

Effects of a 9 months exercise training on inflammatory markers in type 2 diabetic patients

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Summary

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Purpose

Desired effects of a rehabilitative training are: Decreases in inflammation and lipid risk factors, decreases in fasting blood glucose and HbA1c, increases in cardiopulmonary capacity. Though the beneficial effects of intense training are well established, no statistical relevance of such training regimens has been described. So it is the most important prerequisite for a lasting acceptance, that the intervention is only moderate and not stressing. Therefore a major aim of present life style studies should be the evaluation of the lowest but still effective intensity of rehabilitative training.

Methods:

33 type 2 diabetic subjects (17 females, 16 males, 63,8 ± 6,9years, weight 99,2 ± 17,6kg, height 167,6 ± 9,6cm, BMI 35,3 ± 5,3, HbA1c 6,4 ± 0,76%) with insulin regimen exercised two times/week. The first session consisted of 45min endurance training (cycle-, rowing-ergometer, tread mill) and 15min pulley exercises. The second session consisted of 45 minutes of supervised moderate swimming. The program started out with low intensity training and was continuously increased according to the individuals' increasing endurance capacity. The participants frequency of cycle-ergometry training sessions in nine months was 40,5 ± 9,7, and 13 times per each 3 months period. At baseline, after three, six and nine months, fasting blood samples for measurement of inflammatory markers (IL-6, TNF-α, s-CRP) and lipid markers (triglyceride, cholesterol, HDL, LDL) were obtained. Laboratory analyses were performed at 8h after a 12h overnight fast. No health and nutrition intervention was conducted. There was no relevant change in medication throughout the study period. Exclusion criteria were: acute/chronic infections, antibiotic therapy, rheumatoid diseases. No regular physical exercise was done from any patient before the study, most of them did not work.

Results

Rehabilitative training resulted in a significant increase in TNF-α (12,27 ± 7,93 vs. 15,12 ± 9,58pg/l, p<0,002 after 6 months and 14,89 ± 9,25pg/l, p<0,001 after 9 months). Interleukin-6 was reduced, significantly after 3 months (4,3 ± 7,02 vs. 3,92 ± 6,68pg/l), whereas s-CRP remained unaffected. HbA1c (6,4 ± 0,76 vs. 6,51 ± 0,73%) also remained nearly unchanged. Marked changes were seen in endurance capacity (103% increase), and exercise blood pressure (145,3±14,4 : 74,9±6,7 vs. 137,5±17,6:67,2 ± 6,5torr after 9 months), and blood pressure at rest (142,4 ± 19,2:81,6 ± 11,2 vs. 135,6 ± 7:76,7 ± 9,8torr). Circulatory risk factors were also markedly decreased (triglycerides, LDL).

Conclusions:

Even moderate and few endurance/resistance training may improve systemic low grade inflammation as represented by s-CRP. This in turn may be a reason for an improvement of insulin resistance. The role of TNF-α for diabetes in contrast remains further unclear.

Key words: diabetes, exercise training, physical exercise, inflammatory markers, inflammation, s-CRP, TNF-α

Introduction

Numerous studies have shown that physical activity has a short term and long term beneficial effect on insulin sensitivity in healthy and insulin resistant subjects. Similar to insulin, physical exercise increases the rate of glucose uptake into the contracting skeletal muscles, regulated by the translocation of GLUT4 glucose transporters to the plasma membrane and transverse tubules (1). Endurance training leads to lasting reduction of insulin and blood sugar (2,3). Long term training may potentiate the effect of exercise on insulin sensitivity through multiple adaptations in glucose transport (6). The improved glycemic control may thus help improve HbA1c values. Further body weight may also decrease due to higher energy expenditure. Increased physical activity improves insulin sensitivity and glucose metabolism, independent of diabetes and obesity (1,4). However a 14 days interruption of training is enough to reverse the positive effects (5). Exercise thus would produce best effects when performed before the meals due to an increased glucose uptake parallel to reduced

insulin values. Besides all these theoretical considerations the realistic fact is that only few people would accept frequent endurance exercise bouts as their preferred therapy. In contrast high body weight and advanced detraining make this mode of therapy most unappealing. Scientific diabetes meetings are full of contributions with the two topics 1) effects of frequent exercise on diabetes and 2) behavioural lifestyle studies in diabetics. An almost never discussed approach is: how moderate and infrequent training may still have an effect on diabetes and cardio-circulatory parameters. Anyhow we think in the meantime that moderate and infrequent training may be the only way to change diabetic lifestyle to a more active mode, if this is possible at all. Therefore the aim was to create a moderate exercise program which is more likely to be accepted long term in diabetic patients and to look at its effects on diabetes specific, cardio-circulatory and training parameters after 7 months.

