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分担研究報告書

睡眠呼吸障害および血圧の尿中アルブミン排泄量における影響：長浜コホート研究

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研究要旨

尿中アルブミン量の上昇は将来の腎障害のリスクである。睡眠呼吸障害（SDB）が尿中アルブミン量上昇の原因である可能性が既報により示唆されているが、その理由は明らかではない。SDB が日中血圧に加えて夜間血圧を上昇させることにより、尿中アルブミン量を増加させている可能性を大規模集団において検討することを本研究の目的とした。

A. 研究目的

尿中アルブミン量の上昇は将来の腎障害のリスクである。睡眠呼吸障害(SDB)が尿中アルブミン量上昇の原因である可能性が既報により示唆されているが、その理由は明らかではない。SDB が日中血圧に加えて夜間血圧を上昇させることにより、尿中アルブミン量を増加させている可能性を検討した。

B. 研究方法

「ながはまコホート研究」に参加した地域住民 9,850 人を対象に、尿中アルブミン量をスポット尿中の尿中アルブミン／クレアチニン比（UACR）により評価した。睡眠時間と SDB は、それぞれウェアラブルアクチグラフとパルスオキシメーターで評価した。アクチグラフで得られた睡眠時間に応じてパルスオキシメトリーで測定した時間を補正し、アクチグラフ修正 3%酸素飽和度指数（Acti-3%ODI）を算出した。さらに、タイマー付きの血圧計により自宅での起床時と睡眠中の血圧を測定し、UACR・Acti-3%ODI・血圧の 3 者の関係を検討した。

C. 研究結果

6,568 名の参加者において、睡眠パラメータ、UAE、随時血圧の測定が行われた。交絡因子を含めた多変量解析では、Acti-3%ODI と UACR の有意な関連が示された（β=0.06, P<0.001）。さらに、随時収縮期血圧と Acti-3%ODI は UACR に対して正の相互作用を示した（β＝0.06、P<0.001）。解析に登録された 6,568 人のうち、5,313 人が自宅での血圧測定を行った。このコホートでは、起床時と睡眠中の収縮時血圧を解析に含めた後でも、Acti-3%ODI と UACR の関連は有意に保たれた（β=0.06, P<0.001）。さらに、媒介分析により、Acti-3%ODI と UACR の関連の 28.3%（95%信頼区間 14.9-41.7%、P<0.001）が、起床時と睡眠中の収縮時血圧の媒介により説明されることが明らかになった。

D. 考察

SDB と随時収縮時血圧は、慢性腎臓病や心血管イベントの危険因子とされる尿中アルブミン量と独立かつ相乗的に関連していた。媒介解析の結果から、SDB による血圧上昇は、SDB が尿中アルブミン量を上昇させる全てのメカニズムを説明できるわけではないことが示唆された。

E. 結論

SDB は血圧の上昇だけでなく、他の病的経路の関与によっても尿中アルブミン量を上昇させている可能性があることが示された。

F. 研究発表

1. 論文

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ORIGINAL RESEARCH

Association of Sleep-disordered Breathing and Blood Pressure with Albuminuria

The Nagahama Study

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Abstract

Rationale: Although sleep-disordered breathing (SDB) may increase urinary albumin excretion (UAE) by raising nocturnal blood pressure (BP) in addition to diurnal BP, the correlation has not been investigated in a general population.

Objectives: To evaluate the relationships among UAE, SDB, and BP during sleep in a large population cohort.

Methods: Among 9,850 community residents, UAE was assessed by the urinary albumin-to-creatinine ratio (UACR) in spot urine. Sleep duration and SDB were evaluated by a wearable actigraph and pulse oximeter, respectively. We calculated the actigraphy-modified 3% oxygen desaturation index (Acti-3%ODI) by correcting the time measured by pulse oximetry according to sleep duration obtained by actigraphy. Furthermore, participants were instructed to measure morning and sleep BP at home by a timer-equipped oscillometric device.

Results: Measurements of sleep parameters, UAE, and office BP were obtained in 6,568 participants. The multivariate analysis that included confounders showed a significant association of Acti-3%ODI with UACR ($\beta = 0.06$, $P < 0.001$). Furthermore, a positive interaction between office systolic BP (SBP) and Acti-3%ODI for UACR was found ($\beta = 0.06$, $P < 0.001$). Among the 6,568 persons enrolled in the analysis, 5,313 completed measurements of BP at home. In this cohort, the association of Acti-3%ODI with UACR remained significant ($\beta = 0.06$, $P < 0.001$) even after morning and sleep SBP were included in the analysis. Furthermore, a mediation analysis revealed that 28.3% (95% confidence interval, 14.9–41.7%; $P < 0.001$) of the association of Acti-3%ODI with UACR was explained by the mediation of morning and sleep SBP metrics.

Conclusions: SDB and office SBP were independently and synergistically associated with UAE, which is considered a risk factor for chronic kidney disease and cardiovascular events. SDB may raise UAE not only by increasing BP but also by involving other pathologic pathways.

Keywords: sleep disordered breathing; urinary albumin excretion; blood pressure

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