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Effect of Carbon Dioxide (CO_2)-Rich Water Immersion on Changes of Peripheral Blood Flow in Patients with Kidney Disease

Yammar[1]*, Annisa Suwahru[1], Andi Rizky Arbaim Hasyar[1], Irfan Idris[2], Irawan Yusuf[2], Haerani Rasyid[3]

[1]*Postgraduate Program in Physiology Concentration, Hasanuddin University, Makassar, Indonesia*
[2]*Department of Physiology, Faculty of Medicine, Hasanuddin University, Makassar, Indonesia*
[3]*Nephrology-Hypertension Division, Department of Internal Medicine, Makassar, South Sulawesi, Indonesia*
* *Correspondent Author: yammar.ym11@gmail.com*

ABSTRACT

Endothelial dysfunction has been experienced even at an early stage in patients with kidney disease undergoing hemodialysis, characterized by stiffness of the walls of blood vessels, leading to decreased peripheral blood flow. The aims of this study to determine effect of CO_2-rich water immersion on changes of peripheral blood flow. Type of this research was quasy eksperiment design, A total of 30 patients with kidney disease undergoing hemodialysis at Hasanuddin University Hospital were divided into two groups, in which 18 subjects received CO_2-rich water (1,300 ppm) feet immersion at 37-38°C temperature and 12 subjects received freshwater immersion at 36-37°C. The immersions were conducted 2-3 times a week for a period of four weeks and the peripheral blood flow measured using a Laser Doppler Flowmetry on day 1 and 28. The result of this study the peripheral blood flow of the CO_2-rich water immersion group decreased from 12.443 mL/minute to 11.677 mL/minute (decreasing 0.766 mL/minute), while the freshwater immersion group decreased from 8.471 mL/minute to 6.776 mL/minute (decreasing 1.695 mL/minute). This study shows that CO_2-rich water immersion tends to inhibit the decrease of peripheral blood flow more compared to freshwater immersion in kidney disease patients undergoing hemodialysis

Keywords: Carbon dioxide, Freshwater, Kidney Disease, Hemodialysis

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BACKGROUND

In Indonesia, kidney disease is a health problem leading to a high risk of cardiovascular disease with the incidence and prevalence increasing almost every year (Fauziyati, 2016). Recent data reported that in 2018 the number of chronic kidney disease patients in Indonesia was around 3.8% (PERNEFRI, 2018). Patients with stage V chronic kidney disease or End Stage Renal Disease (ESRD) require special care and treatment, namely hemodialysis (Sun et al., 2019)(Lee et al., 2019). Chronic kidney disease patients recovering from hemodialysis (HD) treatment only range from 0.3-8% (Chen et al., 2019)(Wetmore & Collins, 2016). In Indonesia the average HD patients can survive for over 3 years, but the largest proportion survive for 6-12 months (Depkes, 2017). Whereas in Japan, HD patients can survive up to 25 years (Nitta et al., 2020).

Chronic kidney disease patients undergoing HD treatment experience some dysfunction causing increased inflammation and oxidative stress mediators that can lead to further complications including cardiovascular disease and electrolyte abnormalities (Vadakedath & Kandi, 2017)(Russa et al., 2019). Henceforth patients with chronic kidney disease have a higher risk of developing peripheral artery disease (Garimella & Hirsch, 2014) The cause of peripheral artery disease is atherosclerosis, beginning with endothelial dysfunction in the blood vessels and ultimately promotes microcirculation disorders (Michael R. Zemaitis , Julia M. Boll, 2020).

So far there has not been an intervention that can be used as an additional therapy along with hemodialysis to improve microcirculation disorders in patients with kidney disease in Indonesia. Previous studies stated that CO_2-rich water immersion has a beneficial effect in improving microcirculation in ischemic patients (Sato, Kanikowska, & Iwase, 2009)(Sakai et al., 2011)(Finzgar, Melik, & Cankar, 2015)(Makino, Maeda, & Abe, 2015)(Ogoh et al., 2016)(Ogoh et al., 2018).

