

Clinical Research



An Analysis between Pre- and Post-exercise of the Respiratory and Metabolic State for the Acute and Subacute Stroke Patients

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Highlights

- Arterial blood gas analysis (ABGA) was checked by the 52 stroke patients after moderate intensity exercise.
- Respiratory compensation is well preserved of the non-brainstem stroke patients.

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ABSTRACT

To evaluate oxygenation and metabolic state of the non-brainstem stroke patients after the moderate intensity exercise using arterial blood gas analysis (ABGA). Fifty-two stroke patients were recruited. All the subjects were to follow the instructions for the exercise, not suffered cardiopulmonary diseases before, and not diagnosed with brainstem disorders. They were ordered to maintain 70% heart rate of maximal heart rate during exercise and checked blood pressure, pulse rate, respiratory rate (RR), and ABGA before and after the exercise, respectively. O₂ saturation, PaO₂, PaCO₂, O₂ content, HCO₃⁻, pH, and anion gap were compared between the exercise, and those data changes were performed correlation analysis into age and the time after stroke onset. The data comparison was also done into the subgroup of the severity of stroke using National Institutes of Health Stroke Scale (NIHSS). The statistically significant results were observed in the change of O₂ saturation, PaO₂, PaCO₂, O₂ content, HCO₃⁻, pH, and anion gap after the exercise. The decrease of HCO₃⁻ and increase of RR were proportional to age, however the data showed no correlation with the NIHSS. These results suggest relatively preserved respiratory compensation mechanism and homeostatic effect to maintain metabolic balance among the non-brainstem stroke patients.

Keywords: Blood Gas Analysis; Stroke; Exercise; Oxygen Consumption; Bicycling

INTRODUCTION

Decreased saturation level of blood oxygen in the acute and subacute phase of stroke might damage the ischemic penumbra and worsen clinical outcome [1]. Furthermore, patients with acute and subacute stroke frequently develop arterial oxygen desaturations. There is even a research that continuous monitoring is needed to detect drop oxygen saturation and to titrate oxygen administration for the stroke patients [2]. For that reason, there have been many studies that considerable differences in oxygen saturation are seen at the time before and after insertion of nasogastric tube, changes of body position, before, during, and after meals, and sleep-disordered breathing [3-7]. The data of studies above were measured by portable pulse oximeters, in addition to its limitation toward carboxyhemoglobinemia and/or methemoglobinemia, its accuracy toward the old is getting unreliable [8].

Conflict of Interest

The authors have no potential conflicts of interest to disclose.

Therapeutic exercise is important in rehabilitation of stroke patient however, there has been a lack of study how the oxygen saturation is changing before, during and after the exercise. For that reason, we directly analyzed metabolic state and changes of oxygenation (O_2 saturation, PaO_2 , $PaCO_2$, O_2 content, HCO_3^- , pH, and anion gap) via arterial blood gas analysis (ABGA) in pre- and post-exercise status for acute and subacute stroke patients. Moreover, we examined the changes above were correlated with age, the time after stroke onset, and the severity of stroke.

MATERIALS AND METHODS

This research was approved by the Institutional Review Board of Kwangju Christian Hospital, and carried out at a single medical center. All the subjects were recruited prospectively, and the documents of written informed consent were obtained. The subjects were post-stroke of non-brainstem lesion patients within 24 months of onset. Patients were excluded if: 1) the stroke lesion involved around brainstem; according to the preliminary study that brainstem stroke patients used to experience hypoxia even under the resting state so they do not follow the instructions that we planned exercise protocol, 2) onset was over 24 months prior to assessments, 3) considerable cardiopulmonary diseases (e.g., coronary artery disease, valvular heart disease, chronic obstructive pulmonary disease, asthma, pneumonia, and lung cancer). In order to evaluate unnoticed diseases, all subjects were checked by electrocardiography, 2-dimensional transthoracic echocardiography, chest multidetector computed tomography, and pulmonary function test.

From January 2016 to May 2016, 85 hospitalized subjects were first enrolled to the study though, 12 subjects of atrial fibrillation and other arrhythmias, 8 subjects of atelectasis, 3 subjects of pneumonia, and 10 subjects of cognitive impairment who were not able to follow exercise instructions were excluded. Finally, 52 subjects were participated in this study (Fig. 1).

