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Effect of Local Physical Training on the Forearm Arteries and Veins in Patients with End-Stage Renal Disease

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Key Words

Arteries · Endothelium-dependent vasodilatation · End-stage renal failure · Handgrip training · Vascular access · Veins

Abstract

Aim: We investigate the effects of local training on the forearm vessels in patients with end-stage renal disease. ***Methods:*** Fourteen hemodialysis patients were included. Handgrip training was performed for 8 weeks. The following parameters were measured at the beginning of the study and 4 and 8 weeks later: forearm circumference, maximal handgrip strength, and artery and vein parameters, including endothelium-dependent and endothelium-independent vasodilatation (using ultrasound and duplex Doppler scanning). ***Results:*** The maximal handgrip strength increased significantly. The radial artery diameters were significantly higher after 8 weeks of training. The endothelium-dependent vasodilatation was found to be significantly increased after 4 and 8 weeks of training. The maximal vein diameters increased significantly with training, with preserved distensibility. ***Conclusions:*** The present study suggests that regular handgrip training increases the diameters of forearm vessels. It also improves endothelium-dependent vasodilatation. These changes point to the possible beneficial effects of daily handgrip training in chronic renal failure patients before arteriovenous fistula construction.

Introduction

Proper vascular access is of utmost importance for adequate hemodialysis and, consequently, for the long-term survival of chronic hemodialysis patients. The best vascular access in terms of long-term function and low complication rate is the native arteriovenous fistula [1]. The success rate of native arteriovenous fistula construction and function depends mainly on artery and vein status before the operation [2]. Arteries are frequently compromised because of premature atherosclerosis, although arm arteries are usually spared as compared with medium-size conduit arteries [3]. In patients with chronic renal failure, a combination of common atherogenesis risk factors, such as age, diabetes mellitus, hypertension, and dyslipidemia, with factors more specifically related to uremic states, such as dyslipoproteinemia, hyperfibrinogenemia, and hyperhomocysteinemia, is frequently present [4–6]. It has

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been suggested that the uremic state per se is associated with atherogenesis [7]. It was also found that the endothelium-dependent vasoreactivity, considered an indicator of vascular health, is impaired in adult chronic renal failure hemodialysis and prehemodialysis patients and even in children with chronic renal disease [8–10].

Training is known to be associated with structural and functional adaptations in the vasculature, increased capillary density, and increased maximal diameter of resistance arterioles in the skeletal muscles of treadmill-trained rats [11]. Some investigations indicate that regular local physical exercise enhances the local endothelial reactivity in patients with chronic heart failure, possibly through the enhanced endothelial release of nitric oxide [12, 13]. It was also shown that endurance training exerts modulatory influences on femoral and radial vessels [14, 15].

End-stage renal disease patients are frequently encouraged to perform regular forearm training to promote maturation of a new fistula. However, there is no published research to confirm the efficacy of this procedure [1]. Also, whether local regular training (handgrip exercise) can improve the hemodynamics of the forearm vessels before arteriovenous fistula construction and whether it improves the local endothelium-dependent vasoreactivity in patients with-end stage renal diseases is yet to be established.

The purpose of our study was to investigate the effects of daily handgrip training on the forearm arteries and veins in patients with end-stage renal disease.

Patients and Methods

Patients

Fourteen patients (mean age 49 ± 11 years; 7 men and 7 women) with end-stage renal failure were included in the study which was conducted from February to October 2001. To ensure proper supervision of the training program, only patients on hemodialysis were included. The patients had been on hemodialysis for 3 months to 22 years, three times weekly, 4–5 h per session. A native arteriovenous fistula was used as vascular access in all patients. The primary renal diseases were: diabetic nephropathy and chronic glomerulonephritis in 5 patients each and analgesic nephropathy, hypertensive nephrosclerosis, and chronic pyelonephritis in 1 patient each. In 1 case, the primary renal disease could not be established. Twelve patients required antihypertensive therapy, 5 were diabetics, 3 were smokers, and none had a history of cerebral or myocardial infarction. They all had a normal cholesterol level (4.3 ± 0.9 mmol/l). The study was approved by the Ethics Committee, and written informed consent was obtained from all patients after they had been duly informed of the nature of the study.

