Scand J Rehab Med 27: 73–76, 1995

MICRO- AND MACROCIRCULATORY, AND BIOHUMORAL CHANGES AFTER A MONTH OF PHYSICAL EXERCISE IN PATIENTS WITH INTERMITTENT CLAUDICATION

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ABSTRACT. We studied 15 subjects with intermittent claudication, classed as stage II according to Leriche-Fontaine. The patients were subjected to laser Doppler flowmetry, strain gauge plethysmography, Doppler velocimetry, and blood sampling, in basal conditions and after one month of physical training. Symptom-free walking distance at the end of the training period showed a significant increase, while there was no major change in maximal walking distance or the Windsor index. Laser Doppler flowmetry showed no significant change in cutaneous blood flow at rest, after the month of physical training. On the other hand, strain gauge plethysmography showed a significant decrease in rest flow at the end of the training period, while peak flow of postischemic hyperemia did not change appreciably. Biohumoral evaluations showed a significant decrease of white blood cell count, triglycerides and uric acid. Platelet count, prothrombin time, aPTT and plasminogen were unchanged. On the other hand, we recorded a small, but significant, rise of fibrinogen. Our study confirmed the importance of scheduled physical activity in the patient with intermittent claudication, showing that clinical improvement is not accompanied by an increase in the circulatory reserve. The unchanged levels of plasminogen suggest that the fibrinolytic activity does not vary significantly after a course of physical exercise.

Key words: intermittent claudication, physical exercise, laser Doppler flowmetry, strain gauge plethysmography, fibrinogen.

INTRODUCTION

Obliterating disease of the arteries in the lower limbs classed as second stage according to Leriche-Fontaine is managed conservatively, except in a certain percentage of cases characterized by brief, isolated stenosis. Such cases can be treated by the more recent endovascular surgical methods.

Physical exercise, of fundamental importance in functional recovery from claudication, is more efficacious than the various pharmacological treatments (2, 18), though these can as a rule lead more quickly to a new more favourable hemodynamic equilibrium (12). Nevertheless, walking seems to be the most significant factor in functional recovery and to give best results in this respect (16, 17).

Regular physical exercise allows adaptations of both a structural (neoformation of capillaries and development of collateral circulations) and a metabolic nature (increase in the number and size of mitochondria, improved yield of the enzymes in the respiratory chain, etc.). Provided that a well defined protocol is followed—if possible under the supervision of a physiotherapist—walking also affords considerable benefits in terms of statics and improvement of walking technique (11).

In medical treatment, the pharmacological regimen is only one part of the overall approach, which must also include rehabilitation. For this purpose, scheduled physical exercise is of fundamental importance in increasing both symptom-free and maximum walking capacity (4). These benefits are thought to derive from enrichment of the capillary network, enhanced oxygen extraction capacity and raising of the pain threshold (1, 7). Moreover, it is worth noting the influence of physical exercise on coagulation and fibrinolytic systems, and the action this may exert on the development of vascular disorders.

Against this background, we set out to analyze the clinical, instrumental, and biohumoral effects of a scheduled course of physical activity in a group of patients with intermittent claudication.

MATERIALS AND METHODS

We studied 15 subjects (12 men and 3 women; mean age 66 years, range 53–80) with obliterating arterial disease of the lower limbs, classed as stage II according to Leriche-Fontaine. Hemorheological and antiaggregant treatments had been discontinued 15 days beforehand. Ten patients were smokers, but two of these had not smoked for over a year. Only three subjects who had continued to smoke had stopped at the time of the first visit 15 days before the commencement of the study. The other risk factors were represented by hypertension (53%), dyslipidemia (93%) and diabetes mellitus (33%). Of the eight hypertensive patients, six had been receiving calcium antagonist treatment for over a year (in four cases nicardipine and, in two, nifedipine) and two were taking enalapril. This treatment was not changed, since it could reasonably be considered that the patients have gained a stabilized hemodynamic condition.

Patients were subjected to laser Doppler flowmetry (PF3, Perimed, Stockholm, Sweden) and subsequently to strain gauge plethysmography (Periquant 3800, Gutmann, Eurasburg, Germany). Instrumental evaluations were performed after at least 20 minutes' stabilization in a supine position at a constant room temperature (21 ± 1°C). The laser Doppler recording was continued for three minutes to afford an overall evaluation of spontaneous oscillations of the signal, which was recorded with a microcomputer (Olivetti M290S) and a dedicated software package (Perisoft, Gastrosoft Inc., U.K.). Doppler velocimetry of the lower limbs was then performed with a 5-MHz probe (Vingmed SD-50, Vingmed, Horten, Norway) and the Windsor index was calculated as the ratio of ankle systolic pressure to brachial systolic pressure (28). This is the most useful indirect measurement of ankle systolic blood pressure; it relates the pressure drop across an arterial segment to resistance and volume flow.

