Vibration Preconditioning as a Method to Reduce Hyperemia Responses to Plantar Pressure-Induced Ischemia

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Research

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Abstract

Background: One of the main causes for foot ulcers in diabetics is an excessive, constant load on the foot which over time leads to ischemia. The aim of this study is to explore whether vibration preconditioning can alleviate pressure-induced hyperemia responses in foot tissue.

Methods: Fifteen healthy subjects were subjected to compression stimulation with or without vibration preconditioning, determined randomly. Skin blood flow and temperature were measured under the first metatarsal head of the right foot for each subject and compared across the test group.

Results: The results showed that both test groups displayed a reactive hyperemia response, but the peak hyperemia was significantly decreased when vibration was used in combination with compression. In the group subjected to compression only (no vibration), the plantar skin temperature during the first minute after compression was significantly higher than the basal temperature, but this was not so when vibration was applied.

Conclusions: The results of this study suggest that vibration preconditioning before the application of compression can decrease the degree of reactive hyperemia and alleviate pressure-induced ischemic damage. These findings may be used to develop methods to protect against pressure-induced foot lesions in diabetic people.

Background

Diabetes is a serious chronic disease with an increasing prevalence worldwide, primarily due to lifestyle choices [1]. Diabetic foot is one of the most serious complications associated with diabetes, and can have a considerable effect on the health and quality of life for people living with it [2]. The lower extremities in diabetics typically succumb to peripheral vascular disease and peripheral neuropathy. The resulting improper loading of the foot often leads to foot ulcerations due to pressure-induced ischemia [3–5]. The sustained excessive loading causes the capillary vessels to collapse, which disturbs blood regulation, hinders the transportation of nutrients and waste products, and induces tissue ischemia [6–8]. After the release of loading, a reactive hyperemia appears to compensate for the ischemia during compression. However, for diabetics with poor microcirculation, the microvasculature is unable to supply sufficient oxygen to compensate for ischemic damage, which increases the risk of developing foot ulcers [9]. Therefore, to maintain healthy feet, it is important to avoid or reduce pressure-induced ischemia so as to improve tissue viability.

Common methods to treat or prevent diabetic ulcers include drugs, prescription shoes/insoles and mechanical intervention, such as vibration. As a conservative and effective treatment method, vibration has been extensively used to relieve pressure injuries, facilitate wound healing and improve microcirculation. Weinheimer-Haus et al. found that low intensity vibration could promote angiogenesis and wound healing in diabetic mice [10]. Wong et al. showed that vibration could effectively curb oxidative damage and largely maintain the enzymatic anti-oxidative defenses in compressed tissue [11].

Ennis et al. reported that vibration could facilitate angiogenesis and the formation of granulation tissue by promoting the expression of growth factors and reducing hypoxia-inducible factors [12]. Moreover, Ren et al. reported that the increase of plantar skin blood flow appears during and after local vibration stimulation in people with diabetes [13]. Bergstrand et al. pointed out that vasodilation during pressure loading is helpful to relieve the ischemic injury[14]. These studies demonstrate that vibration can relieve pressure injury by improving the cellular biomedical environment, reducing oxidative stress and increasing the supply of blood to tissues. Thus, we suspect that vibration could be integrated with offloading shoes/insoles to reduce ischemic damage caused by mechanical stress in the foot of diabetic people. However, in practice, applying vibration during walking would not be practical and would likely disturb daily activities.

Preconditioning is often used to alter the original state of tissue, and it is widely acknowledged that vibration is an effective preconditioner for improving athletes' performance. Ren et al. demonstrated that local vibration had a residual effect on improving microcirculation after intervention in plantar tissue in diabetics [13]. Weinheimer-Haus et al. also reported that low-intensity vibration has a persistent positive effect on the cellular biochemical environment by promoting wound healing [10]. Thus, the authors speculated that preconditioning plantar tissue using vibration may enhance the viability of the tissue and reduce pressure-induced ischemic damage. Zhu et al. investigated the effect of local vibration preconditioning on plantar skin blood flow after the subject's feet were loaded by walking, and found that local vibration could reduce the walking-induced hyperemic response [15]. However, the characteristics of the subjects' plantar pressure during walking were not controlled and there may be considerable pressure differences between subjects. Also, Pu et al. noted that the accumulated mechanical stimulus was an important factor in assessing the risk of developing diabetic foot ulcers, and has a distinct effect on microvascular responses [16]. Thus, the accumulated pressure should be considered when evaluating the efficacy of vibration preconditioning intervention.

