ImmunoTools *special* Award 2014

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Inflammation and muscle function after long-term physical activity in rheumatoid arthritis

Aims

The goal of our project is to increase the understanding of how Health-Enhancing Physical Activity (HEPA) in rheumatoid arthritis (RA) can affect systemic and local inflammation as well as muscle function.

Background

Systemic and local inflammation is pathognomonic for RA, leading to the characteristic clinical symptoms of chronic pain and fatigue. Reduced physical functionality, particularly aerobic work capacity and muscle function, are as common as activity limitation and poor health perception. Novel developments of medical treatment have markedly improved inflammation control during the past decade. However, not all patients fully respond to medication and it has also been shown that even when inflammation can be controlled with therapeutic medical agents, it does not necessary improve muscle function, which is an important predictor of health perception. Muscle involvement, in particular functional atrophy with progressive loss of muscle mass, is reported in up to 2/3 of patients. Muscle strength training is not only affecting muscle function but also reduces signs of inflammation and pain in patients with RA. Current guidelines on HEPA include muscle strength trainings twice per week in addition to either daily moderate-intensity physical activity or aerobic exercise three times a week. HEPA may help maintaining physical function and long-term health in RA, but a majority of patients do not accumulate enough physical activity. To date, only a few randomized controlled HEPA intervention studies on patients with RA have been performed and more studies, particularly with long-term perspectives are highly needed in this area.

Project description

RA patients will be subjected to a 24-months HEPA programme. During the first year each participant takes part in at least two 45-minute exercise sessions and is encouraged to perform additional moderate-intensity physical activity at least 30 minutes on most of the other days of the week. At baseline, a physiotherapist is present to instruct and assist in adjusting the programme to each participant's needs and preferences. During year two, the participants' will take responsibility for their own HEPA. The patients is assessed at baseline and annually (0, 12, and 24 months) to test mechanisms behind HEPA effects on local muscle

inflammation with: isokinetic strength in knee extensors using a Biodex, muscle biopsies from m. vastus lateralis will be analysed for (i) gene expression by micro-array analysis using Affymetrix and with real-time PCR focusing on genes involved in inflammation and in cellular metabolism, (ii) protein expression by proteomics by immunohistochemistry (IHC) or western blot for molecules that come up in the gene expression analysis and, in addition, proinflammatory and anti-inflammatory cytokines, endothelial cells activation markers, and reactive oxygen species/reactive nitrogen species, (iii) muscle fibre characteristics including fibre type/area, and (iv) body composition with DEXA scan. Age and gender matched biopsies and blood tests from healthy individuals will also be investigated.

To test HEPA effects on systemic inflammation the following values are determined: blood tests investigated for CRP and ESR, and FACS analysis of peripheral blood in the subsample, from which muscle biopsies are taken, to measure expression of inflammatory genes in peripheral blood monocytes using Affymetrix and circulating levels of pro-inflammatory and anti-inflammatory cytokines.

In addition, data on disease activity, medication from the Swedish Rheumatology Register and with questionnaire data on demographics, general health perception, pain and fatigue with visual analogue scales, health-related quality of life, activity limitation, the International Physical Activity Questionnaire, the Exercise Self-efficacy Scale, the modified Fear-avoidance Beliefs Questionnaire, the Stages of Change Questionnaire, and outcome expectations will also be investigated at baseline and annually. These data will be correlated with the results from the muscle biopsies and blood tests.

The successful realization of this study would be greatly improved by reagents from ImmunoTools that will be used for FACS analyses, ELISA and some in vitro studies.