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Hee-Kyung Jin, Tae-Yeon Hwang, Sung-Hyoun Cho*

Effect of electrical stimulation on blood flow velocity and vessel size

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Abstract: Interferential current electrical stimulation alters blood flow velocity and vessel size. We aimed to investigate the changes in the autonomic nervous system depending on electrical stimulation parameters.

Forty-five healthy adult male and female subjects were studied. Bipolar adhesive pad electrodes were used to stimulate the autonomic nervous system at the thoracic vertebrae 1-4 levels for 20 min. Using Doppler ultrasonography, blood flow was measured to determine velocity and vessel size before, immediately after, and 30 min after electrical stimulation.

Changes in blood flow velocity were significantly different immediately and 30 min after stimulation. The interaction between intervention periods and groups was significantly different between the exercise and pain stimulation groups immediately after stimulation ($p<0.05$). The vessel size was significantly different before and 30 min after stimulation ($p<0.05$).

Imbalances in the sympathetic nervous system, which regulates balance throughout the body, may present with various symptoms. Therefore, in the clinical practice, the parameters of electrical stimulation should be selectively applied in accordance with various conditions and changes in form.

Keywords: Exercise level stimulus; Interferential current; Pain level stimulus; Sensory level stimulus; Ultrasonography

***Corresponding author: Sung-Hyoun Cho,** Department of Physical Therapy, Nambu University, Gwangju city, Republic of Korea, E-mail: shcho@nambu.ac.kr
Hee-Kyung Jin, Department of Physical Therapy, Nambu University, Gwangju city, 23 Cheomdanjungang-ro, Gwangsan-gu, Gwangju 506-706, Republic of Korea
Tae-Yeon Hwang, Department of Physical Therapy, Chunnam Techno College, Gokseong-gun, Jeollanam-do, Republic of Korea

1 Introduction

There has been a persistent increase in the incidence of cardiovascular and circulatory diseases owing to the state of blood vessels and circulation characteristics [1]. Thus, blood flow velocity and vessel status are measurable markers that can be used to diagnose health status [2]. Nevertheless, measurement and prediction of circulatory features lack the required precision for clinical diagnosis and treatment. Previous studies have evaluated the characteristics of the vasculature and blood flow [2, 3]. Specifically, it is important to ascertain the heart rate, blood pressure, state of the blood vessels, and blood flow velocity to predict blood flow characteristics.

Therefore, among the diagnostic devices for vascular diseases, such as magnetic resonance imaging, ultrasonography, near-infrared imaging, and laser imaging [4], Doppler ultrasonography was used to detect moving reflectors. Ultrasonography has the advantage of non-invasively measuring blood flow velocity in a quick and continuous manner based on the velocity of sound. Moreover, it enables examination of the state of the blood vessels from the vessel cross-section [5].

As the blood flows through the blood vessels, it maintains a constant shearing force with the endothelial cells in the vessel wall. Thus, the interaction between the vessels and blood is determined by the state of the vasculature and blood flow characteristics [6]. Blood flow velocity is kept constant by a system of self-regulation, primarily controlled by the activity of the brain [7]. Therefore, the characteristics of blood flow and vascular transformation are organically interlinked with the circulatory system of the whole body. In other words, blood flow is proportional to flow velocity and is inversely proportional to the cross-sectional area, which is affected by vascular contraction [8]. However, it is controversial whether an increase in blood flow velocity directly reflects a rise in blood flow [9]. Despite such controversy, blood flow velocity, as measured by vessel size, is a critical index used as an objective diagnostic criterion in functional tests in patients who are not using drugs that affect vascular resistance or in situations where the vascular resistance is not significantly altered [6].

Physiological changes caused by electrical stimulation include an increase in blood flow and an effect on the peripheral circulation [7]. The appropriate dose and duration of electrical stimulation can achieve various physiological responses [10]. Therefore, electrical stimulation affects the control of blood flow, and precise control of such electrical stimulation is essential to avoid tissue damage [5].