The maximal heart rate (HR_{max}) = $220 - \text{age}$ formula was used to objectify the moderate exercise intensity, monitored by pulse oximetry (SPO 7500; SPO medical, Simi Valley, CA, USA) to maintain 70% of HR_{max} during exercise [9-11]. 20 minutes of stationary cycling with resistance (ShinGwang 3000; SGMED, Seoul, Korea) (Fig. 2) is commanded for the exercise under the supervision of physicians not to be strayed from the protocol mentioned above. Moreover, 5 minutes of non-resistant pedaling was done on pre- and post-cycling by for the warm ups and cool downs.

ABGA and vital signs (blood pressure, pulse rate, and respiratory rate [RR]) were measured by physicians 10 minutes prior to exercise, and 10 minutes after the exercise, those were rechecked by the same physicians in the same way. ABGA was performed by collecting blood

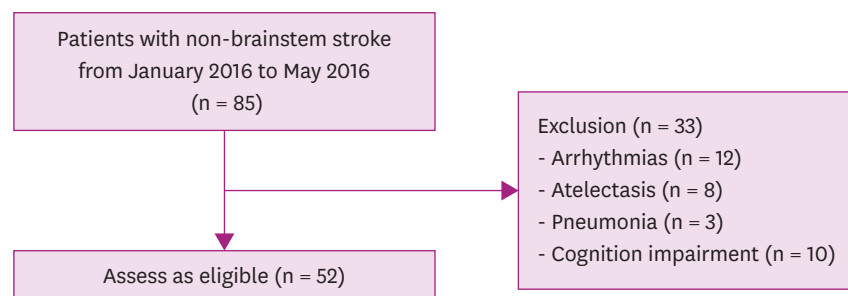


Fig.1. The algorithm for subject enrollment from January 2016 to May 2016.



Fig. 2. Exercise of moderate exercise intensity by stationary cycling with resistance (ShinGwang 3000; SGMED, Seoul, Korea).



Fig. 3. Blood gas analyzer (pHOx Ultra; NOVA Biomedical, Boston, MA, USA).

from a single arterial puncture [12], and subjecting it to analysis on a blood gas analyzer (pHOx Ultra; NOVA Biomedical, Boston, MA, USA) (Fig. 3). All the machines and devices were regularly followed by standard quality control measures. Statistical analysis was performed using the SPSS ver. 21.0 software program (IBM SPSS Inc., Armonk, NY, USA). A paired t-test, Pearson correlation analysis, and one-way analysis of variance (ANOVA) were done to assess the effectiveness and the difference between pre- and post-exercise. A p value of < 0.05 was regarded as statistical significance.

RESULTS

Table 1 presents demographic and clinical information for the 52 patients. The study group was composed of 27 men and 25 women.

Table 2 presents the changes of O_2 saturation, PaO_2 , $PaCO_2$, O_2 content, HCO_3^- , pH, and anion gap between pre- and post-exercise. O_2 saturation, PaO_2 , O_2 content, anion gap, pulse rate,

Table 1. Demographics and clinical characteristics of subjects (n = 52)

Demographic factors	Value
Age (yr)	60.40 ± 15.13
Sex (male:female)	28:24
Stroke etiology	
Ischemic:hemorrhagic	30:22
Onset (mon)	5.84 ± 5.09
Cortical:subcortical	27:25
NIHSS	12.51 ± 6.92

Values are presented as mean or mean ± standard deviation.

NIHSS, National Institutes of Health Stroke Scale.

Table 2. Changes of O₂ saturation, PaO₂, PaCO₂, O₂ content, HCO₃⁻, pH, and anion gap between pre- and post-exercise (n = 52)

Factors	Pre-exercise	Post-exercise	p value
O ₂ saturation	96.5 ± 1.5	97.0 ± 1.2	0.002 [*]
PaO ₂	88.3 ± 13.9	94.3 ± 16.6	0.003 [*]
PaCO ₂	39.4 ± 5.6	36.7 ± 6.5	0.004 [*]
O ₂ content	20.5 ± 2.1	21.4 ± 2.2	0.001 [*]
HCO ₃ ⁻	24.8 ± 0.6	23.1 ± 0.6	0.001 [*]
pH	7.401 ± 0.030	7.407 ± 0.040	0.255
Anion gap	12.5 ± 0.2	14.4 ± 0.4	< 0.001 [*]

Values are presented as mean ± standard deviation.