Therefore, this study investigated changes in skin blood flow and temperature responses in plantar tissue subjected to a fixed pressure stimulus with and without vibration preconditioning. The aim was to investigate whether vibration preconditioning could reduce the degree of reactive hyperemia and alleviate pressure-induced ischemia.

Methods

Participants

According to the estimation of sample size based on the experimental data of preliminary tests and previous studies[15], Eighteen healthy subjects were enrolled in this experiment. The inclusion criteria were: (1) had no calluses, redness, inflammation or wounds on the skin of feet and legs, and (2) had no history of disease such as hypertension, peripheral neuropathy, vascular disease, heart disease, systematic inflammation, or malignant tumors. A total of fifteen subjects (5 males and 10 females) aged 24.27 ± 2.05 years old met the criteria and participated in this study. This study was conducted in

accordance with clinical protocols approved by the institutional review board of Affiliated Hospital of National Research Center for Rehabilitation Technical Aids (registered under study number 20190101) and in compliance with the Declaration of Helsinki. All subjects were briefed on study aims and methods and gave informed written consent prior to participation.

Experimental Procedure

The first metatarsal head (M1) of the right foot of each subject was chosen as the region for analysis because it is one of the most high-risk areas for the development of foot ulcers in diabetics [17]. A laser doppler flowmeter (PeriFlux 5001, Probe 457, Perimed, Stockholm, Sweden) was used to measure the skin blood flow (SBF) and temperature (Temp) of the M1 region at a sampling frequency of 32 Hz, with an accuracy of $\pm 5\%$ and $\pm 0.5\text{ }^{\circ}\text{C}$, respectively. All subjects were asked to rest for 30 min in a room at a temperature of $25 \pm 1\text{ }^{\circ}\text{C}$ before the experiment, and were then randomly assigned to either Vibration Preconditioning or No Vibration preconditioning; both tests were performed on each subject, but the order was random. All tests were conducted in a supine position, and at least an interval of 30-min was needed between each test.

The test period consisted of 4 stages:

- *Baseline stage*; During the first 5 min of the test, the basal SBF and Temp of M1 in the right foot were measured continuously without any interventions.
- *Vibration preconditioning stage*; This stage was only applicable to the Vibration Preconditioning test. For the following 10 min after the Baseline stage, a 30 Hz vibration with an amplitude of 2 mm was applied to the region under M1 of the right foot.
- *Compression stage*; For the following 3 min after vibration ceased, a compression stimulation of 300 mmHg was applied to the region under M1, and the SBF and Temp were measured continuously.
- *Recovery stage*; The compression stimulation was then removed, and the SBF and Temp of M1 were measured continuously for 5 min.

The No Vibration test consisted of Baseline, Compression and Recovery stages, while the Vibration Preconditioning test consisted of all 4 stages.

The vibration and compression stimulations were controlled and delivered through a custom-made device. The vibration head was a cylinder with a diameter of 10 mm and shore hardness of 87°. The compression indenter was calibrated to deliver a pressure of 300 mmHg.

Data Collection

Variations in SBF and Temp during the Baseline, Compression and Recovery stages were analyzed for both tests. The SBF was expressed as raw values (perfusion unit, pu) and normalized values. The mean value of SBF was calculated during the Baseline stage and Compression stage, and the peak SBF and hyperemia was calculated during the Recovery stage [18]. The normalized peak SBF and hyperemia during the Recovery stage were calculated by dividing by their mean values during the Baseline stage respectively. Similarly, the mean value of Temp was calculated during the Baseline stage and Compression stage, and Recovery stage. As the hyperemia mainly appeared in the first minute after the release of compression, the evaluation focused on the mean values of temperature during the first minute of the Recovery stage. All variables in the Recovery stage were normalized by their values during the Baseline stage.

Statistical Analysis

The normality of the variables was checked using a Shapiro-Wilk test, which determined whether a paired t-test or a Wilcoxon matched-pair signed-rank test would be used for evaluating differences in results between the three stages in each test. Differences in SBF and Temp responses between the two tests were also analyzed by a paired t-test or Wilcoxon matched-pair signed-rank test. A statistical significance level of 0.05 was used. All statistical analyses were performed in SPSS (Version 20.0, IBM, Armonk, NY, USA).

Results

The mean SBF during the Baseline and Compression stage and the peak SBF during the Recovery stage were averaged across all subjects for both tests (Fig. 1). As can be seen in Fig. 1, the SBF during the Compression stage in both tests (No Vibration: 3.39 ± 1.10 pu; Vibration Preconditioning: 3.02 ± 0.65 pu) was significantly lower than the Baseline SBF (No Vibration: 13.32 ± 14.63 pu; Vibration Preconditioning: 12.66 ± 11.30 pu). Moreover, significant increase in SBF appeared after the Compression stage, and displayed a reactive hyperemia during the Recovery stage for both tests, and the peak SBF is shown in Fig. 1 (No Vibration: 125.35 ± 65.39 pu; Vibration Preconditioning: 104.93 ± 51.49 pu).