Interferential current (IFC) is one method of electrical stimulation used for pain management, and its clinical applications are diverse; low resistance of the skin and subcutaneous tissues allows focal application of electricity at certain points [10]. IFC uses a current in the mid-frequency range of 1-100 KHz; it is an amplitude-modulated alternative current produced by cross-interference of different currents within the body, thereby transmitting a burst frequency in the biological range into a continual flow of electric potential [11]. In addition, evidence-based approaches of the objective circumstances are required for electrical stimulation conditions and levels [12].

The aim of this study is to quantitatively express blood flow characteristics and functional changes in the vasculature using Doppler ultrasonography. Accordingly, the hypotheses established to examine the study aim are as follows: 1) blood flow velocity will differ per the amplitude and frequency of IFC and 2) vessel size will change depending on the amplitude and frequency of IFC.

2 Methods

2.1 Subjects

This study was conducted on 45 healthy male and female students in Gwangju metropolitan city, South Korea. Subjects who satisfied any the following were excluded from the study: presence of diseases that can affect the blood flow rate, abnormal vital signs (blood pressure, pulse, body temperature, and respiration rate), presence of any state that can affect the experiment and blood test, presence of metal implants, contraindication for electrical stimulation, and ineligibility to participate as determined by the researcher. The subjects were asked to avoid intense exercise, and smoking and intake of beverages and food items that can affect blood flow velocity and vessel size were restricted one hour before the experiment. Accordingly, the experiment was performed on subjects who did not have any health issue and gave voluntary consent to participate in the study.

Eligible subjects were randomly assigned into one of the following three groups: sensory level stimulation group (SSG; n=15), exercise level stimulation group (ESG; n=15), and pain level stimulation group (PSG; n=15).

All procedures in the study were approved by the Local Institutional Review Board of Nambu University. Informed consent has been obtained from all subjects included in this study in accordance with the ethical standards of the Declaration of Helsinki. For the analysis, the three groups were considered to have the same general characteristics with no differences between each group (Table 1).

Table 1: General characteristics of the subjects

Characteristics	SSG	ESG	PSG	F	p
Gender (Male/Female)	7 / 8	8 / 7	8 / 7		
Age (years)	22.00±1.41	22.45±1.44	22.64±1.63	0.527	0.596
Height (cm)	166.27±7.46	167.09±8.50	170.64±8.08	0.615	0.547
Weight (kg)	62.55±4.55	60.82±4.08	65.09±5.93	0.212	0.364
BMI($Kg \cdot m^{-2}$)	22.18±2.48	23.2±4.12	21.76±2.21	0.204	0.641

Values are presented as mean ± standard deviations; SSG: sensory stimulation group; ESG: exercise stimulation group; PSG: Pain stimulation group

2.2 Intervention

ENDOMED 582 (EnrafNonius, Netherlands) was used as an IFC electrical stimulator, and the intervention was performed for 20 min. Pad electrodes (4×4 cm, Protens Electrodes, Bio-protech INC, Korea) were placed on the transverse processes of the T_1-T_4 vertebrae, 2 cm to the left side of the spinous processes (Fig. 1). For psychological stability, the subjects laid down on a bed for 10 min before the intervention [13].

Based on pilot studies, the SSG, ESG, and PSG were tested with sudden frequency 100 bps + intensity 10-20 mA, 5 bps + 45-50 mA, and 100 bps + 80-90 mA, respectively. The inducing method of the electrical stimulation parameters was based on previous studies and pilot studies [14].

2.3 Outcome measures

Using Doppler ultrasonography (MyLabOne, Esoate, Italy), blood flow was measured to determine blood flow velocity and vessel size before, immediately after, and 30 min after electrical stimulation (Figs. 2, 3, and 4).

The signal source of Doppler ultrasonography is blood, in which the particles that induce scattering are smaller than the wavelength of light. The intensity of the scattered signal increases in proportion to the fourth power of the primary frequency. Therefore, an ultrasound frequency was used to measure the increased intensity of scattered reflected signals from the blood, which is a moving reflector [15].

