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Effect of Artificial Carbon Dioxide-Rich Water Immersion on Peripheral Blood Flow in Healthy Volunteers: Preliminary Study about Artificial Carbon Dioxide-Rich Water

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Abstract

BACKGROUND: Peripheral blood circulation disorder is one of the global health problems. Balneotherapy that uses CO_2 springs may be one of the complementary treatment options. The device to produce artificial CO_2-rich water is needed to achieve an improvement effect, at least almost like the improvement effect of natural balneotherapy.

AIM: This study aims to investigate the effect of artificial CO_2-rich water immersion on peripheral blood flow using Bicarbonated JesC CREA BC-2000.

METHODS AND MATERIALS: Thirty-nine healthy volunteers participated in this study. Each subject immersed both of their legs in a mixed solution from water and CO_2 at temperature 38°C. This solution was mixed using a device, namely, “Bicarbonated JesC CREA BC-2000”. Peripheral blood flow was measured for 5 min before immersion (in this study, we denoted it as the mean basal blood flow), 10 min during immersion, and 5 min after immersion using pocket JMS laser Doppler flowmetry MBF-IIA. Repeated analysis of variance was used for statistical analysis.

RESULTS: There is the difference in peripheral blood flow among before, during, and after immersing the legs into artificial CO_2-rich water using Bicarbonated JesC CREA BC-2000 ($p < 0.001$).

CONCLUSION: Bicarbonated JesC CREA BC-2000 may be used as the device to produce an artificial CO_2-rich water bath that may affect peripheral blood flow in healthy volunteers.

Introduction

Balneotherapy, known as spa therapy, has been frequently and widely used in classical medicine to treat various diseases [1], [2], [3], [4]. The temperature of the water and the substances contained in the bath play an essential role in the beneficial effect of balneotherapy [3], [5]. The temperature of water is described as cold (<20°C), hypothermal (20–30°C), thermal (>30–40°C), or hyperthermal (>40°C) [1], [4]. Moreover, natural gas, such as carbon dioxide (CO_2), is one of the substances used for balneotherapy [3], [6], [7]. Both CO_2 [8], [9] and heat [2], [10] have been recognized as triggering factors for vasodilation.

In some regions of Europe, balneotherapy has been linked with the use of CO_2 spring. Balneotherapy by CO_2 spring has been believed to be beneficial in treating hypertension, cardiovascular disorders, and peripheral occlusive arterial disease [5], [6], [7]. The CO_2 spring itself is defined as spring water originating naturally or dug and contains a minimum of 1000 mg/kg of free CO_2 [5], [11]. In some areas, it is quite challenging to find a CO_2 spring as defined. To identify the effect of CO_2 immersion, artificial CO_2-enriched water had been prepared by various methods, such as CO_2 gas that bubbled into bathwater or tablets containing CO_2 dissolved in water [5], [8], [11]. However, it is challenging to maintain CO_2 concentrations above 1000 ppm for several hours with these methods.

Recently, the device has been modified to obtain the artificial CO_2 water bath efficiently and according to the previously developed definition of CO_2 spring, either through the use of special membranes (double-layered composite perforated fiber membranes) or a spa maker with ordinary tap water and high-pressure CO_2 from gas cylinders [5], [8], [9]. On the other hand, the use of devices that produce bicarbonate water for therapy is still relatively new in some region of Indonesia. While, such devices have developed in developed countries, including Japan [8],[12],[13]. Unfortunately, the research about the effects of artificial CO_2-rich water and a suitable device for producing artificial CO_2-rich water with an improvement effect like natural spring balneotherapy is still lacking. Therefore, in this preliminary study, we tried to test the effectiveness of Bicarbonated JesC CREA BC-2000, a high concentration hydrogen carbonate ion spring with a maximum performance of 1300 ppm, in producing artificial CO_2-rich water, which is hypothesized that can improve peripheral circulation.

Methods

Design study

This is a pre-experimental research with the one-group pre-test-post-test design. There was no a control group in this study. While, the research process was carried out with three measurements of peripheral blood flow. They are before, during, and after immersion of the legs in artificial CO_2-rich water bath.