The normalized peak SBF and hyperemia during the Recovery stage for both tests are illustrated in Fig. 2. The normalized peak SBF was significantly lower ($p < 0.05$) in the Vibration Preconditioning test than the No Vibration test. No significant difference ($p > 0.05$) was found in hyperemia between the two tests.

Variations in the mean temperature (Temp) of M1 during the three stages for both tests are shown in Fig. 3. For the No Vibration test, there was no significant difference in Temp between the Compression stage (24.95 ± 2.43 °C) and the Baseline stage (24.85 ± 2.55 °C). However, there was a significant increase in Temp during the first minute of the Recovery stage (25.32 ± 2.50 °C) ($p < 0.05$). For the Vibration Preconditioning test, no significant difference was found in Temp between the Compression stage (24.35 ± 1.83 °C) and the Baseline stage (24.43 ± 2.10 °C). There was a significant increase during the first minute of the Recovery stage (24.65 ± 2.02 °C) in comparison to the Compression stage, but this was still

not significantly higher than the Baseline temperature. Moreover, there was no significant difference in the normalized temperature during the Recovery stage for the two tests.

Discussion

This paper explored the effect of vibration preconditioning on SBF and Temp responses to a fixed pressure stimulus in plantar soft tissue. The results showed that vibration preconditioning could significantly reduce the increase of SBF during hyperemia and may help to maintain a relatively constant temperature in the recovery stage after the release of compression, as shown in Fig. 3 where there is no significant difference between the temperature at the Baseline and Recovery stages in vibration preconditioning test.

When epidermal pressure exceeds capillary pressure, the microvascular network becomes blocked [8]. This hinders the supply of oxygen and nutrition to the tissues and affects the transportation of metabolic waste and toxic substances in the lymphatic system [19–23]. After the pressure is released, the skin blood flow increases to compensate for the reduced oxygen supply to the ischemic tissue [24]. Excessive pressure can lead to an accumulation of xanthine oxidase in hypoxic-ischemic tissue, which may cause oxidative stress during the hyperemia process, and increase the risk of developing pressure ulcers [8, 11, 25]. In this study, a pressure of 300 mmHg was applied to the plantar soft tissue for three minutes to compress and induce local ischemia. When the compression was removed, a protective reactive hyperemia occurred to compensate for the oxygen depletion and accumulation of waste [24]. Thus, all subjects in both tests (Vibration Preconditioning and No Vibration) displayed reactive hyperemia after the release of compression (Fig. 1).

Normally, the level of reactive hyperemia is related to the degree of tissue ischemia [26, 27]. This study used the hyperemia response to assess the degree of ischemia caused by a pressure stimulus [28]. Previous studies have shown that vibration can improve microcirculation, maintain enzymatic oxidation defenses, reduce oxidative stress in hypoxia-ischemic tissue, and protect cell restorability and tissue viability [29, 10, 12, 11]. In our study, vibration was applied as a preconditioning step prior to compression. The results showed that preconditioning with vibration significantly reduced the peak SBF during hyperemia (Fig. 2). This implies that vibration preconditioning can effectively alleviate ischemia, and the size of the vibration in this study was enough to induce fewer peaks of SBF and Temp during hyperemia in the short time after compression (during Recovery stage) to compensate for oxygen depletion. However, there was no significant difference in the SBF hyperemia between the two tests (Fig. 2). A possible reason for this is the inherent ability of the healthy subjects recruited for this study to regulate their SBF, and the vibration stimulation in the Vibration test was of low enough intensity as to not have a demonstrable effect on the hyperemic response. Therefore, the two tests demonstrated a similar level of hyperemia to compensate for the ischemia [24, 16]. Zhu et al reported that the total hyperemia in a subject's foot after a walking stimulus was significantly decreased when vibration preconditioning was used [15]. This contrasts with the results of this study, possibly because of the different parameters for the vibration stimulation. In this current study vibration was applied at 30 Hz, whereas Zhu et al. used a

stronger vibration of 100 Hz, which may produce a stronger SBF response. In addition, the compression stimulus in Zhu's study was applied by asking the subjects to walk for a fixed duration and velocity, but individual variations in plantar pressure could not be accounted for. This would directly affect the SBF response in plantar tissue. This current study applied the same compression stimulus to all subjects. The difference methods of applying pressure may be another reason for the different results between the two studies.

