SHORT COMMUNICATION

Effects of Slow Breathing Exercise in Chronic Kidney Disease Patients

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ABSTRACT

Objective: **Autonomic nervous dysfunction is a well-recognized symptom in chronic kidney disease (CKD). We have reported that slow breathing exercise (SBE) enhances parasympathetic nervous activity in healthy males. This study aimed to evaluate the effects of SBE in CKD patients.**

Methods: **Six male outpatients with severe CKD participated. SBE (six abdominal breaths per minute for each 15-minute session) were performed twice a day for around four weeks. Before and after the SBE trials, electrocardiogram, blood pressure, respiratory rate, skin temperature and skin blood flow were obtained at rest. Autonomic nervous activity was evaluated with power spectral analysis of heart rate variability. High frequency (HF) and low frequency (LF) powers corresponded to the parasympathetic nervous activity and sympathetic-parasympathetic nervous activity, respectively, and LF/HF ratio corresponded to sympatho-vagal balance.**

Results: **After SBE, respiratory rate and LF/HF ratio decreased, diastolic blood pressure tended to decrease, and HF and skin temperature tended to increase.**

Discussions: **Sympatho-vagal balance is shifted to sympathetic dominance in CKD patients compared to healthy adults. Our results showed that SBE can shift autonomic balance to parasympathetic nerve dominance even in severe CKD patients.**

Conclusions: **SBE has the potential to improve autonomic nervous imbalance in CKD patients.**

KEY WORDS

slow breathing exercise, chronic kidney disease, heart rate variability, parasympathetic nervous activity

INTRODUCTION

Autonomic nervous dysfunction is a well-recognized symptom in chronic kidney disease (CKD). The balance of autonomic nervous activity is shifted to sympathetic dominance in CKD patients compared to healthy adults. Sympathetic hyperactivity occurs early in the course of CKD and increases with disease progression[1)].

We had already reported that four-weeks slow breathing exercise (SBE) which incorporate deep breathing into daily life increased parasympathetic nervous activity in healthy male volunteers at rest[2)]. We hypothesized that SBE in CKD patients may relatively suppress sympathetic nerve activity by increasing parasympathetic nerve activity, which may improve the disease state. Therefore, the aim of this study was to investigate whether SBE enhances parasympathetic activity in CKD patients.

MATERIALS AND METHODS

Patients

All subjects were male non-dialysis CKD outpatients in a stable condition. Patients with cardiac rhythm abnormality, moderate to severe valvular heart disease, stroke, respiratory failure, pulmonary disease, end stage kidney disease requiring hemodialysis, degenerative spondylosis with difficulty resting in supine position or optimal medical management for < 3 months were excluded.

We explained about the study protocol in writing and verbally, and confirmed confidentiality for the participants and the right to withdraw from the study without any negative consequences on their treatment needs. Written informed consent was obtained from every patient before participation in this study, which was approved by the Institute of Ethical Guidelines under the approval of the Ethics Review Board of Ibaraki Christian University and the Ethics Committee of the Tokiwa group Jyoban Hospital.

Received on June 8, 2021 and accepted on July 29, 2021

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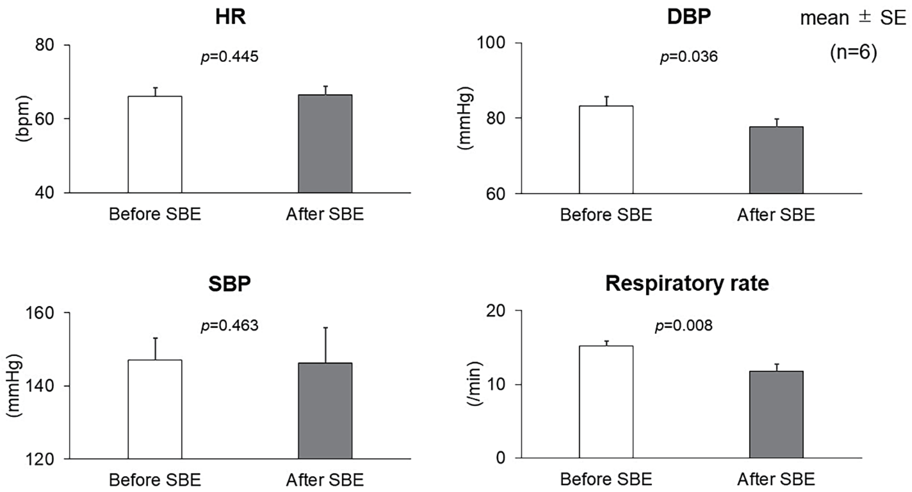

Figure 1: Changes of HR, BP and respiratory rate.
Diastolic blood pressure (DBP) and respiratory rate decreased significantly. HR and systolic blood pressure (SBP) were no change, respectively.

