ASSESSMENT OF PERIPHERAL ARTERIAL TONE
- CLINICAL APPLICATIONS IN SLEEP MEDICINE

AKADEMISK AVHANDLING

Som för avläggande av medicine doktorsexamen vid Göteborgs Universitet kommer att offentligen försvaras i Kammaren, Vita stråket 12, Sahlgrenska Universitetssjukhuset, Göteborg, tisdag den 1 juni 2010, klockan 9.00

av
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The thesis is based on the following papers:

I. Zou D, Grote L, Eder DN, Peker Y, Hedner J.
Obstructive apneic events induce alpha-receptor mediated digital vasoconstriction.
Sleep 2004; 27(3): 485-9.

II. Zou D, Grote L, Eder DN, Radlinski J, Hedner J.
A double-blind crossover study of doxazosin and enalapril on peripheral vascular tone and nocturnal blood pressure in sleep apnea patients.
Sleep Medicine 2010; 11(3): 325-28

III. Zou D, Grote L, Peker Y, Lindblad U, Hedner J.
Validation a portable monitoring device for sleep apnea diagnosis in a population based cohort using synchronized home polysomnography.
Sleep 2006; 29(3): 367-74.

IV. Zou D, Grote L, Radlinski J, Eder DN, Lindblad U, Hedner J.
Nocturnal pulse wave attenuation is associated with office blood pressure in a population based cohort.
Sleep Medicine 2009; 10(8): 836-43.

V. Grote L, Sommermeyer D, Zou D, Eder DN, Hedner J
Oximeter based autonomic state indicator algorithm for cardiovascular risk assessment.
Chest. In press.

Assessment of Peripheral Arterial Tone
– Clinical Applications in Sleep Medicine

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Abstract:

Circulatory and vascular control differs between wakefulness and sleep. Few studies have used physiological recordings during sleep for assessment of cardiovascular (CV) function and risk. This thesis addresses the physiological link between nocturnal peripheral vascular tone, measured by a novel finger photoplethysmographic signal – PAT (peripheral arterial tone), and obstructive sleep apnea (OSA). The validity of using such a signal for OSA diagnostics and CV risk classification is also studied.

The amplitude of the PAT signal was periodically attenuated, reflecting vasoconstriction, during the immediate post apnea/hypopnea period. These attenuations were largely reversed by cumulative dosages of phentolamine (α-receptor antagonist) infusion via the brachial artery during sleep in eight patients with severe OSA. This effect suggests that OSA-related PAT attenuation is mediated via a sympathoadrenergic α-receptor mechanism.

Adrenergic α-receptor mechanisms were further evaluated in a double-blind crossover study comparing equipotent dosages of doxazosin (a peripheral α-receptor inhibitor) and enalapril (an angiotensin-converting enzyme inhibitor) on digital vasoconstriction and nocturnal blood pressure (BP). While the nighttime beat-to-beat finger BP was significantly higher under doxazosin treatment, the apnea related PAT attenuation decreased during doxazosin compared with enalapril treatment ($P<0.001$) in 16 hypertensive OSA patients. An analysis of sleep related changes of PAT demonstrated that attenuations were influenced by apnea related oxygen desaturation and rapid eye movement sleep.

A portable monitoring device, Watch_PAT100 (WP100), was validated against unattended polysomnography (PSG) for OSA diagnosis in 98 subjects recruited from the Skaraborg Hypertension and Diabetes Project. The WP100 records PAT, pulse rate, oxygen saturation and actigraphy for automatic analysis of the sleep-wake state, respiratory disturbance index (RDI), apnea-hypopnea index (AHI) and oxygen desaturation index (ODI). The WP100 RDI, AHI, and ODI correlated closely with the corresponding indices obtained by PSG. The area under the ROC curves for WP100 AHI and RDI were 0.93 and 0.90 when the AHI and RDI thresholds 10 and 20 were applied respectively. A new standard for limited-channel device validation using simultaneous PSG recording in the home environment was proposed.

The relationship between nocturnal PAT attenuation and office BP was investigated in 81 subjects from the same study population. Episodic attenuations of the PAT signal were identified and characterized. In a generalized least squares regression model, we found an association between median PAT attenuation (PWA.att) and office BP which was independent of gender, age, body mass index, antihypertensive medication, number of attenuation episodes, AHI, ODI and arousal index. Each 10% increase in PWA.att was associated with an increase of 5.0 mmHg systolic BP and 3.0 mmHg diastolic BP, respectively. Continuous assessment of PAT during sleep appears to reflect vascular regulation and homeostasis.

An autonomic state indicator algorithm based on a novel finger pulse oximetry sensor was developed and validated for CV risk assessment according to the ESH/ESC risk factor matrix. Five signal components reflecting cardiac and vascular activity (pulse wave attenuation, pulse rate acceleration, pulse propagation time, respiration related pulse oscillation and oxygen desaturation) were extracted in 99 subjects and used to construct an algorithm. The capacity of the algorithm for CV risk prediction was validated in 49 additional subjects. The sensitivity and specificity of the algorithm to distinguish high/low CV risk in the validation group was 80% and 77%, respectively. The area under the ROC curve for high CV risk classification was 0.84. Based on this data, we propose that information derived from a photoplethysmographic signal obtained during sleep may be applied as a useful tool for CV risk classification.

This thesis supports the notion that PAT, as a measure of finger pulsatile volume changes, reflects the sympathetic autonomic activity and can be used for the detection of sleep disordered breathing. Information derived from an oximeter based pulse wave signal may be used to assess CV function and CV risk.

Keywords: Arousal, autonomic nervous system, blood pressure, cardiovascular risk, obstructive sleep apnea, peripheral arterial tone, portable monitoring, pulse wave attenuation

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