METHODS

This study is a quasy experimental design, conducted at Hasanudddin University Hospital in 2020, involving 30 patients with kidney disease undergoing hemodialysis. The patients were randomly divided into two groups, in which 18 patients received CO_2-rich water immersion and 12 patients received freshwater immersion. Each group received the intervention 2-3 times a week for a period of four weeks set up in accordance with the patients scheduled hemodialysis. The immersions conducted about 10 minutes prior to the hemodialysis procedure. This study was approved by the Health Research Ethics Committee of the Hasanuddin University Faculty of Medicine, Makassar, Indonesia: 333/UN4.6.4.5.31/PP36/2020.

Method of data collection

Data collection begins with conducting interviews and looking up the patients' medical records related to weight, age, gender, blood pressure, GFR value and HD frequency.

Experimental protocol

CO_2-Rich Water and Freshwater Feet Immersion

A box shaped plastic container is filled with 24 liters of CO_2-rich water. This CO_2-rich water discharged from a sink connected to a special device that produces CO_2 (JesC CREA, BC2000) made in Nagoya Japan. The sink is also connected to a heating device (Ariston). The liquid accommodated is 24 liters of water with 1300 ppm of CO_2, pH = 4.5-

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5.6 and a temperature of 37-38ºC. Subjects were asked to immerse both feet for 10 minutes while peripheral blood flow measured.

As for freshwater immersion, the plastic container filled with 24 liters of water directly from the sink and then only connected to the heater. The water is set to 36-37°C temperature without CO_2 enrichment. The procedure of Immersion and peripheral blood flow measurement are the same.

Measurement of Peripheral Blood Flow

Peripheral blood flow was measured with a Laser Doppler Flowmetry (Pocket LDF MBF IIA Series, Hiroshima, Japan) connected to a computer (Toshiba) via a software (LDF Recorder, version 1.02, Japan). The LDF sensor was set on the dorsal part of the left foot between the first toe (thumb) and second toe (hallux) before taking measurements. Peripheral blood flow were measured for ten minutes at immersion on day 1 and day 28. The Immersion tool is shown in figure 1

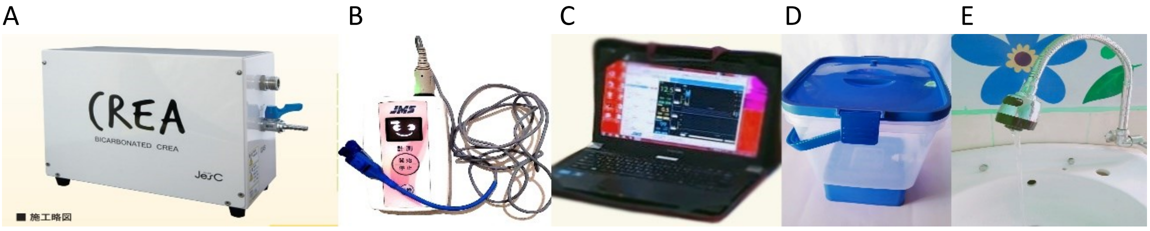

Figure 1: A. JesC CREA, BC2000, B. Laser Doppler Flowmetry, C. Computer (Toshiba) D. Plastic Container, E. Sink (Water Source)

Immersion of both feet with CO_2-rich water and freshwater while measuring the peripheral blood flow is shown in figure 2.

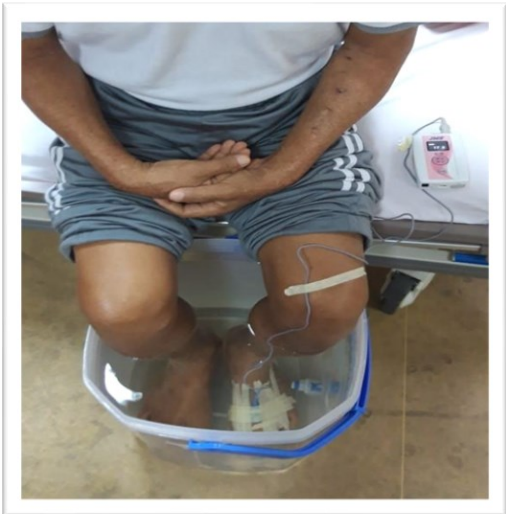

Figure 2: Immersion of both feet while measuring the peripheral blood flow

Data Analysis

The data were processed using SPSS program version 22. Differences in peripheral blood flow in the CO_2-rich water immersion group on day 1 and day 28, as well as in the freshwater immersion group were analyzed with Wilcoxon test. The changes of peripheral blood flow

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between the CO_2-rich water and the freshwater groups on day 1 and day 28 were measured with Mann-Whitney test and considered significant if p value <0.05.

