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THE EFFECT OF EXERCISE TRAINING ON THE AUTONOMIC FUNCTION, DISEASE ACTIVITY AND FUNCTIONAL CAPACITY IN FEMALES SUFFERING FROM RHEUMATOID ARTHRITIS

by

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in

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DEDICATION

This dissertation is dedicated to all Rheumatoid Arthritis sufferers

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SYNOPSIS

Title	**The effect of exercise training on the autonomic function, disease activity and functional capacity in females suffering from rheumatoid arthritis**
Candidate	**Dr DC Janse van Rensburg**
Supervisor	**Prof JA Ker**
Degree	**MD (Internal Medicine)**

Rheumatoid Arthritis (RA) is a chronic disease and one of the more common auto-immune diseases. It generally occurs more amongst females than males. Patients with RA rely almost solely on pharmaceutical intervention to manage the disease. This study firstly compared the autonomic function of RA females to that of healthy females, whereupon the emphasis shifted to the effect of exercise intervention on the following three aspects relating to the effects of RA:

- Autonomic function (as measured by heart rate variability)
- Disease activity (as measured by Disease Activity Score, Visual Analogue Scale and Health Activity Questionnaire)
- Functional capacity (as measured by strength, flexibility and aerobic capacity)

After a 3 month intervention period it was found that exposing Rheumatoid Arthritis patients to exercise had a meaningful effect on their autonomic function, disease activity and functional capacity.

Key words: autonomic nervous system dysfunction / impairment, rheumatoid arthritis, heart rate variability, exercise, disease activity, functional outcome

ABSTRACT

Introduction: Rheumatoid arthritis (RA) is a chronic disease and one of the more common auto-immune diseases. Patients with RA rely almost solely on pharmaceutical intervention to manage the disease. Autonomic impairment has been proven in previous studies on patients with RA. The positive effect of exercise on autonomic impairment has also previously been demonstrated, but not in the RA population. The purpose of this study was firstly to confirm autonomic impairment in a South African based female population with RA and secondly to evaluate the effect of exercise on the autonomic cardiac function (as measured by short-term heart rate variability), disease activity and functional capacity.

Methods: The study was conducted at the University of Pretoria during 2009 and 2010. In the first phase of the study female RA patients were recruited from all rheumatology practices in Pretoria and healthy controls were recruited from family and friends of the research team and of the RA group. Cardiac autonomic function was compared between the two groups by means of short-term heart rate variability. Three techniques were used: time domain, frequency domain and Poincare plot analysis.

In the second phase of the study, females with confirmed RA were randomly assigned to an exercise group and a control group. The exercise group was requested to train under supervision two to three times per week for a period of twelve weeks, while the control group continued with their sedentary lifestyle. At study completion the two groups were compared for the effect of exercise intervention on the following three aspects:

- Autonomic function (as measured by heart rate variability)
- Disease activity (as measured by Disease Activity Score, Visual Analogue Scale and Health Activity Questionnaire)

- Functional capacity (as measured by strength, flexibility and aerobic capacity)

Results: In the first phase of the study comparing females with RA (n=45) to healthy females (n=39), the basal heart rate was significantly higher in the RA group. In the supine position significant differences existed between the RA group and the control group ($p \leq 0.01$). Indicators of parasympathetic activity showed significantly lower variation in the RA group [RMSSD=14.70, pNN50=0.50, SD1=10.50, HF(ms^2)=31] compared to the control group [RMSSD=29.40, pNN50=7.8, SD1=20.9, HF(ms^2)=141.00]. Indicators of sympathetic variation were also significantly lower in the RA Group [SD2=36.70, LF(ms^2)=65) compared to the Control group (SD2=49.50, LF(ms^2)=175]. In the standing position 8 variables indicated autonomic impairment by significant differences ($p \leq 0.01$) between the 2 groups. The response of the RA Group to an orthostatic stressor showed less vagal withdrawal, [p-values for RMSSD=0.038, pNN50=0.022, SD1=0.043 and HF(ms^2)=0.008 respectively]; and lower sympathetic response [p-values for SD2=0.001 and LF(ms^2)<0.001] when compared to the Control group.

In the second phase of the study, comparing an RA exercise group to a RA sedentary group, three aspects were evaluated:

1. Heart rate variability

   At baseline the control group (n=18) had significantly higher variability compared to the exercise group (n=19) for most heart rate variability (HRV) indicators. At study completion the variables showing significant changes (p=0.01 to 0.05) favoured the exercise group in all instances. Wilcoxon signed rank tests were performed to assess changes within groups from start to end. The exercise group showed significant improvement for most of the standing variables, including measurements of combined autonomic influence e.g. SDRR (p=0.002) and variables indicating only vagal influence e.g. pNN50 (p=0.014). The control group mostly deteriorated with emphasis on variables measuring vagal influence [RMSSD, pNN50, SD1 and HF(ms^2)].