Fasting venous blood samples were collected between 8 a.m. and 9 a.m. after at least a 15-minute resting period in a supine position at the beginning of the study and after one month of physical training.

After instrumental evaluations, both symptom-free walking distance (SFWD) and maximal walking distance (MWD) after the onset of symptoms were evaluated. These measurements were performed on a treadmill with a 0° inclination and a speed of 4 km/h.

After these basal measurements, the informed consent of patients, according to Helsinki declaration, was obtained prior to commencing an exercise schedule of two half-hour sessions per day. Exercise consisted of cyclette or treadmill, with zero resistance. After 30 days, the basal instrumental evaluations and blood sampling were repeated.

Data were subjected to statistical analysis by Student's *t*-test for paired data allowing for Bonferroni's correction, and levels of probability less than 5% were considered statistically significant.

RESULTS

All patients completed the protocol. Symptom-free walking distance at the end of the training period showed a significant increase, while there was no major change in maximal walking distance (Fig. 1). Similarly, local blood pressure measurements showed no appreciable variation in the Windsor index (0.665 ± 0.048 vs 0.589 ± 0.051; mean ± s.e., n.s.). Cutaneous blood flow, measured by laser Doppler flowmetry, showed no significant change after one month of physical training (3.057 ± 1.134 vs 3.114 ± 0.567 perfusion units; n.s.). In terms of macrocirculation, strain gauge plethysmography showed a significant decrease in rest flow at the end of the training. Peak flow did not change appreciably (Fig. 2).

Biohumoral evaluations showed a significant decrease of white blood cells count (6880 ± 385 vs 7446 ± 429 WBC/mmc, $p < 0.05$), triglycerides (170 ± 16 vs 227 ± 32 mg/dl, $p < 0.01$), and uric acid (5.16 ± 0.37 vs 6.11 ± 0.33 mg/dl, $p < 0.01$). Platelet count, prothrombin time, aPTT, plasminogen, and total cholesterol were unchanged; on the other hand we found a small, but significant, rise of fibrinogen (Table I).

DISCUSSION

Scheduled physical exercise for a patient with intermittent claudication is now widely recognized as an important therapeutic factor for purposes of satisfactory functional autonomy (16, 17). Various studies underline that the indication can also be extended to claudicant subjects with associated ischemic heart disease, excluding only those patients in whom exercise would aggravate stenocardic symptoms. Not even diabetes mellitus gives grounds for considering that the benefits of exercise would not meet expectations (9, 14).

Our study shows first and foremost that microcirculatory flow, measured by laser Doppler flow-

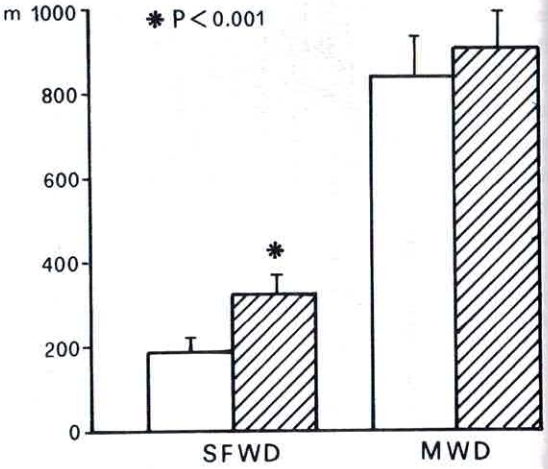

Fig. 1. Changes in symptom free walking distance (SFWD) and maximal walking distance (MWD) before (*open columns*) and after (*hatched columns*) the period of physical training (M ± SE).