Blood flow (mL/s) is the volume of blood flowing from the heart to the aorta over the course of a minute when

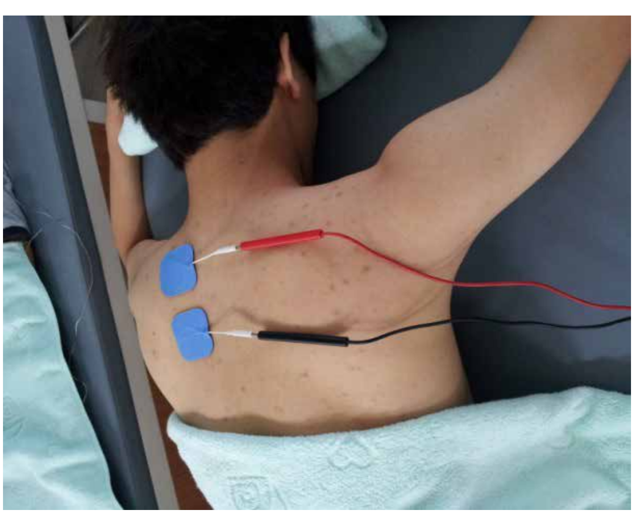

Figure 1: Method of IFC electrode application

Figure 2: Device of real-time ultrasonography

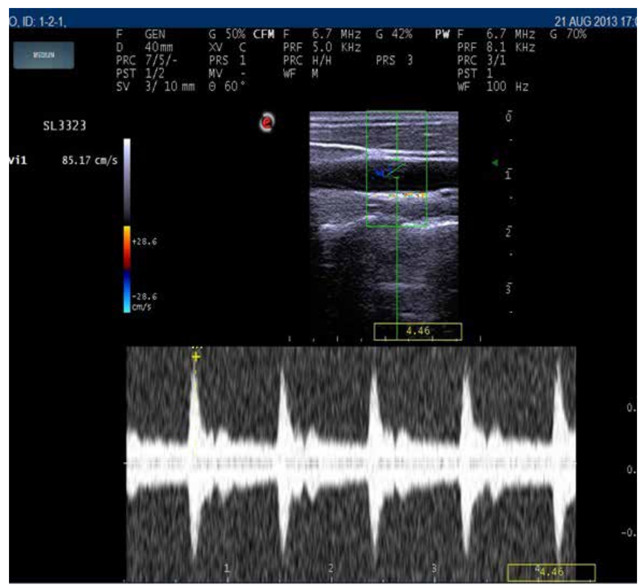

Figure 3: Measurement of change in the blood flow velocity

Figure 4: Measurement of carotid artery vessel size

blood is flowing from the artery to the vein and the same volume of blood is flowing from the artery to the vein through peripheral resistance. It is determined by hydraulic resistance depending on blood flow velocity and vessel diameter [16].

After applying an appropriate amount of ultrasound gel to the left carotid artery, the ultrasonography probe was attached to a fixator and placed against the skin at an angle of approximately 60-70° to observe and measure blood flow. Measurements were repeated three times, and the mean was calculated [17].

2.4 Statistical analysis

All data were analysed with the SPSS 22.0 version for Windows. The Shapiro-Wilk test was used to check the normal distribution of the general characteristics and values measured. Thus, normal distribution was accepted. One-way analysis of variance (ANOVA) was then used to investigate the difference in the general characteristics between the groups. Two-way repeated measures ANOVA was used to investigate the change in blood flow velocity and vessel size of each group depending on time. The significance of the values measured was analysed by a post hoc analysis using the Tukey's method. The level of statistical significance was set at $p<0.05$.

3 Results

3.1 Changes in blood flow velocity

Changes in blood flow velocity of each group are shown in Table 2. Sphericity was assumed because there was no statistically significant difference in the Mauchly's sphericity test ($p>0.05$). For the tests of within-subject effects, blood flow velocity was significantly different immediately and 30 min after stimulation ($p<0.05$). Further, the interaction between ESG and PSG was significantly different immediately after stimulation ($p<0.05$).