Population and study setting

Subjects and data collection

In this preliminary study, we investigated the effect of using artificial CO_2-rich water on changes in blood flow in healthy volunteers. There were 53 volunteers who participated in this study, but only 39 people met our inclusion criteria. Before conducting the experiment, each volunteer was asked to answer several questions related to their medical histories, both the presence of diabetes and the presence of other cardiovascular diseases. Then, observations were made regarding the presence or absence of wounds on the legs, and blood pressure was also checked using a sphygmomanometer. Volunteers with hypertension (>140 mmHg), leg injuries, and admitting a history of cardiovascular disease or diabetes mellitus were excluded from the study. Thus, at the end of the observation, 39 samples were obtained in this study. Each subject signed an informed consent. All experiments were carried out at Hasanuddin University Medical Research Center at 6^{th} floor of the Hasanuddin University Hospital.

The protocol of CO_2-rich water bathing and blood flow measurement

Peripheral blood flow was measured using a non-invasive measurement method that shows the value of every second by the pocket laser Doppler flowmetry MBF-IIA series (JMS, Hiroshima, Japan). This device has a sensor pad set on the dorsal left foot between the first and second finger of each subject. The data of the peripheral blood flow were stored in the pocket laser Doppler flowmetry software (version 1.02, Japan). The mean value of every minute was calculated using Microsoft Excel 2010. All the data were shown on a personal computer (Toshiba, Tokyo, Japan). The measurements were made for 5 min before immersion, 10 min during immersion, and 5 min after immersion, respectively.

During the experiment, before measurement of peripheral blood flow, subjects were asked to sit without shoes and socks. None of the subjects wore tight pants that might affect the blood flow in the legs, so before doing the immersion, we only asked them to lift the pants/skirt above their knees. They were instructed, not to talk or move during the measurement. Each subject was asked to immerse both legs under their knees into a container with artificial CO_2-rich water, an output that comes out of a highly concentrated hydrogen carbonate ion spring (Bicarbonated CREA BC-2000, JesC, Nagoya, Japan) as a device for obtaining CO_2-rich water with maximum concentrations 1300 ppm. This device was connected to a water heater (Ariston, TI-SHAPE 15 OR 500 ID, Marche, Italy), which was set at temperature of 38°C, as a warm water source and a gas cylinder containing CO_2 as a CO_2 source. After the artificial CO_2-rich water comes out, the temperature is measured again with a mercury thermometer to ensure that the output temperature is 38°C. While, the pH of this output was measured by a pH meter (Sato, SK-620PH II, China), with its range between 4.5 and 5.6.

Data analysis

To record the difference of the peripheral blood flow before, during, and after immersing the legs in CO_2-rich water, repeated analysis of variance (ANOVA) was used. The data (mean ± Std. deviation) were considered significant at $p < 0.05$ and were calculated using the SPSS 16.0.

Ethical aspect

The Ethics Committee Health Research in the Medical Faculty of the Hasanuddin University approved this experimental protocol with Letter No 387/H4.8.4.5.31/PP36-KOMETIK/2018.

Results

Characteristics of the subjects

The characteristics of the respondents are shown in Table 1. Thirty-nine respondents were enrolled in this study, consisted of 53.8% of male, and 46.2% of female. The mean age of the subjects was 32.90 ± 13.613 years. The mean body mass index was 23.98 ± 5.066 kg/m^2, which indicates that

Table 1: Demographic characteristics of respondents

Parameter	Frequency (n = 39)
[a]Sex	
Male	21 (53.8)
Female	18 (46.2)
[b]Ages (years)	32.90 ± 13.613
[b]BMI (kg/m^2)	23.98 ± 5.066
[b]SBP (mmHg)	114.21 ± 10.270
[b]DBP (mmHg)	74.31 ± 8.234

N: Number of subjects; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; BMI: Body mass index. [a]Parameters with categorical data, values are expressed as n (%). [b]Parameters with numerical data, values are expressed as mean ± SD.

the subjects in this study had a body mass index in the normal category. Furthermore, the mean blood pressure of all respondents was in the normal category, namely, 114.21 ± 10.270 and 74.31 ± 8.234 mmHg for systolic blood flow and diastolic blood flow, respectively.

Association between Artificial CO_2-rich water immersion and the peripheral blood flow

Using repeated measurement ANOVA test, it was found that there was a significant difference between mean basal blood flow, mean blood flow during legs immersion in CO_2-rich water bath, and mean blood flow after legs immersion (p = 0.000, Table 2).