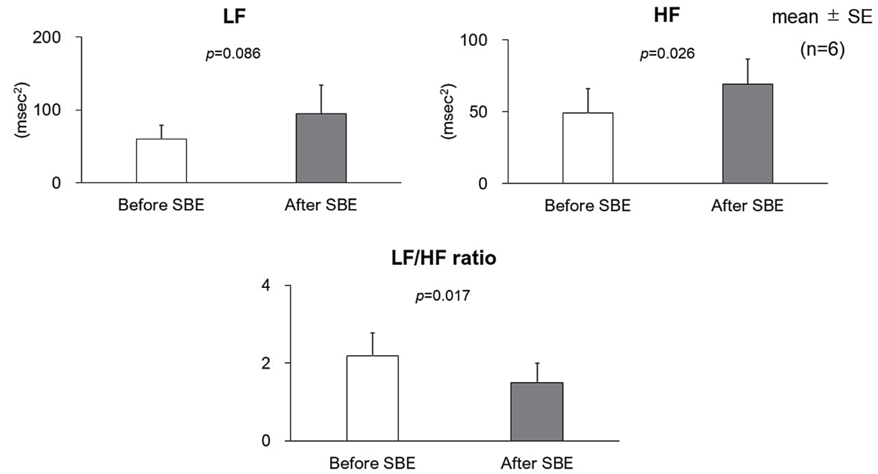

Figure 2: Changes in autonomic nervous activity.
HF values and LF/HF ratio were significantly increased and decreased, respectively.

Measurement schedule and methods of SBE

At first visit, we checked ECG sinus rhythm presence and physiological parameters to confirm the condition of the subjects prior to SBE. The subjects started and continued them until the next visit. The entire SBE performance period lasted more than four weeks. At the second visit, we checked the same physiological parameters and the condition of the subjects after performing SBE.

SBE was performed as previously described[2]. Briefly, SBE entailed breathing six abdominal breaths per minute[3-6] for 15 minutes, twice a day for around four weeks. Subjects repeatedly inhaled for three seconds through the nose and exhaled for six seconds through the mouth.

Measurements

At each outpatient's visit before and after SBE trials, measurements of physiological parameters were performed with subjects resting in supine posture for 15 minutes. Heart rate (HR) was measured continuously using a wireless electrocardiograph (RF-ECG, GMS, Tokyo) and blood pressure (BP) of the left upper arm was measured at 5-minute intervals using an electronic sphygmomanometer (H55, Terumo Corporation, Tokyo). Respiratory rate was obtained using the 1-minute breath count at 5-minute intervals[7]. Skin temperature at the sites the thumb, foot dorsum and hand dorsum were measured continuously using a body surface skin thermometer (N543, Nikkiso therm, Tokyo, Japan) and data were extracted using dedicated software (NT Logger Monitor N543, Nikkiso therm, Tokyo, Japan). Skin blood flow at the right thumb was measured continuously using laser doppler flowmetry (PeriFlux System 5000 / PF 5010 LDPM Unit, PERIMED, Sweden) and data were extracted using dedicated software (PeriSoft for Windows Version 2, PERIMED, Sweden). Power spectral analysis of heart rate variability (HRV) was performed using maximum entropy method software (MemCalc/Bonaly Light, GMS, Tokyo, Japan). We separated the frequency range into two classes according to previous studies; low frequency (LF) class between 0.04 and 0.15 Hz and high frequency (HF) class between 0.15 and 0.4 Hz[8]. The ratio of LF and HF power (LF/HF) was also calculated. It is known that LF corresponds to both sympathetic and parasympathetic nervous activities, HF corresponds to parasympathetic nervous activities and LF/HF ratio corresponds to sympatho-vagal balance[9]. Blood test results were collected from medical records at the outpatient visit on both pre-and post-SBE days. The eGFR category was based on CKD clinical practice guidelines[10].