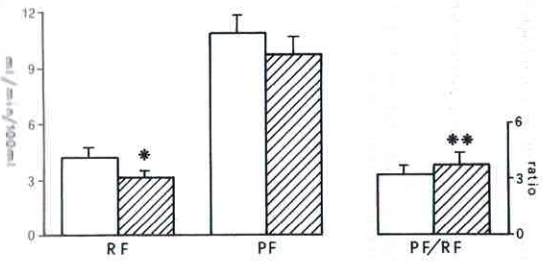

Fig. 2. Changes in rest flow (RF), peak flow (PF) and PF/RF ratio before (*open columns*) and after (*hatched columns*) the period of physical training (M ± SE). $*p < 0.001$; $**p < 0.01$.

metry, does not show significant variations after a course of physical training. In other words, hemodynamic changes determined by the period of training do not involve the dermal and cutaneous microcirculation. This is consistent with the finding that physical exercise modifies the metabolism of the striated muscle cells. Training enhances the capacity of muscle to extract oxygen; there is also a change in muscular metabolism, with a reduction in oxygen consumption at any given level of exertion (7). In other words, after physical training, blood flow seems to favour the muscle mass with an unchanged level of cutaneous microcirculatory delivery.

In measuring overall blood flow in the limb, we observed a statistically significant decrease in rest flow. This may possibly be related to the metabolic changes: higher oxygen uptake and better "energy yield".

Muscular effort in conditions of relative ischemia is an important stimulus for the development of new capillaries and collateral circulations (27). In some studies, this is considered to be related to an increase in the Windsor index, and thus to decreased resistances downstream from the stenosis (22). However, there is no general agreement regarding this finding, and many authors have observed their patients to be free of the perfusion pressure changes which would be expected in the presence of an increased ankle-arm index (10, 20). An excellent study by Johnson et al. (15) showed no significant changes in maximal blood flow in the common femoral arteries after 5 months' training. In our study, there were no variations in peak flow or the Windsor index, suggesting that the circulatory reserve as a whole remains unchanged—hence the absence of significant changes in MWD. This result is consistent with the findings of other authors, who have not found changes in blood flow in the lower limbs of claudicant patients undergoing physical exertion (3, 5, 23). In the study by Johnson and coworkers, after the third month of exercise, there was a statistically significant increase in MWD in comparison with the basal value for the parameter. In our study, possibly the absence of significant effects on MWD is attributable to the far briefer period of training involved, though the protocol was not the same and the difference in overall workload was thus not proportional to the different duration.

Table I. *Changes in biohumoral parameters after physical training* (*M* ± *SE*)

Biohumoral parameters	Before training	After training
WBC (cells/mmc)	7446 ± 429	6880 ± 385**
Platelets (10^3/mmc)	251 ± 13	250 ± 11
Triglycerides (mg/dl)	227 ± 32	170 ± 16*
Cholesterol (mg/dl)	249 ± 11	240 ± 10
Uric acid (mg/dl)	6.11 ± 0.33	5.16 ± 0.37*
PT (ratio)	0.981 ± 0.018	0.969 ± 0.009
aPTT (ratio)	1.044 ± 0.042	1.064 ± 0.030
Fibrinogen (mg/dl)	340 ± 17	389 ± 20**
Plasminogen (mg/dl)	108 ± 2.8	104 ± 3.2

$*p < 0.01$, $**p < 0.05$ vs values before physical training.

The increase in fibrinogen at the end of the training period is consistent with the observations of other authors (13, 26), although some references report that fibrinogen does not change after exercise (19) or even decreases (25). The varying results might be due to the different study populations. In our study the results do not show an increase in clotting tendency as confirmed by unchanged PT, aPTT, and platelet count.

Fibrinolytic activity has not significantly varied with regard to the levels of plasminogen. Some authors have reported an increase in fibrinolytic activity mainly by an elevation of tissue plasminogen activator (8, 21). Moreoever, Stratton et al. emphasized a decreasing PAI-1 activity (24).

Other authors report a significant increase in plasminogen levels after a course of physical training, but in their study the blood sampling was carried out at peak exercise (6), thus in a different hemodynamical and functional condition than for our subjects.

Our study confirmed the importance of scheduled physical activity in the patient with intermittent claudication, showing that clinical improvement is not accompanied by an increase in the circulatory reserve. On the other hand, plasminogen levels as well as parameters of coagulation did not show significant changes. The findings for blood flow were considered to be related, albeit indirectly, to the improvement in

muscular metabolic function. In this respect, the decrease in overall rest flow indicates that physical exercise is accompanied by increased tolerance of exertion, probably due to a redistribution of flow within the muscles to ensure a more efficient blood supply to the active component (27).

ACKNOWLEDGEMENT

This work was partly supported by a grant from Centro Regionale di Medicina dello Sport.

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