Methods

50 type 2 diabetic subjects ($61 \pm 7,4$ years, weight $98,4 \pm 19$ kg, height: $169,2 \pm 8,7$ cm, BMI $34,3 \pm 5,9$, HbA1c $6,6 \pm 0,9\%$) participated in this study. 32 of these patients had an oral medication and 18 an insulin therapy. The patients had no relevant change in medication throughout the study period. No regular physical exercise was done from any patient before the study, most of them were unemployed and the exercise training was funded by their insurance companies. Two training sessions weekly were performed, one with 45 min of endurance/ resistance training (cycle-ergometer, treadmill, rowing) and 15 min of

pulley exercises, the 2nd with 45 min of moderate swimming. The program started out with low intensity training for each form of exercise and was continuously increased according to the individuals' increasing endurance capacity. Before and after each exercise set heart rate, blood pressure, blood glucose, and work load were measured and recorded. Data at baseline and after 7.1 ± 3.2 months of training were analysed. The cardiac load was estimated using the rate-pressure product, divided by 1000.

Results

Body composition and metabolic parameters

	weight (kg)	BMI	HbA1c (%)
initial	$98,4 \pm 19$	$34,3 \pm 5,9$	$6,6 \pm 0,9$
final	$98,0 \pm 18,4$	$34,1 \pm 5,5$	$6,3 \pm 0,7$
p	n.s.	n.s.	0,004

Table 1. Weight (kg), BMI, and HbA1c (%) before and after the 7 months training period.

Cardio-circulatory parameters for resting conditions

	baseline	after 7 months	p
heart rate (bpm)	$80,1 \pm 15,8$	$76,4 \pm 13,2$	$p < 0,001$

blood pressure (torr)	syst. 147,6±18,9 diast. 82,9±11,4	syst. 140,0±16,4 diast. 80,3±11,4	p<0,005 n.s.
rate-pressure product	11,8 ± 2,4	10,7 ± 2,0	p<0,001

Table 2. Pre-exercise heart rate at rest (beats x min⁻¹), pre-exercise blood pressure at rest (RR_{sys} and RR_{dia}, mmHg), and rate-pressure product (HR x RR_{sys} / 1000) before and after 7 months.

Effects on blood glucose

	baseline	after 7 months	p
pre-exercise blood glucose	8,2 ± 3,0	8,2 ± 2,8	n.s.
post-exercise blood glucose	6,4 ± 2,7	6,1 ± 2,3	n.s.
p	p<0,0001	p<0,0001	

Table 3. Pre- and post-exercise blood glucose (mmol x l⁻¹) before and after 7 months.

Cardio-circulatory and training effects for exercise conditions

	baseline	after 7 months	p
endurance capacity (W)	40 ± 14	68 ± 21	p<0,001
heart rate (bpm)	102,7 ± 15,8	105,9 ± 17,5	n.s.
blood pressure sys. (torr)	151,6 ± 20,3	149,4 ± 21,8	n.s.
rate-pressure product	15,7 ± 3,8	15,9 ± 3,7	n.s.

Table 4. Endurance capacity (Watt), heart rate (beats x min⁻¹), blood pressure (RR_{sys} and RR_{dia}, mmHg), and rate-pressure product (HR x RR_{sys} /1000) for exercise conditions before and after 7 months of exercise training. Please note that the rate-pressure product was similar although endurance capacity was increased.

Discussion

A seven months rehabilitative exercise training two times a week had only minor effects on body weight and HbA1c values. The major effects were related to a significant improvement of the all day circulatory capacity by about 70%. This can be explained by a very low training intensity at the beginning because even low grade training exposure could be maintained only for few minutes by most patients. Training capacity after the 7 months recreational training was 68 Watt. The endurance capacity of the diabetic patients was limited by presence or high degree of complicating diseases, poor pre-training fitness and physical inactivity. Unexpectedly the training program had only minor effects on body weight. The mean weight loss of 0,4kg was not significant. But it should not be

disregarded that the majority of the participants complained a constant weight gain before joining this program. Weight gain was also the most important trigger for the acceptance of the exercise program. Insofar stagnant weight can be seen as a success. Further in some patients treated with sulfonylureas or insulin hypoglycaemia occurred due to exercise. This in turn was a welcome justification for higher energy intake before or after sports. Finally this kind of exercise training causes no weight loss without improved and reduced nutrition and sports adapted medical management. The change of HbA1c was significant but moderate and can be explained in the same way. In contrast resting blood glucose values markedly decreased from 8.2 to 6.4 mmol x l⁻¹ (p<0,0001)

after exercise. The minor change in HbA1c values may also be an effect of the observation period, since HbA1C follows a substantial change of blood glucose with a delay of several months. In contrast to the metabolic changes the seven months rehabilitative exercise training two times a week markedly improved endurance capacity. Further the heart stress resulting from the combined effects of blood pressure and heart rate was markedly reduced. This is best shown by the cardiac load (systolic blood pressure

x heart rate). According to this parameter the heart stress per watt during training had been reduced by about 40%. These quite impressive results may have their explanation in the extremely detrained status of the patients, when an even moderate training impulse creates a relevant stimulus of physiological reaction.

Conclusions

A six months rehabilitative exercise training in type 2 diabetic patients had only minor effects on diabetes and metabolic parameters but induced a significant improvement of the endurance capacity. These results

may indicate that a moderate exercise stimulus of 45 min two times a week may be the lowest level of efficiency for metabolic and cardio circulatory effects in extremely detrained diabetic patients.

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