Preliminary Study on the Assessment of Peripheral Vascular Response to Cold Provocation in Workers Exposed to Hand-Arm Vibration Using Laser Doppler Perfusion Imager

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Received March 10, 2005 and accepted June 1, 2005

Abstract: Measurements of changes in finger skin blood flow with laser Doppler perfusion imaging (LDPI) in response to cold provocation test (10°C, 10 min) were performed in 12 men suffering from vibration induced white finger (VWF) and 13 exposed controls. The mean perfusion values in both groups reduced markedly as a result of immersion of the hand in cold water. In the controls, however, the mean value increased gradually until the end of the cold provocation, while that in the VWF subjects remained at the lowest level. After removal of the hand from the cold water, the skin blood perfusion in the controls recovered rapidly and nearly reached the baseline value. In the VWF subjects, it had a slight increase immediately following the cold immersion but no tendency to rise as the time span increased. Analysis of covariance controlling for possible confounders revealed that the VWF subjects had significantly lower perfusion values compared to the controls in the last several minutes of the cold provocation and the following recovery. These findings suggest that the LDPI technique enables visualizing and quantifying the peripheral vascular effects of cold water immersion on the finger skin blood perfusion and thus has the potential of providing more detailed and accurate information that may help detect the peripheral circulatory impairment in the fingers of vibration-exposed workers.

Key words: Hand-arm vibration, Finger skin blood perfusion, Laser Doppler perfusion imaging, Cold provocation test

Introduction

Long-term exposure to hand-transmitted vibration at work can be the cause of various symptoms, e.g., an evolution of early sensory neural disorders with paraesthesias and pain gradually becoming persistent, and increasing motor neural and musculoskeletal symptoms in hands and arms (HAVS)1–3. Of these, the best-documented symptom is cold-induced vibration white finger (VWF), also known as “occupational Raynaud’s phenomenon”, characterized by symmetrical intermittent reversible vasospasm of the digital arteries. Several objective tests have been developed to detect circulatory impairment in the fingers of vibration-exposed workers5. Measurement of finger skin temperature in combination with local cooling of the fingers and hands has been most commonly used in the survey of vibration syndrome. The cold provocation will simulate the interruption of digital blood flow that is presumed to occur in cold environments. Laser Doppler velocimetry has been widely used as a noninvasive method for the measurement
of finger blood flow to surface tissue\(^4,5\). The technique can be used for investigating the response to vasoconstrictive stimulus such as cold water immersion test and it has been applied in the case of some workers who use hand-held vibrating tools\(^6–8\). In conventional instruments, however, the laser light is transmitted to and from the tissue by optical fibers, and the perfusion within only a small area of an approximately 1 mm\(^3\) tissue volume at the tip of the probe is recorded. Therefore, no information is attained as to how the perfusion varies over the skin surface regardless of the fact that tissue perfusion frequently shows a substantial spatial variation resulting in significant differences in perfusion values even at adjacent sites. Laser Doppler perfusion imaging (LDPI) is a new technique for mapping cutaneous blood flow\(^9\). The method employs a two-dimensional horizontal scanning of the flow in a specific tissue, and makes it possible to visualize the spatial variation over the region of interest. By the introduction of the imaging concept in laser Doppler image scanning technology, the limitations in genetic laser Doppler flowmetry will be overcome, and the spatial heterogeneity in tissue perfusion can be investigated. It can, therefore, allow for a detailed analysis of the peripheral vascular response following the immersion of the hand in cold or hot water.

The present study was undertaken to evaluate the peripheral circulatory function of the workers exposed to hand-arm vibrations by monitoring the response of finger skin blood perfusion to a cold provocation test using the LDPI technique.

### Subjects and Methods

#### Study subjects

The present subjects examined were 12 men suffering from VWF who had worked on private forestry enterprises using chainsaws. In addition, among public service workers who were mainly working to maintain the public roads or afforesting and gardening on a farm by using bush cutters, 13 men without any sings of symptoms related to vibration syndrome were selected and treated as exposed controls. No subject was found to be affected with metabolic, cardiac, or occlusive arterial diseases, and none of them took any medication at the time of examination. The demographic data of the two groups as well as the outline of disorders in the VWF subjects are shown in Table 1. There was a significant difference in age between the groups (\(p<0.01\)). The VWF subjects had been exposed to a high level of vibration for a significantly longer time compared to the exposed controls (\(p<0.05\)). The controls had not used a chainsaw and were not operating a bush cutter habitually in their routine work. On the Stockholm Workshop scale\(^{10}\), four subjects with VWF had Raynaud’s phenomenon in their tested hand classified as Stage 3 (severe), six of them were Stage 2 (moderate), and two into Stage 1 (mild). All the subjects with VWF suffered from numbness in their hands; nine were recognized to be in the stage of 2SN and three were in 1SN\(^{11}\). The subjects signed a written informed consent form after receiving a detailed explanation of the study aims and procedures. The protocol of this study was approved by the Ethic Committee of the Wakayama Medical University.