Table 2: Peripheral blood flow in different conditions

Condition	Mean ± Std. deviation (mL/min)	p-value
Blood flow before CO_2-rich water immersion	4.34 ± 0.166	<0.001
Blood flow during CO_2-rich water immersion	6.57 ±0,272	
Blood flow after CO_2-rich water immersion	4.72 ± 0.159	

CO_2: Carbon dioxide.

It appears that the value of mean peripheral blood flow increased during the legs immersion in CO_2-rich water of the basal value and then decreased after immersion, with the value that was close to the basal mean blood flow (Figure 1).

Based on the Bonferroni test that is shown in Table 3, it was found that peripheral blood flow during immersion was significantly different from basal blood flow and blood flow after immersion (respectively, p = 0.000 and p = 0.000). However, there was no significant difference between basal blood flow and blood flow after immersion (p = 0.092).

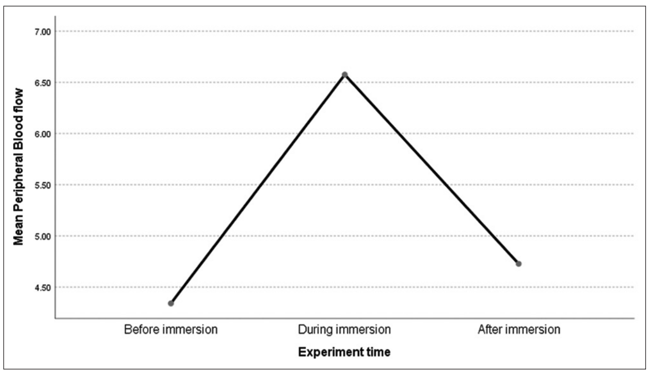

Figure 1: Graph of mean peripheral blood flow: Before exposed to CO_2-rich water immersion, during exposed to CO_2-rich water immersion, and after exposed to CO_2-rich water

Table 3: Pairwise comparison of mean peripheral blood flow

Condition	Comparison condition	Mean difference	Sig.[b]
Before immersion	During immersion	-2.23*	<0.001
	After immersion	-0.38	0.092
During immersion	Before immersion	2.23*	<0.001
	After immersion	1.84*	<0.001
After immersion	Before immersion	0.38	0.092
	During immersion	-1.84*	<0.001

Asterisk (*) indicates that the mean difference is significant at the 0.05 level; b, adjustment for multiple comparisons: Bonferroni.

Correlation of the respondent characteristics and the peripheral blood flow during legs immersion in artificial CO_2-rich water bath

In this study, to ensure that this increase in peripheral blood flow was purely influenced by artificial CO_2-rich warm water, multivariate analysis was performed. This multivariate analysis by linear regression test shows no correlation between sex, age, body mass index, systolic blood pressure (SBP), or diastolic blood pressure (DBP) on changes in peripheral blood flow during immersion of the legs in artificial CO_2-rich warm water (Table 4).

Table 4: Linear regression analysis of characteristics respondents related to peripheral blood flow during immersion

Demographic characteristics of respondents	Coefficient	Standard error	p-value
Sex	1.058	0.730	0.158
Ages (years)	0.035	0.023	0.143
BMI (kg/m^2)	−0.059	0.096	0.546
SBP (mmHg)	−0.007	0.044	0.871
DBP (mmHg)	0.012	0.051	0.808

SBP: Systolic blood pressure; DBP: Diastolic blood pressure; BMI: Body mass index

Discussion

This pre-experimental design study found an increase in peripheral blood flow during legs immersion into artificial CO_2-rich water from the basal control value before immersion in healthy volunteers. Furthermore, after the legs were removed from the immersion, the peripheral blood flow during the immersion decreases almost near the basal peripheral blood flow value. Thus, it suggests that artificial CO_2-rich water immersion may affect peripheral blood flow in healthy volunteers. Meanwhile, the decrease in blood flow after the legs is removed from the bath, close to the basal blood flow value, may be because the changes in environmental temperature by bathing affect the expansion and contraction of blood vessels through the autonomic system [12].