Data analysis

For the analysis of physiological indices, stable data taken over five minutes during the 15 minutes measurements were used. All values are expressed as the mean ± SEM. Student's *t*-test was used to compare values between the pre-SBE and the post-SBE. A value of $P < 0.05$ was considered significant. Statistical analyses were performed using JMP 14 (SAS Institute Inc., Cary, NC, USA).

RESULTS

Six male patients (mean age: 66.0 ± 9.4 years, mean BMI: 22.8 ±

2.1 kg/m^2, CKD stage 4 or higher) participated in this study. The underlying diseases were nephrosclerosis in four patients and diabetic nephropathy in two patients. The mean implementation period of SBE was 5.0 ± 1.3 weeks, and the mean implementation rate was 77.2 ± 29.1%.

HR and systolic BP did not change. Diastolic BP decreased significantly from 83.3 ± 2.3 mmHg to 77.7 ± 2.2 mmHg (P = 0.036) and respiratory rate decreased significantly from 15.2 ± 0.7 breaths/min to 11.8 ± 0.9 breaths/min (P = 0.008) (Fig.1). Skin temperature of the thumb tended to increase from 29.7 ± 2.0°C to 31.7 ± 1.3°C (P = 0.050), but the thumb skin blood flow remained the same. As regard autonomic nervous activity, LF power did not change, but HF power increased significantly from 48.9 ± 17.3 msec^2 to 69.3 ± 17.4 msec^2 (P = 0.026), and LF/HF ratio decreased significantly from 2.2 ± 0.6 to 1.5 ± 0.5 (P = 0.017) (Fig.2). On the other hand, eGFR was unchanged from 13.4 ± 2.4 ml/min/1.73 m^2 to 12.1 ± 2.1 ml/min/1.73 m^2.

DISCUSSION

In this study, respiratory rate was decreased from 15.2 breaths/min, which is similar results for normal respiratory rate in the 60s.[11)], to 11.8 breaths/min. Decreased respiratory rate increases tidal volume to maintain minute ventilation and increases cardiopulmonary extension receptor stimulation[12,13)]. These reduce sympathetic efferent fiber discharge, resulting in vasodilation. In addition, slow abdominal breathing is more effective because it causes a shift from smaller-amplitude to larger-amplitude[13,14)].

One of the hallmarks of altered autonomic nervous system function in CKD is sympathetic overactivity, and although the mechanism is not adequate[1)], reducing this potent sympathetic activity has become a therapeutic strategy. In this study, it was not clear whether the sympathetic overactivity was actually alleviated, but there was a reduction in LF/HF ratio and a reduction in diastolic blood pressure. These may be attributed to decreased peripheral vascular resistance due to decreased sympathetic nerve activity in autonomic nervous system function. The decrease of sympathetic nerve activity through SBE caused the vasodilation of the periphery, increasing peripheral circulation. The association with cardiovascular function is important in patients with kidney disease, and a decrease in diastolic blood pressure was observed even in patients with severe CKD, suggesting that SBE has a clinical effect.

The SBE implementation period was set as a single outpatient period, and there was a difference in the number of days to the next outpatient day depending on the subject. The results of both young healthy males[2)] and CKD patients with a 70% or higher implementation rate may provide one criterion for performing effective SBE, but the effect may vary depending on the duration and frequency of implementation. Therefore, further investigation of improved therapies using SBE is required.

SBE did not lead to any adverse events, such as syncope or arrhythmia inductions. Although SBE in patients with CKD considered in this study may be relatively safe, the possibility of adverse events emerging depending on the underlying disease and complications cannot be ruled out. Therefore, in future clinical studies, it will be necessary to give guidance so that SBE can be correctly and safely carried out.

CONCLUSION

SBE could shift autonomic balance to parasympathetic nerve dominance even in severe CKD patients. Increasing parasympathetic nervous activity may promote peripheral circulation as shown by increased skin temperature in this study. SBE has the potential to improve the autonomic nervous imbalance in CKD patients.

ACKNOWLEDGEMENTS

This work was supported by Japan Society for Promotion of Science KAKENHI Grant (grant numbers JP17H05107).

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