#### Experimental protocol

Simultaneous measurements of the finger skin blood flow and temperature were performed at one-minute intervals before, during, and after the hand was immersed into the cold water (10\(^\circ\)C, 10 min). The finger skin blood flow was measured by the laser Doppler perfusion imager (PeriScan PIM-II, PERIMED Co, Sweden). The scanner head was
placed parallel to the surface of the finger, and the laser beam scanned over the area of \(3 \times 3\) cm at the palmar side of distal phalanx of the subject’s most severely affected finger. During scanning, the area of interest was placed right under the scanning head with the laser beam pointing at the center of the measurement area. The distance between the tissue surface and the lower part of the scanner head during image capturing was fixed to 15 cm. When capturing perfusion images, the ambient light level was kept at a minimum in order to avoid the influence on laser light and the recorded numerical blood perfusion values. The finger skin temperature was also taken by an electrode thermistor (Takara Thermistor D922, TECHNOL SEVEN Co., Japan) attached to the skin on the dorsal side of the index finger. All measurements were performed in a quiet, air-conditioned room (24.4 ± 0.4°C) after the subjects had a sufficient rest for equilibration to room temperature. To avoid nicotine-induced vasoconstrictive effects of the digital vessels, smokers refrained from smoking for at least two hours before testing.

**Laser doppler perfusion imaging**

Laser Doppler perfusion imager is a camera-like device intended for two-dimensional mapping of the superficial tissue blood perfusion (Fig. 1). The low power (1 mW) laser beam (wavelength, 670 nm) successively scans the tissue step-wise throughout a large number of measurement sites\(^1\). In the tissue, the light is scattered and frequency shifted as it interacts with the moving blood cells according to the Doppler principle. The sampling depth is in the order of a few hundred micrometers\(^2\). In the step-wise scanning technique, the laser beam is arrested during a time period of about 50 milliseconds to record the back-scattered light. A fraction of the back-scattered and Doppler-broadened light is detected by a photo-detector positioned in the scanner head. The recorded Doppler signal is fed to a computer via an optical isolation box, demodulated, and converted into an electrical signal. The signal is further processed to a scale which is linearly with tissue perfusion defined as the product of the blood cell velocity and concentration. All perfusion signals are eventually combined to form a color-coded image using a scale ranging from dark blue (lowest value) to red (highest value) and then displayed on a monitor screen (Fig. 2). In addition, a numerical perfusion value is obtained for each measurement site in terms of voltage (V) and used as the basis for calculation of the mean perfusion values in a region of interest. System specific changes in the mean values are treated as the evaluation parameter for quantification of alternations in skin blood perfusion. In the present analysis, we calculated the mean perfusion values in an area of 10 mm\(^2\) in the tip of tested finger for each image recorded during the course of observation (The area size corresponds to 81 measurement sites).

![Cross section of the Scanning Head](image)

**Fig. 1.** The PIM-II laser Doppler Perfusion Imager system for non-invasive imaging of superficial tissue. Based on the well-known laser Doppler principle, it collects back-scattered light without touching the tissue and generates color-coded images of the spatial distribution of the tissue perfusion.
Statistical analysis

All statistical analysis was conducted using the SPSS statistical package 12.0 (SPSS Software, Inc., Chicago, Illinois). Analysis of covariance (ANCOVA) was used for comparisons of the data between the groups controlling for the effects of a subject’s age and room and water temperatures during immersion test as a covariate. The correlation coefficients were also computed by the Pearson product-moment correlation method. Results are expressed as mean ± SEM, number of cases, or percentages. The level of significance was defined as $p<0.05$.

