STUDY PROTOCOL WITH SAP

Development of Structured Exercise Program for T2DM Management

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CENTER FOR SPORTS AND EXERCISE STUDIES, INDONESIA MEDICAL EDUCATION AND RESEARCH INSTITUTE, FACULTY OF MEDICINE UNIVERSITAS INDONESIA

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Title: DEVELOPMENT OF STRUCTURED EXERCISE PROGRAM FOR T2DM MANAGEMENT

Background.

Given the many forms of interval training, it is important to investigate the appropriate intensity, duration, frequency, and type of exercise for diabetic patients. One significant issue for exercise-based T2DM management is oxidative stress, as both high plasma glucose and the exercise itself will increase production of reactive oxygen species (ROS). However, exercise can still play a useful role in good T2DM management. At moderate intensity, yielding low levels of ROS, cell signaling and regulation of gene expression influence the expression of important enzymes associated with the antioxidants that defend against ROS. Therefore exercise programs for patients with Type 2 Diabetes Mellitus (T2DM) must be demonstrably safe, effective, and beneficial.

Objectives.

To review the effect of combined high intensity interval training (HIIT) and resistance training to meet three criteria

1) Safe: showing lowered oxidative stress (lowered MDA and higher SOD measure)
2) Effective: showing better glycaemic control (lowered HbA1c)
3) Beneficial: showing better fitness level (increased VO2max)

Design

Randomized controlled trial (RCT)

Methods.

1) Subject recruitment: T2DM patients who were registered at primary clinics near the training facility
2) Eligibility criteria
   - Aged 18–64 years
   - Showing controlled plasma glucose levels (average fasting plasma glucose < 250 mg/dL or HbA1c ≤ 10.5%), with regular intake of oral hypoglycemic agents for at least 6 months.
3) Exclusion criteria
   - Suffered from diabetic complications such as
     - macroangiopathy (ECG readings showing signs of coronary heart problems, or foot ulcers),
     - severe retinopathy (severe NPDR)
     - severe nephropathy (macroalbuminuria)

- restricted locomotion

4) Before and after measurements
   - Physical fitness included VO2max, grip strength, sit and reach, and back extension, which was measured using the CSEP protocol
   - Blood work for HbA1c, malondialdehyde (MDA) level, and superoxide dismutation (SOD) activity.
   - Body composition:body mass index (BMI) and body fat percentage (Bioelectrical Impedance Analysis (BIA) - (Tanita MC780MA portable).
   - Quality of Life measure using the EuroQol EQ-5D questionnaire

   (One-sided blinding meant that those measuring fitness levels were unaware of subjects' group allocation, and all blood samples were numbered by recruitment order to conceal group allocation.)

5) Subjects were randomly allocated to experimental (EXP) and control (KTR) groups, using block of 4 randomization until there were 25 subjects in each group.

6) Health checks before starting exercise session:
   - Resting blood pressure should not exceeded 180/100 mmHg
   - Heart rate should not exceeded 100 per minute
   - Random blood glucose level outside 100–300 mg/dL.

7) The 12-week combined high intensity interval training (HIIT) and resistance training was conducted at the Center for Sports and Exercise Studies - Indonesian Medical Education and Research Institute, Faculty of Medicine Universitas Indonesia, Jakarta, Indonesia.
   - Detail of HIIT load is shown in Table 1.

Table 1. Dose of high-intensity interval training (HIIT)

Week	Intensity		Duration		Comparable intensity (METs)	Training device
	VO_2peak	HRmax				
1–2	50%	60–70%	20 minute continuous		Moderate intensity (3.8)	Treadmill/ Ergocycle
3–6	HIE: 80%	90%	1 min	4 cycles = 20 min	Moderate intensity (4–6)	Treadmill/ Ergocycle
	LIE: 50%	70%	4 min		High intensity (6–8)	
7–12	HIE: 85%	92%	1 min	6 cycles = 30 min	Moderate intensity (4–6)	Treadmill/ Ergocycle
	LIE: 60%	75%	4 min		High intensity (6–8)	

Note:

1. Comparable intensity refers to *compendium of physical activities*.
2. Comparison of VO_2peak to HRmax is calculated using Swain formula.

- The resistance training comprised nine exercises for core, upper, and lower extremities to train all body muscles (single leg raise (leg extension), shoulder press, chair squat, back row, chest press, lateral pull down, hamstring curl (leg curl), back up, and crunches). Detailed of training load is shown in Table 2.

Table 2. Dose of resistance training

Week	Set	Repetition	Load (RPE)	Training device
1–2	1	8	No external weight/minimal (3–4)	Resistant band & dumbbell
3–6	1	10	External weight resistance (5–6)	Weight training machine & weight strap
7–8	2	10	External weight resistance (7–8)	Weight training machine & weight strap
9–12	2	10	External weight resistance (8–9)	Weight training machine & weight strap

8) During the training program, subjects were asked not to alter their daily physical activities, food intake, or medication to ensure that training effects were maintained
   - All subjects were provided with OMRON HJ325 pedometers to be worn throughout the study period other than when performing the program exercises.
   - Each subject was asked to record their physical activity every four weeks, using Bouchard's three-day physical activity record
   - Each subject was asked to record their food intake using 3-day food intake record, which were analyzed using Nutri Survey software (SEAMEO-TROPMED RCCN – University of Indonesia).

Statistical Analysis Plan

- Group numerical data were reported as means ± standard deviation; non-normally distributed data were reported as median and interquartile range (IQR).
- At the outset, randomization of EXP and KTR groups was tested using independent sample t-testing for mean differences or chi-square testing for differences in proportions.
- Between-group effects were analyzed in terms of post-study and pre-post differences (Δ/delta) measurements, using independent samples t-testing for normally distributed data and independent samples Mann-Whitney U testing for non-normally distributed data.
- Statistical analysis was performed using SPSS (Statistical Package for the Social Sciences) version 20 for Windows.