3.2 Changes in vessel size

Changes in vessel size of each group are shown in Table 3. Sphericity was assumed because there was no statistically significant difference in the Mauchly's sphericity test ($p>0.05$). For the tests of within-subject effects, vessel size was significantly different before and 30 min after stimu-

Table 2: The change of the blood flow velocity (unit: cm/s)

Group	Pre-test (M±SD)	Post-test (M±SD)	Post-30 (M±SD)	F(p)		
				Group	Period	Group x Period
SSG	71.35±5.08	72.79±5.36	70.81±4.85	0.457 (0.637)	11.681 (0.000*)	7.041 (0.000*)
ESG	70.30±3.30	74.65±3.48	70.82±3.95			
PSG	70.97±4.36	69.96±4.90b	70.01±4.29			

*$p<0.05$; Values are presented as mean ± standard deviations; SSG: sensory stimulation group; ESG: exercise stimulation group; PSG: Pain stimulation group; Pre-test: before electrical stimulation; Post-test: after electrical stimulation directly; Post-30: after 30 minutes from immediately the electrical stimulation

Table 3: The change of vessel size (unit: mm)

Group	Pre-test (M±SD)	Post-test (M±SD)	Post-30 (M±SD)	F(p)		
				Group	Period	Group x Period
SSG	6.07±0.44	5.96±0.28	6.00±0.40	0.910 (0.410)	5.440 (0.010*)	10.367 (0.000*)
ESG	5.86±0.42	6.16±0.34	5.66±0.38			
PSG	5.96±0.39	6.00±0.35	5.83±0.36			

*$p<0.05$; Values are presented as mean ± standard deviations; SSG: sensory stimulation group; ESG: exercise stimulation group; PSG: Pain stimulation group; Pre-test: before electrical stimulation; Post-test: after electrical stimulation directly; Post-30: after 30 minutes from immediately the electrical stimulation

lation ($p<0.05$), and the interaction between ESG and PSG was significantly different immediately after stimulation ($p<0.05$).

4 Discussion

The sympathetic nervous system regulates metabolism and maintains homeostasis against external influences and changes in environmental factors [18]. Therefore, blood flow velocity, which can be used to examine the state of the cardiovascular system, is related to cardiovascular diseases. Studies on blood flow velocity and vessel sizes are essential for the prevention and treatment of diseases of the sympathetic nervous system.

This study compared the changes in blood flow velocity and vessel size using three levels of electrical stimulation. The main element of electrical stimulation is the regulation of frequency, amplitude, and pulse duration, which shows a high therapeutic efficacy [19]. Moreover, various physiological responses can be induced per the dosage and stimulation duration [10]. In other words, the vessels dilated from low frequency-high intensity ESG stimulation contract the skeletal muscles to increase blood flow velocity [20]. Previous studies visualised data on the changes in blood flow velocity and vessel size in terms of shape, size, colour, position, and orientation to confirm and compare the study results at a glance [21].

Visualisation of data helps express results graphically, enabling intuitive understanding of and insights into the information. Visualisation also aims to efficiently convey the meaning of the data, its analytical power, and reliability. Therefore, visualisation of blood flow velocity and vessel size measurements by Doppler ultrasonography greatly help with data comprehension and analysis [22]. This study used the carotid artery, which is the largest artery that pumps blood from the heart into the systemic circulation, for the measurements; it is easy to detect stenosis or blockage based on the differences in blood flow velocity and the use of red and blue colours to indicate blood flow [23]. However, signals from Doppler ultrasonography are not completely stable, since blood flow velocity keeps changing and vectors of blood flow are non-linear; however, in this study, blood flow velocity and vessel size could be easily and rapidly quantified based on the visual models with statistically identical features [24]. Blood flow velocity increases geometrically relative to the Doppler angle. Beyond 70°, abrupt increase in flow velocity cannot be measured accurately. In other words, a Doppler angle of 1° shows a difference in blood flow of 82 cm/s compared to an angle of 80°. Therefore, a Doppler angle of 60° is appropriate for examination. Our study has used a Doppler angle of 60° based on previous studies [21].

