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The effects of physical activity on disease activity in patients with rheumatoid arthritis

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Abstract

Rheumatoid arthritis (RA) is an autoimmune condition with a predilection for peripheral synovial joints. It affects 0.5 to 5% of the adult population worldwide. The chronic inflammation of RA results in destruction of the synovial joints, decreased mobility and chronic pain. Patients who have RA experience a poorer health related quality of life (HRQoL) in comparison to the general population. They are less habitually physically active than a healthy population, to the point of not meeting the required guidelines of physical activity to maintain a healthy wellbeing. Moreover, patients with RA are prone to developing osteoporosis as a consequence of systemic inflammation and a sedentary lifestyle.

The aims of the research undertaken for this thesis were to: 1) objectively quantify habitual physical activity levels in RA patients in comparison to a healthy population, 2) ascertain any associations between habitual activity levels and disease activity in patients with RA, 3) determine the changes in habitual physical activity levels in patients newly diagnosed with RA in response to commencement of DMARD therapy, 4) determine the predictive factors causing the changes seen in disease activity in response to commencement of DMARD therapy in patients with RA, 5) determine the associations between habitual physical activity levels and bone health in patients with RA, and 6) determine the effects of a WBV therapy intervention on functional ability, and bone health, as well as on disease activity and habitual physical activity levels in patients with RA. These aims were addressed by conducting three studies.

In the first study habitual physical activity levels was assessed over a two week period in a cohort of 50 female RA patients in comparison to 22 healthy matched control participants, using an Actical accelerometer. Patients also completed various disease activity questionnaires, namely the Health assessment questionnaire (HAQ), and the Short Form-36 questionnaire (SF-36), and were assessed for rheumatoid disease activity by a physician using the simplified disease activity index (SDAI). All data are presented as mean (SD). The RA patients had a disease duration of 99(77) months, with moderate functional disability (HAQ score of 1.3(0.9)) and moderate disease activity (SDAI score of 18.38(11.76)). Patients had a poor HRQoL as assessed by the SF-36 with a score of 44(18). Accelerometry showed that the RA group spent significantly more time in sedentary behaviours than did the control group, spending 71(11)% of their awake day in sedentary activities as opposed to 62(11)% in the control group ($p<0.01$). The RA group had significantly lower mean activity counts in the morning ($p<0.01$) and the late afternoon ($p<0.01$) than the control group. Within the RA group, patients who were more physically active scored significantly better in many components of the SF-36, indicating an association between better HRQoL and increased habitual physical activity levels. The HAQ scores, corrected for age and disease duration, correlated negatively with physical activity levels in the RA group ($r^2=0.12$, $p=0.03$).

In the second study habitual physical activity levels were observed longitudinally in 18 RA patients before and three months after commencing DMARD therapy. The accelerometer was worn for two consecutive weeks before and after starting DMARD therapy. Patients also completed the same disease activity assessments as the patients in Study 1. The RA group was compared to a matched control group of 18 healthy participants. After three months of DMARD therapy, RA patients improved

significantly on all measured indices of disease activity and accelerometry metrics. The activity counts in sedentary activities declined from a mean (SD) of 995(283) to 837(253) counts, $p<0.01$, whilst light activities increased from a mean (SD) of 3461(1453) to 4451(92057) counts, $p=0.04$, indicating increased habitual physical activity levels after commencing DMARD therapy. Moreover, significant differences in mean activity counts observed between the control and RA groups in the morning ($p=0.05$) and afternoon ($p=0.02$) at baseline, were attenuated after three months of drug therapy, to the point where habitual physical activity levels were equivalent between the groups throughout the day. Multiple regression analysis showed that change in early morning stiffness was most strongly predicted by change in sedentary and moderate activity ($\beta=0.69$, $p=0.04$ and $\beta=-0.93$, $p=0.02$ respectively), while a fall in CRP levels was most strongly associated with change in moderate activity ($\beta=-0.92$, $p=0.03$). Spearman's correlation tests showed further positive associations between improvements in physical activity and improvements in disease activity.