2. Disease activity

At baseline the two groups were comparable. At the end of the intervention, the exercise group had significant improvement for the tender joint count (p=0.015), swollen joint count (p=<0.001), physician global assessment (p=0.003) and DAS score (p=0.003) compared to the control group. To assess changes that happened within each group from start to end, Wilcoxon signed rank tests were performed. The exercise group improved significantly with regards to tender joint count (p=0.002), swollen joint count (p=0.001), physician global assessment (p=0.001), DAS score (0.001) and the visual analogue scale (p=0.032). The sedentary group improved significantly only in the health assessment questionnaire (p=0.032).

3. Functional capacity

Comparing the groups at baseline the exercise group had better knee- and hip flexion on the left hand side but it took them longer to complete the arm curl test. At study completion the exercise group was mostly favoured with regards to flexibility (significant p-values ranging between 0.001 – 0.049), strength (handgrip right p<0.001, leg strength p=0.035, arm curl test p=0.010, sit to stand test p=0.025) and aerobic fitness (1 mile walk test p<0.001 and VO_2 max p=0.007). Changes within each group were assessed by Wilcoxon signed rank tests. The exercise groups showed significant changes for many parameters in the three categories, i.e. flexibility (8 of 18), strength (5 of 5), and aerobic fitness (4 of 8). The control group mostly deteriorated in flexibility, while their strength also improved, but not to the same extent as for the exercise group. Their aerobic fitness did not change.

Discussion: In the first phase of this study, using standardised methods to measure short-term HRV, females with RA showed less variability compared to a healthy age- and sex matched control group. An inability of the autonomic nervous system to efficiently compensate to internal and external environmental changes may predispose RA patients to arrhythmias thereby increasing cardiovascular mortality.

All 3 methods used showed the same outcome, implying decreased HRV and thus an increased risk for arrhythmias in RA patients. Evaluating the autonomic nervous system might be critical in planning management of RA.

In the second phase study results indicated that twelve weeks of exercise intervention, had a positive effect on cardiac autonomic function as measured by short-term HRV, in females with RA. Several of the standing variables indicated improved vagal influence on the heart rate. Exercise can thus potentially be used as an instrument to improve cardiac health in a patient group known for increased cardiac morbidity.

The exercise programme was also effective in decreasing perception of pain as well as disease activity in female RA patients. Given our findings it seems warranted to include physical exercise as part of the treatment prescription of patients with class I and II RA.

Lastly this research has shown that regular, controlled exercise for RA patients with controlled disease can decrease joint stiffness and improve joint mobility, strength and aerobic capacity without exacerbating pain or disease activity. Also, if one observes the decline in the sedentary group for many parameters, it is important to note that this happened over a relative short time period and that even a small change may have a detrimental impact on the RA patient.

The current report supports previous literature on autonomic impairment in patients suffering from RA as well as the meaningful positive effect of exercise on disease activity and functional capacity. It is the only study on the effect of an exercise intervention on the cardiac autonomic function of RA patients.

Future research in this field should aim for larger study samples, longer intervention periods and perhaps add analysis of blood pressure variability to support results obtained by HRV analysis.

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List of publications, oral and poster presentations from the study

Publications

1 Efficacy of an exercise program on the functional capacity and disease activity in females with Rheumatoid Arthritis.
South African Orthopaedic Journal Vol 9(2) 2010: 34-42

2 Land- and water-based exercises in Rheumatoid Arthritis.
South African Journal of Sports Medicine Vol 23(3) 2011: 84-88

3 Autonomic dysfunction in Rheumatoid Arthritis.
Article accepted for publication in International Journal of Rheumatic Diseases

4 Effect of exercise on cardiac autonomic function in female Rheumatoid Arthritis patients.
Article accepted for publication in Clinical Rheumatology

Oral presentations

5 Efficacy of an endurance exercise program on the functional capacity and disease activity in females suffering from Rheumatoid Arthritis: pilot study.
21st National Congress of the South African Rheumatoid Arthritis Association 2009

6 Efficacy of an exercise program on the functional capacity and disease activity in females with Rheumatoid Arthritis: randomised controlled trial.
Conference of Science and Medicine in Sport 2010 (Australia)

7 Testing of Autonomic Dysfunction in Rheumatoid Arthritis patients: pilot study.
Faculty Day, University of Pretoria 2011

8 Testing of Autonomic Dysfunction in Rheumatoid Arthritis patients: HRV of Healthy Control Group vs Rheumatoid Arthritis Group.
South African Rheumatoid Arthritis Association Congress 2011

9 Heart rate variability and exercise.
14th Biennial South African Sports Medicine Association Congress 2011

Poster presentations

10 The prescription of exercise to counter autonomic dysfunction in Rheumatoid Arthritis patients: a pilot study.
American College of Sports Medicine Congress 2011 (Denver, Colorado)

11 Effect of exercise on cardiac autonomic function in female Rheumatoid Arthritis patients.
International e-Conference on Kinesiology and Integrated Physiology 2011(University of Houston)