The most important principle of the circulatory system is to regulate blood flow per the demands of the local tissues. IFC stimulation induces sympathetic tone to block vasoconstriction fibres, which inhibits nerve activity and reduces tension in the arterial muscles, improving blood circulation [25]. The high frequency-low intensity SSG showed an increased blood flow velocity as vessel size decreased; this demonstrates that the tonicity of the sympathetic nervous system can be manipulated by electrical stimulation to improve blood circulation [26].

However, there was a clear difference in this study between increased blood flow velocities from sensory and exercise stimulations. The velocity increase by exercise stimulation is caused by vasodilation and prostaglandin in the skeletal muscles as the afferent fibre receptors of the skeletal muscles are stimulated, resulting in a central sympathetic response [27]. In other words, promising results can be expected if low frequency-high intensity exercise stimulation is used clinically to alleviate the symptoms of focal ischemia, via an increase in vessel size and flow velocity. On the other hand, blood flow velocity and vessel size influence circulatory function, and electrical stimulation also causes physiologic changes by activating sympathetic tone via muscle contraction [28]. In addition, electrical stimulation is effective at reducing the incidence of cardiac vein thrombus and the risk of pulmonary embolism [29] and increases venous return due to increased venous and muscular tension caused by sympathetic tone [30]. By the same electrophysiological mechanisms, high frequency-low intensity sensory stimulation induced vasoconstriction and increased blood flow velocity in this study; thus, it is thought that such stimulation could also enhance normal venous return. Moreover, after compression of the veins in the leg using an obstructive blood flow measurement technique, blood flow towards the heart increased by electrical stimulation; this means that it is appropriate to use electrical stimulation to reduce the risk of embolism [31].

Moreover, it has been reported that blood flow velocity gradually increases in vascular stenosis, before decreasing after a certain severity of stenosis has been exceeded [32]. In another report, the accumulation effect of swelling and effusion in experimental animals was reduced by high frequency-high intensity needle electrode electrical stimulation. Such results imply that physiological changes by electrical stimulation are feasible, given that high frequency-high intensity electrical stimulation in this study resulted in vascular contraction and reduced blood flow velocity [33].

Based on the findings of this study and previous studies, appropriate use of electrical current stimulation under various conditions can be considered as a very important application in physical therapy. This study is a fundamental study, which identifies that blood flow velocity and vessel size may vary depending on the amplitude and frequency of IFC stimulation. The present study is significant as it identified that the changes in the autonomic nervous system induced by IFC electrical stimulation can lead to good treatment outcomes when any imbalance in the autonomic nervous system, which maintains an appropriate balance for the human body, has presented with various symptoms. Accordingly, our findings may serve as basic indices for improvement in the autonomic nervous system from various conditional variables and complex electrical stimulation variables.

However, the human body maintains homeostasis from appropriate interaction between stimulation and inhibition of all organs. Thus, it is necessary to verify the effects of electrical stimulation by performing at least two examinations; vasomotion should be examined along with cardiovascular examination, sweat test, endocrine function test, and measurement of the amounts of neurotransmitters. In other words, the results of this study, which examined the effects on the autonomic nervous system only through vessel size and blood flow velocity, may be limited.

Furthermore, this study evaluated healthy subjects. However, the autonomic nervous system may respond sensitively to electrical stimulation in the patients as they have increased tonicity in the sympathetic nervous system due to pain. Accordingly, future studies will need to compare various pain models.

5 Conclusion

The results of our study can be applied to conduct different electronic stimulation variables depending on specific situations and purposes to patients during clinical trials. However, this study was conducted on healthy adults; it will be applied to various patients in the clinical field in the future. Further trials will be needed to apply our findings on a wide range of patients and conditions. This study provides types of stimulation for different terms and changes in clinical data.

Conflict of interest statement: Authors state no conflict of interest.

Abbreviations: ESG, exercise level stimulation group; IFC, Interferential current; PSG, pain level stimulation group; SSG, sensory level stimulation group

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