Results

The changes in finger skin temperature in response to the cold water immersion were shown in Fig. 3A. The baseline finger skin temperature of VWF subjects and controls was not significantly different (VWF: $31.5 ± 0.7^\circ$C vs. controls: $31.7 ± 0.6^\circ$C on average during 5 min rest period before immersion, $p=0.44$). As a result of the immersion of the hand into cold water, the skin temperature of both groups was gradually decreased, and the VWF subjects had a lower temperature compared with the controls; however, there were no significant differences between groups (VWF: $11.7 ± 0.6^\circ$C vs. controls: $12.4 ± 0.5^\circ$C at the 10th min during immersion, $p=0.09$). During a recovery period of 10 min following the cold water immersion, the controls were likely to have recovery in their skin temperature from the 3rd min after removal of the hand from cold water. Significant differences in the finger skin temperature of the controls compared to the VWF subjects were found from the 5th min to the 10th min after the cold provocation test (VWF: $18.5 ± 1.3^\circ$C vs. controls: $25.0 ± 1.7^\circ$C at the 10th min after immersion, $p<0.05$).
Examples of the relative changes in skin blood perfusion imaging in the tip of the test finger in one of each group before, during, and after the cold water immersion are shown in Fig. 4. At each point in the image, the skin blood perfusion is color coded using a scale ranging from dark blue (lowest value) to red (highest value). The difference in the responses of skin blood perfusion under the condition of cold immersion between the VWF subjects and controls was clearly demonstrated in this sequence of images.

Figure 3B summarizes the mean values of skin blood perfusion in the fingertip during the course of observation for both groups of subjects. The baseline blood perfusion values of VWF subjects were lower than the controls; but significant differences could not be obtained (VWF: $1.05 \pm 0.08$ V vs. controls: $1.38 \pm 0.11$ V on average during 5-min rest period before immersion, $p=0.49$). When the hand was immersed in the cold water the skin blood perfusion reduced markedly, and a cold-induced vasoconstriction was noticed in both the VWF subjects and controls. In the controls, there was a slight gradual increase in blood perfusion which was rather stable the last 3 min of the cold immersion, while the perfusion in the VWF subjects remained at the same lowest level which was observed immediately after the immersion. Furthermore, during the recovery period following the cold provocation, the skin perfusion in the controls recovered rapidly and nearly attained the baseline value by 5 min after the removal of the hand from cold water. In the VWF subjects, the skin perfusion had a slight increase immediately following the cold water immersion and no tendency to rise as the time span increased. The significant differences in the finger skin perfusion of the VWF subjects and controls were found at the last 2 min of the cold water immersion (VWF: $0.32 \pm 0.04$ V vs. controls: $0.60 \pm 0.05$ V at the 10th min during immersion, $p<0.05$) and throughout the following recovery period (VWF: $0.39 \pm 0.10$ V vs. controls: $1.20 \pm 0.13$ V at the 10th min after immersion, $p<0.01$) after statistically controlling for age and room and water temperatures.

In each phase of the cold water immersion test, there were significant linear relationships between the values of finger skin blood perfusion and finger skin temperature. The correlation coefficients for the regression lines in total subjects were relatively high at baseline resting condition prior to cold immersion ($r=0.73$, $p<0.01$) and during the recovery period after the end of the immersion ($r=0.78$ at the 10th min after the immersion, $p<0.01$) but had a tendency to be low when the hand was being immersed in cold water ($r=0.40$ at the 10th min during the immersion, $p<0.05$).

**Discussion**

This study was designed to test the possibility of LDPI technique to investigate peripheral vascular response to cold water immersion in workers exposed to hand-arm vibration. We have found the significant difference in the patterns of the finger skin perfusion during and following the cold water immersion between subjects with VWF and exposed controls without any symptoms of vibration syndrome. It seems, therefore, possible that repeated image scanning of finger skin blood perfusion based on the LPDI technique will become a valuable means for detection of impaired vascular regulation in the fingers of vibration-exposed workers.

Conventional laser Doppler blood flowmetry can be used for identifying the presence of and response to a vasoconstrictive stimulus such as a cold water immersion test, and it has been used with some workers operating
vibrating tools\textsuperscript{6–8}). A clear drawback to laser Doppler flowmetry is, however, that the probe covers only a small area (less than 1 mm\textsuperscript{2}) and, therefore, local differences in skin blood flow may markedly influence results obtained. In fact, some researchers have found the reduction to be greater in men with the symptoms related to HAVS than in exposed controls\textsuperscript{7} but others have not\textsuperscript{8}. The LDPI technology is considered a further development of the genetic laser Doppler flowmeter of which the intended use is to continuously monitor the tissue blood perfusion in a single spot. By the introduction of the imaging concept, the spatial heterogeneity in the tissue blood perfusion can be investigated, while at the same time, averaging the blood perfusion over an area of a specific extension increases the reproducibility. Furthermore, the visualization of skin blood perfusion over larger area in the hands has the benefit of detecting the impaired vascular regulation in the fingers among VWF patients which generally appears with spatial variations\textsuperscript{2, 3}.