RESULTS

Table 1. Characteristics of Research Subjects

Variable	CO_2-Rich Water n=18	Freshwater n=12	*p
[a] age	44.88 ±13.450	48.41±13.701	0.433
[b]Gander			-
Male	8 (44.4)	10 (83.3)	
Female	10 (55.6)	2 (16.7)	
[a] Weight (Kg)	55.27±8.975	63.41±10.182	0.082
[a] Systolic (mmHg)	141.67±20.934	128.25±23.518	0.134
[a] Diastolic (mmHg)	81.67±6.183	76.00±10.054	0.187
[a] GFR (mL/Min/1.73 $\boldsymbol{m^2}$)	7.02±3.162	7.64±3.630	0.767
[b] Hemodialysis Frequency (x)			-
Twice a week	11 (61.1)	6 (50.0)	
Three times a week	7 (38.9)	6 (50.0)	

n= Total Sample
*p= Mann whitney test
[a]=Variable Numerical Data (Mean±SD)
[b]=Variable Categorical Data (%)

Table 1 shows that the groups that received CO_2-rich water and freshwater immersions were homogeneously distributed. Age, weight, blood pressure and GFR were more or less the same, except that there were more females in the CO_2-rich water immersion group.

Table 2. Differences of Peripheral Blood Flow in the CO_2-Rich Water Immersion Group and the Freshwater Immersion Group

Day	**Group**	**Blood Flow**	***n***	**Mean of Blood Flow (mL/menit) ± SD (Standard Deviation)**	***p**
Day 1	CO_2-Rich Water	During Immersion	18	12.443 ± 4.842	0.435
Day 28	CO_2-Rich Water	During Immersion	18	11.677 ± 4.747	
Day 1	Freshwater	During Immersion	12	8.471 ± 2.967	0.239
Day 28	Freshwater	During Immersion	12	6.776 ± 1.493	

**p*:*Wilcoxon*

Table 2 shows that there were decreases of peripheral blood flow in both CO_2-rich water and freshwater immersion groups. However, the decrease of peripheral blood flow in the CO_2-rich water group was very minimal compared to the freshwater group, although it is not statistically significant (Wilcoxon test, p> 0.05). And if the number of blood flow decrease measured (table 3, Figure 3), it showed that the decrease of peripheral blood flow in the CO_2-rich water immersion group on day 28 was 0.766 mL / minute, while in the freshwater group the decrease was 1.695mL /minute. The data indicated that the decrease of peripheral blood flow in the CO_2-rich water immersion group was only 1/3 compared to that of the freshwater group, although it was not statistically significant (Mann Whitney test, p> 0.05). It seemed that the CO_2-rich water feet immersion of the patients with kidney disease undergoing hemodialysis inhibited the decrease of peripheral blood flow and this indicated an inhibition of the process of microcirculation damage.