^{*}Statistically significant at the p < 0.005.

and RR were increased, PaCO₂ and HCO₃⁻ were decreased, and pH was not changed. There was statistical significance on both the increase of O₂ saturation, PaO₂, anion gap, pulse rate, and RR and the decrease of PaCO₂ and HCO₃⁻. Moreover, increase of O₂ content showed significance (p = 0.001) however, change of pH was not revealed meaningfulness (p = 0.255).

Then, we analyzed the data changes with age and the time after stroke onset in Pearson correlation. As age more increased, we found more decreased HCO₃⁻ (correlation coefficient r = 0.450, p = 0.001) and more increased RR (correlation coefficient r = 0.432, p = 0.001) (Fig. 4). Those were revealed statistical significance.

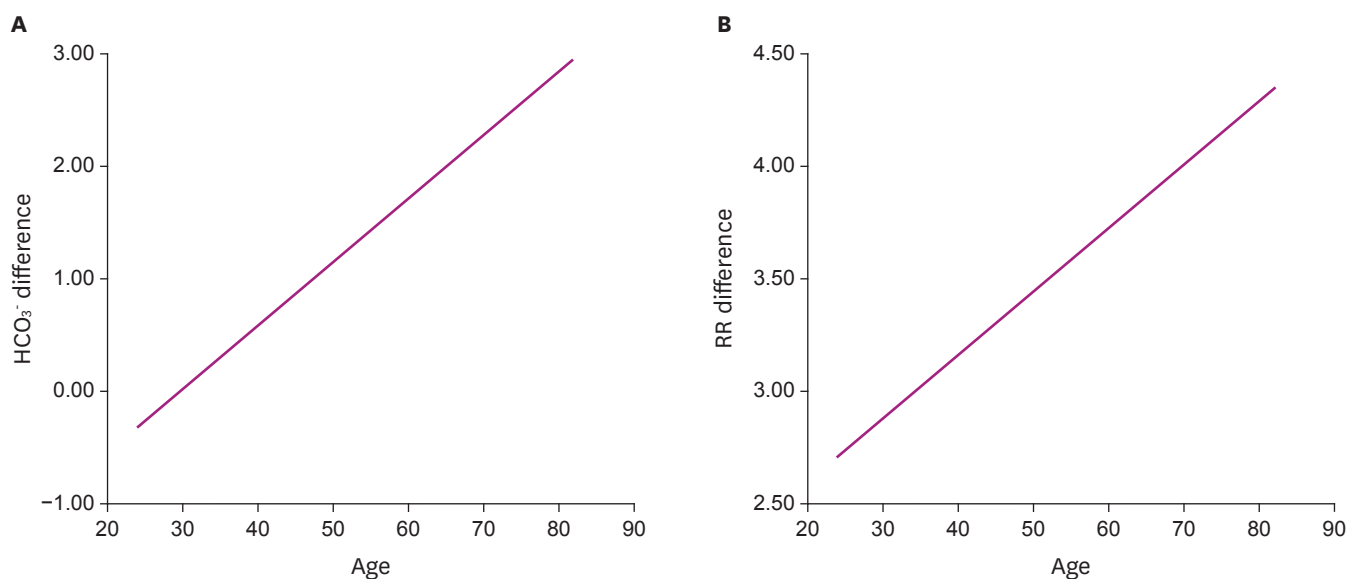


Fig. 4. (A) The decrease of HCO₃⁻ (mEq/L) and (B) the increase of RR (breaths per minute) were proportional to age. RR, respiratory rate.

Table 3. The correlations of between NIHSS and the pH, PaO₂, PaCO₂, O₂ saturation, HCO₃⁻, O₂ content, pulse rate, RR, and anion gap

Factors	p value of NIHSS correlations
pH difference	0.391
PaO ₂ difference	0.279
PaCO ₂ difference	0.210
O ₂ saturation difference	0.293
HCO ₃ ⁻ difference	0.436
O ₂ content difference	0.081
Pulse rate difference	0.429
RR difference	0.265
Anion gap difference	0.075

Values are presented as mean or mean ± standard deviation.

NIHSS, National Institutes of Health Stroke Scale; RR, respiratory rate.

*Statistically significant at the p < 0.005.