Methods

Handgrip Training Protocol

The patients were asked to perform the handgrip exercise with the arm without previous or present vascular access, using a rubber ring (4.5 cm inner and 7.5 cm outer diameter; maximal compression force: 50 N). They were asked to squeeze the rubber ring 20 times per minute, altogether 30 min each day. On the dialysis day, the training was performed during the hemodialysis procedure and supervised by the dialysis staff.

Measurements

The following parameters were measured at the beginning of the study and 4 and 8 weeks later during the course of the training program: forearm circumference, maximal handgrip strength, radial artery parameters (diameter and flow velocity), brachial artery parameters (diameter before and after hyperemic test and flow velocity), and vein diameters before and after placement of the tourniquet. The arm without permanent vascular access was chosen for the study. The measuring locations of the artery and vein parameters were marked at the beginning of the study using water-resistant, harmless paint to ensure that all further measurements were made on exactly the same spot.

The forearm circumference was measured at a 25% distance from the olecranon process to the wrist of the forearm being trained.

The maximal handgrip strength was measured using a hand dynamometer (model AD 141; Aesculap, Tuttlingen, Germany). The pressure on the dynamometer scale is expressed in millimeters. The average strength of two consecutive handgrips, each lasting approximately 3 s, was calculated.

Arteries: All measurements were performed by means of two-dimensional (B-mode) ultrasound and duplex Doppler scanning using a model 128 XP/10 computed sonography system (Acuson, Mountain View, Calif., USA). A two-dimensional linear electronic probe (Acuson L7) at 7.0 MHz, a pulse wave Doppler at 5.0 MHz, and a color Doppler at 5.0 MHz were used. The arterial flow velocity was measured by a pulsed Doppler signal at an up to 60-degree angle to the vessel, and the time-averaged flow velocity was calculated. Patients were advised to rest for 10 min at room temperature before measurements of both the radial (wrist) and brachial arteries (2–8 cm above the elbow) were performed while the patients in supine position. The baseline values of both the radial and brachial arterial diameters (d) and the flow velocity were measured three times, and their mean values were calculated (TAV = time-averaged velocity). The radial and brachial blood flows (Q) were also calculated using the formula $Q\ (ml/min) = \pi d^2/4\ (cm^2) \times TAV$.

A modified protocol proposed by Celermajer et al. [16] was used to estimate the endothelium-dependent vasodilatation of the brachial artery. The pneumatic tourniquet, placed proximally to the place where the brachial artery diameter was measured, was inflated to a pressure of 250 mm Hg for 4 min, and the brachial artery diameter was measured 60 s after cuff deflation. The increase of diameter was expressed as a percentage of the baseline value.

To estimate endothelium-independent vasodilatation, nitroglycerin spray (400 μg) was administered sublingually, and the brachial artery diameter was measured 3 min later. Again, the increase of diameter was expressed as a percentage of the baseline value [16].

Veins: The same ultrasound equipment was used to measure the vein parameters. The vein diameter was measured three times at three previously marked locations on the forearm, before and 1 min after placement of a pneumatic tourniquet around the upper arm

Table 1. Results of forearm artery, endothelium-dependent vasodilatation, and endothelium-independent vasodilatation measurements before and after 4 and 8 weeks of training

Variable	Before training	After 4 weeks of training	After 8 weeks of training	r-Anova p value
Diameter arteria radialis, mm	1.85±0.09	1.86±0.10 NS (p = 1.00)	1.91±0.08 p = 0.025	0.034
Arteria radialis flow velocity, cm/s	15.65±0.80	17.12±0.53 NS (p = 0.130)	16.36±0.62 NS (p = 0.553)	NS (p = 0.141)
Arteria radialis blood flow, ml/min	25.17±2.18	28.99±3.24 NS (p = 0.124)	28.66±2.50 NS (p = 0.058)	NS (p = 0.053)
Diameter arteria brachialis, mm	3.88±0.18	3.87±0.19 NS (p = 1.00)	3.91±0.19 NS (p = 0.995)	NS (p = 0.466)
Arteria brachialis blood flow, ml/min	128.7±12.20	128.6±12.58 NS (p = 1.00)	130.6±13.01 NS (p = 1.00)	NS (p = 0.874)
EDV, %	6.0±0.40	8.6±0.50 p < 0.001	10.3±0.74 p < 0.001	<0.001
EIV, %	11.1±0.65	11.2±0.31 NS (p = 1.00)	11.7±0.55 NS (p = 1.00)	NS (p = 0.537)

