk of OSA (odds ratio: 3.5 (95% confidence interval: 1.9, 6.3)) (**Table 2**).

Quartile specific odds ratios confirmed an increasing risk of OSA with increasing ET-1 levels after multivariable adjustment and are displayed in **Figure 1**.

Conclusion

Elevated plasma levels of ET-1 are strongly associated with an increased risk of OSA among young and healthy adults. These findings underscore the potential adverse effects of OSA on endothelial function, which may be one mechanism by which OSA is associated with future cardiovascular events.

GAPP studie www.blutdruck.li

Contact: tobias.schoen@usb.ch

Disclosures: J.T. and J.E. are employees of Singulex.