The results of this study are in line with the research of Nishimura *et al*. (2002) which showed an increase in cutaneous blood flow in the forearm reaching 200–250% during bathing in carbon dioxide-rich water from the control value before bathing and tended to decrease after leaving out of the tub [8]. Similarly, the research of Ogoh *et al*. (2018) showed an increase in popliteal artery blood flow for 20 min of immersing the leg in warm carbonated water [14]. Furthermore, Watanabe *et al*. (2006) showed three peaks of changes in peripheral blood flow associated with bathing in inorganic salts and carbon dioxide, the first occurred shortly after the start of immersion, the second occurred just before the end of immersion, and the third occurred after immersion [12]. In addition, animal studies have shown that repeated carbonated water immersion enhances angiogenesis and muscle blood flow in ischemic limbs [15]. Thus, these studies indicate that CO_2-rich water has a beneficial effect on peripheral circulation improvement, especially when administered repeatedly. It should be noted, these studies in human subjects also used artificial CO_2-rich water baths. Although these studies used the device to produce artificial CO_2-rich water and the blood flow measurement device was different from this study, the peripheral blood flow improvement was almost the same as our results. That way, not only natural CO_2 springs but artificial CO_2-rich water may also produce beneficial effects for the body. Therefore, these results indicate that the device used for mixing the CO_2 and warm water in this study may be considered to produce artificial CO_2-rich water that is beneficial for the body. In addition, the use of the blood flow meter that we use may also be considered to be used in further research related to peripheral blood flow measurement.

Balneotherapy or spa therapy has been used for long time in classical medicine. It also has been believed to have benefit in body health. Over the past few decades, this kind of therapy has played an essential role in the treatment for many diseases, such as; hypertension, cardiovascular disorders, and peripheral occlusive arterial diseases; the mechanical effect is obtained from hydrostatic pressure, where immersion allows the patient to mobilize joints and strengthen muscles with minimal discomfort, also causes fluid transfer from the extremities to the trunk, resulting in hemodilution and increased diuresis; thermal effects caused by high-temperature water may cause superficial vasodilation; the chemical effect is obtained through various spa water compositions and physical properties (such as salty, sulfurous, bicarbonate, carbonic, radon rich, selenium rich, arsenical, and ferruginous) [1]. In this study, we mix the CO_2 in 38°C water, which allows for both thermal and chemical effects. Both CO_2 [8], [9] and heat [2], [10] have been recognized as triggering factors for vasodilation. Thus, the artificial CO_2-rich water in this study may increase the blood flow through the vasodilation mechanism produced by the combination of warm water and CO_2.

In some European regions, balneotherapy is carried out using CO_2 springs, defined as springs originating naturally or dug and containing minimum concentrations of 1000 mg/kg of free CO_2 [5], [14]. In addition, for its result effectiveness in flow-mediated vasodilation, the water spa temperature is generally thermal [3], [14], [10]. Indeed, it had been known that water is a good conductor of heat [16], high temperatures can cause vasodilation [2], [10], and CO_2 is a powerful vasodilator [8], [9]. Recently, the device has been modified to obtain the artificial CO2 water bath efficiently and according to the previously developed definition of CO_2 spring, either through the use of special membranes (double-layered composite perforated fiber membranes) or a spa maker with ordinary tap water and high-pressure CO_2 from gas cylinders [5], [8], [9]. In this study, we used Bicarbonated JesC CREA BC-2000, a device with a special membrane (multilayer composite fiber membrane), to obtain CO_2-rich water with a maximum CO_2 concentration of 1300 ppm. Thus, this device makes it possible to produce artificial CO_2-rich water that can affect peripheral blood flow.

The results of multivariate analysis in this study showed that gender, age, body mass index, basal SBP, and DBP did not affect the change of peripheral blood flow during immersion. It suggests that artificial CO_2-rich water was responsible for the changes in blood flow in this study. In other words, gender, age, body mass index, and basal SBP and DBP were not confounding factors in changes in peripheral blood flow during the legs were immersed in CO_2-rich water in this study.

Finally, it should be mentioned that this study has a particular limitation, such as the inability to elucidate the physiological mechanisms associated with vasodilation by artificial CO_2-rich water produced by the device used in this study. It happened because this our preliminary study, we did not measure blood samples on the research subject. It is hoped that in future research, this mechanism will become clear. Therefore, future studies regarding blood sample investigations and factors involved in vasodilation may be more interesting.

Conclusion

This study noted that the use of Bicarbonated JesC CREA BC-2000 produced artificial CO_2-rich water that might increase peripheral arterial blood flow during immersion, and decreased after immersion to a value close to basal blood flow. Therefore, it is drawn that the device we use can be considered to produce artificial CO_2-rich water that produces beneficial effects on health. Unfortunately, in this study, we have not analyzed the blood plasma of the study subjects to find the vasodilation mechanism that might be the cause of the increase in blood flow. This kind of investigation is needed in future studies.

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