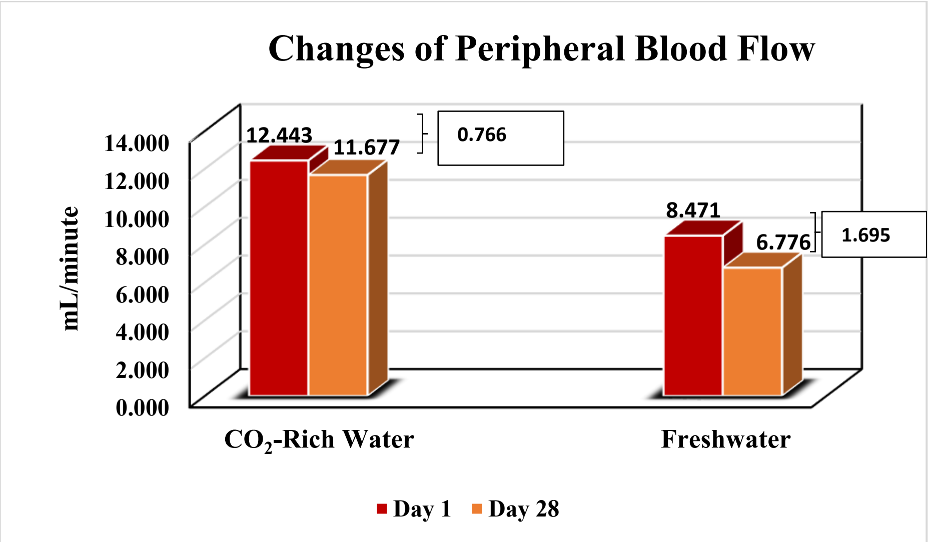

Figure 3. Changes of Peripheral Blood Flow in the CO_2-Rich Water Immersion Group and the Freshwater Immersion Group

Table 3. Differences of Peripheral Blood Flow Changes Between CO_2 Water and Freshwater Immersion Groups

Blood Flow	**Mean of Blood Flow (mL/menit) ± SD (Standard Deviation)**		***p**
	CO_2-Rich Water	**Freshwater**	
During Immersion	0.766 ± 4.131	1.695 ± 3.798	0.641

**p*:*Mann-Whitney*

I.

DISCUSSION

Since the Middle Ages, the beneficial effects of using carbon dioxide balneotherapy had been known and clinically applied to humans (Pagourelias & Zorou, 2011)(Kälsch et al., 2017). Several previous studies showed that CO_2-rich water immersion can increase blood

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flow and can be used as a treatment for patients with peripheral artery and cardiovascular diseases (Xu, Elimban, & Dhalla, 2017).

Hence, up till now a number of studies regarding the effects of CO_2-rich water immersion are still carried out. Among them is our study, which aims to determine whether CO_2-rich water immersion has an effect on changes of peripheral blood flow in patients with kidney disease. Our study results showed that feet immersion with CO_2-rich water in patients with kidney disease undergoing hemodialysis inhibited a decrease in peripheral blood flow, and this indicated an inhibition of the process of microcirculation damage compared to the freshwater immersion. The immersion with CO_2-rich water can improve endothelial mediated vasodilator function and reduce stiffness in the arteries (Ogoh et al., 2018). Thus, carbonated water immersion can be used as an additional therapy for hemodialysis to inhibit microcirculation damage in patients with kidney disease.

Another study is a recent study by Rizky showing that CO_2-rich water immersion can lead to an increase of peripheral blood flow in healthy people (Rizky et al., 2020). The different results of the study from ours may well be because our study subjects were patients with kidney disease undergoing hemodialysis that of course had microcirculation damage. A theory suggests that sufferers of chronic kidney disease induce loss of microvascular tissue including arterioles, capillaries and venules leading to reduced blood flow velocity, decreased vascular tone and impaired oxygen absorption, all of which have an important role in forming most of the microcirculation and providing physiological functions of the endothelium (Prommer et al., 2018)(Querfeld, Mak, & Pries, 2020).

Carbon dioxide is a vasodilator substance that has a direct effect on blood vessels by triggering an increase in peripheral blood flow (Rizky et al., 2020). The mechanism underlying this phenomenon is that CO_2 diffuses into the subcutaneous tissue through the skin layers (Makino et al., 2015). An increase in subcutaneous PCO_2 tension will show a vasodilating effect so that the blood flow rate increases (Nishimura et al., 2002). The transfer of CO_2 to the skin has a local vasomotor effect without affecting systemic hemodynamics (Izumi et al., 2015). The mechanism of CO_2 effect on vascular smooth muscle is based on the presence of extracellular acidosis that can reduce smooth muscle contraction of cutaneous blood vessels in arteriolar walls, leading to the decreased resistance and increased of blood flow (Yoshimura et al., 2020).

Finally, this study has certain limitations, namely the small number of samples and the female gender of CO_2-rich water immersion samples compared to the freshwater immersion samples. Further research requires a large number of samples and the samples gender evenly distributed

CONCLUSION

This study shows that the CO_2-rich water immersion tends to inhibit the decrease of peripheral blood flow compared to the immersion of freshwater in patients with kidney disease undergoing hemodialysis.

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