The patients were classified into the 3 group on the basis of National Institutes of Health Stroke Scale (NIHSS) as having very severe neurologic impairment (NIHSS > 25: the group was excluded due to cognitive impairment not to follow the exercise protocol), severe impairment (NIHSS 15–24: group A), mild to moderately severe impairment (NIHSS 5–14: group B), and mild impairment (NIHSS < 5: group C) [13]. Therefore, we studied that measured data changes (O₂ saturation, PaO₂, PaCO₂, O₂ content, HCO₃⁻, pH, anion gap, blood pressure, pulse rate, and RR) after the exercises were correlated with each group through one-way ANOVA. There was not statistical significance between stroke severity and the data changes.

In addition, there were not statistical significance between NIHSS and the data (O₂ saturation, PaO₂, PaCO₂, O₂ content, HCO₃⁻, pH, anion gap, blood pressure, pulse rate, and RR), either (Table 3).

DISCUSSION

Whole animal and in vitro studies indicate that ventral and dorsal respiratory group on medulla oblongata and pneumotaxic center on pons regulate respiration according concentrations on chemoreceptors of CO₂ and hydrogen ions, those are distributed throughout the brainstem [14]. Peripheral chemoreceptor system is also involved in respiration by detecting lack of O₂ on carotid and aortic bodies, then it makes respiration center in brain excited [15]. In this study, we excluded the patients with brainstem lesions in computed tomography and magnetic resonance imaging.

Nevertheless, some studies reported that respiration center is not only controlled by brainstem, but also regulated by other brain area [16-18]. Accordingly, we hypothesized that even the patients with other brain lesions (cortex, basal ganglia, cerebellum, and any lesions other than brainstem) were decreased respiratory control reaction during exercise. The goal of this study was to figure those things out.

In the healthy athlete, arterial PO₂, PCO₂, O₂ saturation, pH, and anion gap remain almost exactly normal during strenuous exercise [15]. Our patients (non-brainstem stroke) were not strayed from normal ranges [19] before and after the exercise, either. There are several possible explanations for it. First, adaptation or neuroplasticity of respiratory center on brainstem to decreased signal of it. Several studies reported that the neuroplasticity of respiratory center on

brainstem [20], even if signal decreased or absent from other brain areas to respiratory center on brainstem, it is supposed compensatory neuroplasticity occurred to maintain respiratory homeostasis. Second, we guess that carotid and aortic bodies increase its respiratory drive by detecting decreased oxygen level [21]. It is statistically significant that the increase of RR after the exercise of our patients. Among 52 patients, 5 of them, relatively lower scores of NIHSS with higher physical functions, did not show the increase of RR after the exercise. We assume that further study is needed by setting healthy people as a control group.

We excluded the patients with cognitive impairment not to follow the exercise protocol before we had initiated this study. They were mainly NIHSS > 25 that the effects of the exercise may not be objectively evaluated. Besides, patients with history of considerable cardiopulmonary diseases were also excluded. Therefore, it is not reasonable that our results may be extended to the patients with brainstem disorders and/or cardiopulmonary diseases.

We deduce the decrease of HCO_3^- was the result of buffering effect toward increased lactic acid after the exercise. Consequently, respiratory alkalosis, we observed through the increase of PaO_2 and the decrease of PaCO_2 , and metabolic acidosis, caused by the increase of lactic acid (increased anion gap) were counterpoised each other and maintained normal range of pH. We supposed that this buffering system was considered properly activated in non-brainstem stroke patients.

It was interesting that as age more increased, more decreased HCO_3^- and more increased RR were seen. It may be explained that age more increase, the exercise ability is more decrease that makes lactic acid production and RR more increase.

The limitations of our study were that the lack of parametric approach toward each subgroup of brain lesions, the 10 minutes before and after the blood ABGA might not reflect real-time blood status, and lack of data toward direct measurements of carboxyhemoglobin or methemoglobin.

In conclusion, statistically significant results were observed in the change of O_2 saturation, PaO_2 , PaCO_2 , O_2 content, HCO_3^- , pH, and anion gap 10 minutes before and after the exercise of moderate intensity for the non-brainstem stroke patients, and the data were not strayed from normal ranges. Only increase of HCO_3^- and decrease of RR were proportional to increase of age, whereas age, the time after stroke onset, and the scores of NIHSS were not correlated with the aforementioned statistically significant results. These suggest that it is relatively well preserved that the respiratory compensation to maintain metabolic homeostasis for the non-brainstem stroke patients.

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