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Response of Peripheral Vascular System to Cold Pressor Test Measured Using Near Infrared Spectroscopy

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Abstract: We measured the responses of oxygenation and carotid artery diameter (Di) to the cold pressor test (CPT), which is the standard method for measuring endothelial function. The subjects were 10 elderly hypertensive women (hypertensive group) and 10 healthy elderly women (control group). Oxygenated Hb (oxy-Hb) was measured around the gastrocnemius muscle during a 90-sec CPT. Compared with the control group, greater changes in oxy-Hb and Di were found in the hypertensive group. Δoxy-Hb correlated with ΔDi. These data suggest that the response of oxygenation to the CPT may be useful to evaluate endothelial function.　(J Jpn Coll Angiol, 2011, **51**:255–257)

Key words: endothelial function, near infrared spectroscopy, cold pressor test

Introduction

Although blood pressure is the gold standard for diagnosing hypertension, it is unsuitable for evaluating arterial function in the early stages of cardiovascular disease. Arterial compliance/stiffness is determined by functional and structural components related to the intrinsic elastic properties of arteries.[1, 2] To evaluate endothelial function, the arterial structure must be measured, which can be carried out via the cold pressor (CPT) or flow-mediated dilation test.[3, 4] The CPT, which results in the production of NO via sympathetic activation, is one of several novel methods for evaluating endothelial function.[5] These methods are complicated and time-consuming. At the clinical level, an easier screening tool/method is required.

Near infrared spectroscopy (NIRS) can monitor the balance between oxygen consumption and supply by measuring optical absorption changes in oxygenated and deoxygenated hemoglobin (Hb)/myoglobin. Some studies have suggested that oxygen status as determined by NIRS is influenced by arterial function.[6, 7] Therefore, NIRS measurements may facilitate the evaluation of an individual's risk of cardiovascular disease. However, no previous studies investigated arterial function in comparison with NIRS findings.

In the present study, we compared the responses of oxygenation and carotid artery diameter to the CPT between hypertensive and healthy elderly patients.

Methods

Subjects

We enrolled 30 elderly women. Ten subjects with a history of antihypertensive medication or smoking were excluded. The 20 remaining subjects were divided into two groups according to their systolic/diastolic blood pressure (SBP/DBP): a hypertensive group of subjects who had SBP of over 140 mmHg or DBP of over 90 mmHg (n=10, age: 69.3±6.4 yrs, height: 150.1±3.4 cm, weight: 53.8±5.4 kg, SBP: 153.7±20.8 mmHg, DBP: 86.4±6.9 mmHg) and a control group of subjects who had SBP of less than 140 mmHg and DBP of less than 90 mmHg (n=10, age: 70.6±3.3 yrs, height: 151.3±5.2 cm, weight: 51.5±8.3 kg, SBP: 123.7±15.6 mmHg,

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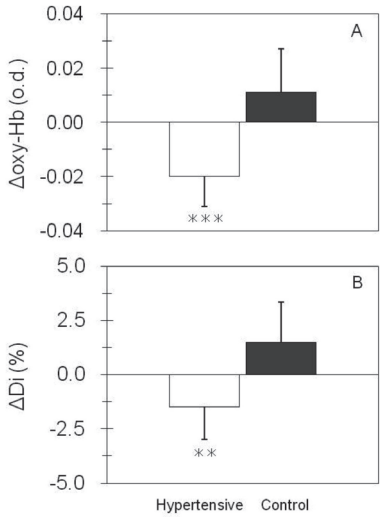

Figure 1 Comparisons of Δoxy-Hb and ΔDi during a CPT between the hypertensive and control groups.
Data are mean ± SD.
* * (p<0.01), * * * (p<0.001): significantly different from the control group

DBP: 72.3±6.3 mmHg).

CPT: cold pressor test

The subjects remained in a supine position with their knees at a right angle for 20 min. Then, a CPT was performed by immersing the left foot up to the ankle in ice slush for 90 sec, a modification of previous methods.[4, 8] The subjects were instructed to avoid breath-holding, muscle contractions, and Valsalva maneuvers. The left side of the common carotid artery was imaged using a 7.5-Mhz linear array transducer ultrasound system (SSA-340A: Toshiba Med Co Ltd) before the baseline and for 20 sec during the CPT. Longitudinal artery images were recorded on videotape for subsequent off-line analysis. The rate of change in arterial diameter (ΔDi) was calculated by comparing baseline findings with those at the end of the CPT using image analysis software (NIH imager). To measure oxygenated Hb (oxy-Hb), an NIRS probe (HEO-200: OMRON Co Ltd) was positioned over the left gastrocnemius muscle throughout the CPT. The difference between the data at rest and the data obtained in the last 10 sec of the CPT was adopted for Δoxy-Hb. In both Δ values, a positive number indicates an increment, and a negative numbers indicates a decrement.