NS = Not significant; EDV = endothelium-dependent vasodilatation (increase of the brachial artery diameter after hyperemic test expressed as percent baseline value); EIV = endothelium-independent vasodilatation (increase of the brachial artery diameter after nitroglycerin administration expressed as percent baseline value).

which was inflated to a pressure of 100 mm Hg. The distensibility was expressed as the percent average increase in tourniquet measurements [2]. In order to minimize the impact of patients' hydration status on the venous diameter, all measurements in individual patients were always performed at the same time in relation to the hemodialysis session. The patients had approximately the same average body weight at the beginning of the study and 4 and 8 weeks later (before training 72.95 ± 3.55 kg, after 4 weeks 72.78 ± 3.53 kg, and after 8 weeks 72.27 ± 3.47 kg).

Statistics

The results are expressed as mean values ± SD for descriptive data and as mean values ± SE for comparative data. Repeated-measures analysis of variance (r-Anova) was used to compare data at baseline and after 4 and 8 weeks of training. If the r-Anova was significant ($p < 0.05$), paired t tests were performed with Bonferroni adjustment for three-way comparison. The results of measurements were analyzed using the SPSS package for Windows, version 10.1.

Results

Forearm Circumference

There was a small, yet statistically insignificant increase in the mean forearm circumference from 25.97 ± 0.52 cm before training to 26.22 ± 0.53 cm after 4 weeks ($p = 0.054$) and to 26.23 ± 0.55 cm after 8 weeks ($p = 0.125$) of training, i.e., by approximately 1%.

Maximal Handgrip Strength

The maximal handgrip strength measured with a dynamometer increased significantly from 24.1 ± 2.95 mm before training to 26.2 ± 3.06 mm after 4 weeks ($p = 0.005$) and to 28.5 ± 3.17 mm after 8 weeks ($p < 0.001$) of training.

Effect of Training on Arteries

The effect of training on the arteries is presented in table 1. The radial artery diameters remained practically unchanged for the first 4 weeks, but were found to be significantly increased ($p = 0.025$) after 8 weeks of training. On the other hand, both radial artery mean flow velocity and radial artery mean blood flow showed only a statistically insignificant tendency to increase after 4 and 8 weeks of training.

Brachial artery diameters and brachial artery mean blood flow remained unchanged throughout the training period. The change in the diameter of the brachial arteries after a 4-min upper arm occlusion, expressed as percent increase in diameter *(endothelium-dependent vasodilatation)*, was significantly higher after 4 weeks ($p < 0.001$) and 8 weeks ($p < 0.001$) of training, while the diameter of the brachial artery after the nitroglycerin application *(endothelium-independent vasodilatation)* remained unchanged throughout the training period.

Table 2. Effect of training on veins

Variable	Before training	After 4 weeks of training	After 8 weeks of training	r-Anova p value
Average vein diameter before compression, mm	2.25 ± 0.14	2.35 ± 0.12 NS (p = 0.470)	2.44 ± 0.12 p = 0.015	0.005
Average vein diameter after compression, mm	2.97 ± 0.18	3.10 ± 0.19 p = 0.007	3.18 ± 0.18 p < 0.001	<0.001
Distensibility of veins, %	33.1 ± 4.94	31.9 ± 4.07 NS (p = 1.00)	30.3 ± 3.53 NS (p = 1.00)	NS (p = 0.511)

NS = Not significant.

Effect of Training on Veins

The effect of training on the veins is presented in table 2. The average vein diameters before placement of the tourniquet remained unchanged for the first 4 weeks, but were found to be significantly increased after 8 weeks of training (p = 0.015). The average vein diameters after placement of the tourniquet were already significantly higher after 4 weeks (p = 0.007) and even higher after 8 weeks (p < 0.001) of training. The distensibility of the veins, expressed as percent increase of the diameter after inflation, remained unchanged.

Discussion

The native arteriovenous fistula continues to be considered the best vascular access in terms of long-term survival and low complication rate and is the procedure of first choice by most authors. The success rate of native arteriovenous fistula construction and function depends mainly on the artery and vein status before the operation. Therefore, every effort to improve the artery and vein status before surgery could be beneficial. It seems reasonable to conduct studies in order to establish the possible benefits of local physical activity. If this is proven to be effective, the patients should be encouraged to perform noninvasive activities which could enhance the quality and survival rate of fistulas and possibly reduce complications (like distal ischemia). Chronic hemodialysis patients already having an arteriovenous fistula on the other arm were included into the study to assure compliance and supervision of training during the hemodialysis procedures.