In the third study, the effects of 12 weeks of whole body vibration (WBV) therapy in stable and established RA was studied by randomising patients to either a WBV therapy group (n=16) or a standard care control group (CON, n=15). All data are presented as mean (SD) or mean (SEM). Patients were fitted with an accelerometer for a one week period, completed the same questionnaires as done in the previous two studies, and had dual X-Ray absorptiometry (DXA) scans to measure BMD and body composition at baseline, end of therapy and 12 weeks post-therapy.

Patients in the WBV and CON groups were well matched at baseline for all variables. During baseline analysis, all patients were divided into two subgroups – those with normal bone mass (n=21), and those with low bone mass (n=8). Compared to subgroup

of patients with low bone mass (n=8), the subgroup of patients with normal bone mass (n=21) reported less functional disability (HAQ score (0.96(0.71) vs. 1.57(0.74), p=0.05) and had a trend towards lower RA disease activity as assessed by CDAI (7.7(6.1) vs. 13.8(10.8), p=0.07). The normal bone mass subgroup also had higher overall habitual physical activity (p<0.01). They spent on average two hours less per day in sedentary activity (65(4) vs. 73(2) % time per day, p<0.01), over 70 minutes more time in light activity (23(1) vs. 18(2) % time per day, p<0.01), and over 50 minutes more in moderate activity per day (12(3) vs. 8(2) % time per day, p<0.01), than the low bone mass subgroup. The normal bone mass subgroup broke up their sedentary time more frequently per day than low bone mass subgroup (72(21) vs. 53(18) times per day, p=0.03). Patients who met the minimum recommended physical activity guidelines for a rheumatic population had significantly better Z scores at the hip than those who failed to meet the minimum guidelines (p=0.03).

Thereafter, at the end of the 12 week intervention, the patients who underwent WBV therapy experienced significant improvements in HAQ scores (1.22(0.19) to 0.92(0.19), p=0.02), fatigue levels assessed by a self-report Lickert scale (4.4(0.63) to 1.1(0.65), p<0.01), and whole body BMD (1.09(0.03) to 1.10 (0.03) $g.cm^{-2}$, p=0.05). By contrast, in the CON group there was no significant change in HAQ scores or fatigue levels, and whole body BMD declined significantly (1.07(0.03) to 1.05(0.03) $g.cm^{-2}$, p<0.01), while a significant increase was seen in the WBV group (1.09(0.03) to 1.10(0.03) $g.cm^{-2}$). Rheumatoid disease activity remained stable in both groups throughout the intervention period. Ten minute bouts of light and moderate physical activity were significantly reduced in the CON group over the intervention period (2.8(0.61) to 1.8(0,64) bouts/day, p=0.01), but were preserved in the WBV group (3.1(0.59) to 3.0(0.61) bouts/day, p=0.70). Twelve weeks post therapy, fat mass was decreased

(37(3) to 35(3) kg) in the WBV but increased in the CON group (31(3) to 35(3) kg, $p<0.01$), while lean mass decreased in the CON group (42(2) to 40(2) kg), and was increased in the WBV group (46(2) to 45(2) kg, $p<0.01$). In summary this study showed that intermittent WBV results in sustained improvements in functional ability, attenuation of bone mass loss at the hip, and improvement in fatigue levels in established RA.

Altogether, these studies demonstrate that RA patients are indeed more sedentary in comparison to a healthy, matched control group, and that habitual physical activity levels measured by accelerometry correlate with patient-reported functional ability. Accelerometry measures were found to be responsive to change in relation to disease activity. Besides improving RA disease activity indices, DMARD therapy increased habitual physical activity levels and patterns of daily physical activity in RA patients started to resemble those of the control group. The research also showed that BMD is positively associated with increased habitual physical activity in RA patients and, lastly that WBV therapy improved functional ability and fatigue levels, and attenuated bone loss at the hip, without significant impact on rheumatoid disease. Hence, increased habitual activity needs to be encouraged, and WBV therapy is a feasible, safe and simple intervention for improving functional ability, HRQoL, and BMD in patients with established RA.