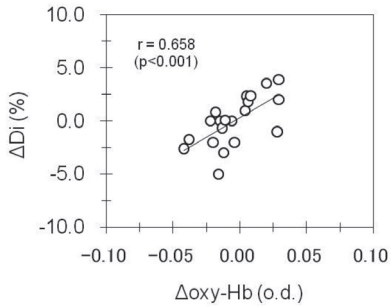

Figure 2 Relationship between Δoxy-Hb and ΔDi during a CPT.

Statistics

All parameters were compared between the two groups using a non-paired t-test. Simple linear regression analysis was used to determine the relationship between measurements. The level of significance was set at p<0.05. All values are presented as the mean ± SD.

Results

The Δoxy-Hb values in the hypertensive and control groups were –0.020±0.011 and 0.011±0.0163 (**Figure 1A**), and the ΔDi values were –1.49±1.50% and 1.50±1.85% (**Figure 1B**), respectively. The negative values of both Δoxy-Hb and ΔDi were greater than their positive values. There were significant differences in Δoxy-Hb (p<0.001) and ΔDi (p<0.01) between the two groups. There were also significant linear relationships between ΔDi and Δoxy-Hb (r=0.658, p<0.001; **Figure 2**).

Discussion

We measured the responses of oxygenation and carotid artery diameter to the CPT and found greater changes in Δoxy-Hb and ΔDi in the hypertensive group than the control group. Our findings concerning carotid artery diameter are consistent with those of previous studies.[8, 9] The greater changes in ΔDi during the CPT in the hypertensive group may be the result of the balance between adrenergic vasoconstriction and vasodilatation. The normal vasodilator response to a CPT can be blocked by competitive inhibition of L-arginine, a substrate for NO synthase,[5] and L-arginine may have normalized the vasoconstrictor response in the hypertensive group.[10] Previous studies have suggested that NIRS has potential for

evaluating the level of oxygen supply and vasoconstriction/dilation.[6, 7] Thus, greater change in oxy-Hb might reflect abnormal vasodilation during a CPT in hypertensive groups.

In the present study, Δoxy-Hb correlated with ΔDi ($p<0.001$). NIRS was applied to superficial capillaries/vessels around the gastrocnemius muscle. The response of an artery to the CPT was evaluated at the carotid artery. Because the measurement areas were different, it remains an unsettled question whether we could compare the oxygenation at peripheral areas to carotid artery changes. However, our findings suggest that oxygenation by NIRS might be able to evaluate arterial function, especially endothelial function.

Limitations

Measuring and analyzing arterial function using NIRS is easier and takes less time than using an ultrasound echo device. However, there were some limitations to our study. First, NIRS measurements reflect the changes in oxygenation near the surface, including arteriole, venule, and capillary changes. Further studies are needed to clarify the contribution of each vessel's oxygenation determined using NIRS. Second, the NIRS signal was influenced by subcutaneous fat. In our subjects, subcutaneous fat around the gastrocnemius muscle using a skinfold caliper was 5.0±1.4 mm in the hypertensive and 4.7±1.6 mm in the control group (n.s.). Therefore, calibrating data using an occlusion test or analyzing data using kinetics for oxygenation should be considered in the case of a clinical trial. In addition to these points, the CPT sometimes causes elevated blood pressure. Though using this method has some disadvantages, it has the advantage of being non-invasive while still facilitating easy detection and early diagnosis of endothelial dysfunction.

NIRS can be used not only for measuring metabolism in human tissues, but also has the possibility of diagnosing and evaluating various diseases. We included a small number of elderly people as subjects. To confirm this method of evaluating endothelial function, a larger number of subjects should be targeted, considering a greater variety of ages, past illnesses, or severities of disease.

Conclusion

We measured the responses of oxygenation and carotid artery diameter to a CPT. Compared with the control group, greater differences in Δoxy-Hb and ΔDi were found in the hypertensive group. Δoxy-Hb correlated with ΔDi. These findings suggest that oxygenation measured using NIRS might useful to evaluate endothelial function.

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