Duplex sonography is an ideal noninvasive method for evaluating both arteries and veins prior to arteriovenous fistula construction [17]. However, one should be aware that sonography is a highly operator-dependent method which can result in technical errors, especially when measuring vessels with a very small diameter and all the more so when calculating blood flow. This also appears to be a shortcoming of this and similar studies [12, 16].

The slight increase in forearm circumference in the trained extremity and the increase in maximal handgrip strength observed in our study were expected on the basis of similar results reported by Katz et al. [13] and Sinoway et al. [18] as well as the well-known effects of physical training on healthy individuals.

The radial artery diameter increased after regular physical training. Miyachi et al. [14] demonstrated that endurance training increases the femoral arterial cross-section area, presumably via flow-induced adaptation. Hornig et al. [12] did not report any increase in radial artery diameters after 4 weeks of training. The increase in radial artery diameter in our patients could be the result of a longer training period, since, as well, the initial 4 weeks of training appeared to be insufficient to produce any significant increase. It is known that if the metabolism in a given tissue increases for a prolonged period (as is in the case of protracted training), the vascularity also increases. This occurs more slowly in old well-established tissues and may take even months in elderly people. The increases of radial artery mean flow velocity and mean blood flow were not significant, as already reported by Katz et al. [13] who measured the blood flow using a plethysmographic technique.

Moreover, no changes in brachial artery diameter and brachial artery blood flow were detected after 4 or even 8 weeks of training. Such a result was expected, as the handgrip exercise mostly affects forearm muscles and vessels. The intermittent increase of blood flow induced by physical activity probably increased the capability of the endothelium to release nitric oxide, as the endothelium-dependent vasodilatation is largely mediated by nitric oxide [19]. The results of our study have shown that regular handgrip exercises improve the endothelium-dependent vasodilatation locally in patients with end-stage renal disease, even though a significant number of patients in our sample were exposed to additional atherosclerosis risks, such as diabetes, hypertension, and/or a smoking history. We can speculate that this can be beneficial for hand ischemia after arteriovenous fistula construction, especially in diabetics. The total body production of nitric oxide is significantly reduced in end-stage renal disease patients [20, 21]. The reduction of nitric oxide points to worsening atherogenic and thrombogenic endothelial properties in end-stage renal disease patients on hemodialysis. Experimental data demonstrated that the nitric oxide synthase gene expression in endothelial cell cultures is increased after exposure to increased shear stress [22] and that chronic increased blood flow causes an increased endothelial release of nitric oxide [23, 24]. It was proven that handgrip training is not associated with the systemic effect and that an improved endothelium-dependent vasodilatation induced by training is specific to the trained extremity in patients with chronic heart failure [13]. The age-associated loss in endothelium-dependent vasodilatation may also be restored by regular aerobic exercise in middle-aged and older sedentary men [25]. Regular physical exercise improves both basal endothelial nitric oxide formation and agonist-mediated endothelium-dependent vasodilatation of the skeletal muscle vasculature, and the correction of endothelium dysfunction is associated with a significant increase of the exercise capacity in patients with chronic heart failure [26].

On the other hand, the results of our study have shown that regular handgrip training has no influence on the endothelium-independent vasodilatation in patients with end-stage renal failure. Annuk et al. [10] reported that no differences were found in the blood vessel smooth muscle function in patients with renal failure as compared with healthy controls. Our findings are also in agreement with the results of Hambrecht et al. [26] who reported that regular exercise did not alter the responsiveness of smooth muscle cells of the peripheral vasculature to exogenous application of nitroglycerin in patients with chronic heart failure. It seems that the vasodilatatory dysfunction is limited to the bioavailability of nitric oxide.

Our study has shown that regular local training increases the diameter of forearm veins before and after compression. This is in agreement with the results obtained by Miyachi et al. [14] who found that endurance exercise can induce an increase in peripheral (femoral) vein size in healthy humans. All of these findings are consistent with the hypothesis that endurance training exerts modulatory influences on the venous circulation. This hypothesis seems to apply also to patients with end-stage renal disease.

It may be concluded that regular handgrip training increases the diameter of the forearm arteries and veins. It improves endothelium-dependent vasodilatation which had already been impaired in patients with end-stage renal disease. These changes in the forearm vessels after local training point to the possible beneficial effects of daily handgrip training in chronic renal failure patients before arteriovenous fistula construction.

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