It has been shown that hand-arm vibration induces a decrease in blood flow in normal fingers as a result of vascular injury and abnormalities in vasoregulatory function\textsuperscript{14, 15}. The clinical condition of VWF includes components of an exaggerated vasoconstriction and impaired vasodilatation manifested under cold conditions. Cold provocation testing of the hand simulates the interruption of finger blood flow that is presumed to occur in cold environments. The two general approaches to cold provocation tests are blood pressure and skin temperature measurements, the later being a presumed surrogate for blood flow\textsuperscript{16}. The finger systolic pressure tests, measurement of critical opening pressure after local cold provocation, may record the interruption of digital blood flow in a context of vasoconstriction, whereas skin temperature recovery tests are a measure of vasodilatation\textsuperscript{17}. Therefore, inconsistent findings such as an absence of abnormal finger blood pressure against a delayed skin temperature recovery could be observed in some cases\textsuperscript{16}. It has also been noted that there is lack of concordance between skin temperature recovery and symptoms of vibration-related vasospastic disease assessed by the Stockholm workshop scale\textsuperscript{18}. In this investigation, the mean skin perfusion value measured by LDPI and skin temperature in fingers were closely correlated with each other at baseline and the recovery phase but were weakly correlated when the hand was being immersed in cold water, indicating that skin temperature cannot fully represent the state of digital perfusion during the immersion. The finger systolic pressure test has been used in many laboratories as a standard method for demonstrating increased vascular cold reactivity in patients with VWF\textsuperscript{19, 20}. It seems possible that repeated monitoring of skin blood perfusion before, during, and after the cold provocation test can reveal the different aspects of vascular reflection to cold, namely the vasoconstrictive response to cold exposure and the following vasodilatation.

We demonstrated that the changes in mean perfusion values in response to cold conditions in the VWF subjects and controls were clearly different. In the controls, even during cold water immersion, the digital skin perfusion gradually increased, but such recovery could not be observed in the VWF subjects. A more extreme vasoconstrictive response to cold can inhibit the normal periodic increase in skin blood perfusion. The excessive vasoconstrictive response in VWF patients is thought to be attributed to both of enhanced sympathetic vasomotor activity in response to cold and digital vessel abnormalities which are characterized by a medial muscular hypertrophy with narrowed lumen and impaired endothelium\textsuperscript{21–23}. These pathophysiological features may account for the absence of blood flow recovery observed during the cold immersion among the subjects in VWF group. Furthermore, in the recovery phase, skin blood perfusion of the controls rapidly increased, while that of the VWF subjects had no tendency to recover as the time span increased. Such hemodynamic behavior may also be associated with prolonged vasoconstriction and/or delayed vasodilatation due to enhanced sympathetic activity to cold exposure and vascular abnormalities in finger arteries. In addition, as for the recovery of digital circulation following the cold provocation, it seems that measurement of the blood perfusion could expeditiously detect differences between the vascular capacity of VWF patients and workers free from vibration-related symptoms when compared to the results obtained for skin temperature. This might be due to the fact that skin temperature generally has a less pronounced increase and requires a longer recovery time than the blood perfusion.

There are several potential limitations in this study. First, the study samples were consisted of relatively small sample size and selected without the application of a pair-matching procedure. Although the possible confounding effect of age difference between the groups was statistically controlled, this might influence some of the results in the present analyses. Second, in the LDPI technique, standardized protocol for assessment of skin blood perfusion has not fully been demonstrated and interpretation of clinical data seems to be complex. As these procedures should be further developed, LDPI may provide a beneficial method for clinical investigation and monitoring of the peripheral circulatory functions of vibration-exposed workers. Third, our effort
in this preliminary investigation was focused on examining the possibility of LDPI technique for the assessment of peripheral vascular response to cold provocation in the VWF patients. Further research with use of large number of samples and well-controlled design will be required to demonstrate the usefulness of this method as a reliable objective test for detecting peripheral circulatory impairment among vibration-exposed workers.

**Conclusion**

The results of this study suggest that the LDPI employing multiple points recording and spatial mapping, will become an important quantitative tool for the study of changes in finger skin blood flow after application of cold water immersion. Therefore, it seems that the technique can provide more detailed and accurate information that may help detect the impaired vascular regulation in the fingers among workers exposed to hand-arm vibration.

**Acknowledgements**

This work was financially supported by a research grant from the Ministry of Education, Culture, Sports, Science and Technology of Japan (grant No.15590511) and by a Trust Grant from Japanese Ministry of Health, Labour and Welfare for scientific research on accidents.

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