The results of this study also revealed a significant increase in plantar skin temperature after the removal of compression during both tests. Moreover, Temp was significantly higher during the first 1 min of the Recovery stage than the basal temperature in the No Vibration test, but not in Vibration Preconditioning test. The results of increase in temperature in the recovery stage were in accordance with the variations of SBF, and the significant increase in Temp may imply a greater reactive hyperemia in the No Vibration test. Skin temperature is mainly regulated by the sympathetic nerve, which also plays a vital role in regulating vasomotion. Thus, skin temperature has been used as an alternative to SBF for characterizing microvascular responses [30]. However, the regulation of temperature related to central and peripheral blood flow is mainly regulated by dry heat exchange [31, 32]. And the mechanisms underlying the regulation of skin temperature and blood flow are distinct [33, 32]. Therefore, the correlation between skin temperature and SBF is nonlinear [34]. As shown in Fig. 1, there was a significant difference in SBF between the two tests during the Recovery stage, but there was no significant difference in Temp. This implies that the Temp response and SBF response to vibration preconditioning are likely governed by distinct mechanisms.

Compression for 3 min at 300 mmHg is commonly used to investigate post-occlusion microvascular responses because it is sufficient to cause tissue ischemia and induce compensative hyperemia [18, 9]. In our study, the same compression stimulation was applied to the plantar tissue in both tests to induce ischemia. It has been reported that low intensity vibration at 30–35 Hz can effectively reduce damage caused by mechanical strain and oxidation [35, 11]. Therefore, this study used a preconditioning vibration step with a frequency of 30 Hz and an amplitude of 2 mm.

This study has some limitations that should be acknowledged. First, the vibration stimulus had fixed parameters (frequency, amplitude and intermittent duration). Variations in these parameters could affect the physiochemistry and microcirculation responses. To determine the optimal parameters, further investigation is required to understand the relationship between the vibration parameters and the protective effect of vibration preconditioning. Similarly, the compression stimulation also had fixed parameters (duration and intensity) in this study. Changing these parameters could induce different levels of ischemic damage and disturb the protective effects of vibration preconditioning. Thirdly, only healthy subjects were enrolled in this preliminary study. These experimental results were also applicable for diabetic people who have the same physiological hyperemic responses. Future studies are warranted to verify the clinical effectiveness of vibration preconditioning in people with diabetes.

Conclusions

This study investigated the effect of vibration preconditioning on microvascular responses to pressure stimulus in plantar soft tissue. The results demonstrated that vibration preconditioning can effectively reduce peak skin blood flow and alleviate the degree of reactive hyperemia. This indicates that vibration preconditioning may be a practical method for alleviating pressure-induced ischemia in diabetics and could be used to protect their feet from pressure injuries.

Abbreviations

M1: First metatarsal head; SBF: Skin blood flow; Temp: Temperature; PU: Perfusion unit

Declarations

Ethics approval and consent to participate

This study was conducted in accordance with clinical protocols approved by the institutional review board of Affiliated Hospital of National Research Center for Rehabilitation Technical Aids (registered under study number 20190101) and in compliance with the Declaration of Helsinki. Informed consent was obtained from all individual participants included in the study.

Availability of data and materials

The dataset(s) supporting the conclusions of this article is(are) included within the article.

Conflict of interests

The authors declare that they have no conflict of interest.

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Authors' Contributions

Y.J., F.P., & Y.F. contributed to the concept and design of the study. H.L., W.R., Y.D., & W.Y. contributed to the data collection, analysis and interpretation of the results. W.R., Y.J., F.P., & Y.F. drafted and critically revised the manuscript. All authors agree to approve the final version of the manuscript, and be accountable for all aspects of the work.

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Figures

Figure 1

Variation in SBF during the Baseline (mean SBF), Compression (mean SBF) and Recovery (peak SBF) stages. SBF: Skin blood flow. "*" indicates a significant difference between stages for No Vibration test, and "#" indicates a significant difference between stages for Vibration Preconditioning test. The significance level was set at 0.05

Figure 2

Comparison of SBF response variables during the Recovery stage of No Vibration test and Vibration Preconditioning test. SBF: Skin blood flow. “*” indicates a significant difference in the variable between the two tests

Figure 3

Variation in Temp during Baseline (mean Temp), Compression (mean Temp) and Recovery (mean Temp of the first minute) stages. Temp: Temperature. “*” indicates a significant difference between stages for No Vibration test, and “#” indicates a significant difference between stages for Vibration Preconditioning test. The significance level was set at 0.05