Contemporary Clinical Trials Communications 10 (2018) 177–189

Contents lists available at ScienceDirect

Contemporary Clinical Trials Communications

journal homepage: www.elsevier.com/locate/conctc

Meal-exercise challenge and physical activity reduction impact on immunity and inflammation (MERIIT trial)

Diana Silva[a,b,*], Rita Moreira[c], Oksana Sokhatska[a], Marília Beltrão[a], Tiago Montanha[d], Vanessa Garcia-Larsen[e], Rodrigo Villegas[f], Milton Severo[g], Andreia Pizarro[d], Mariana Pinto[a,c], Carla Martins[b], Ana Duarte[h], Luís Delgado[a,b], João Rufo[a,g], Inês Paciência[a,g], João Paulo Teixeira[h], Carla Costa[h], Pedro Moreira[c], Joana Carvalho[d], André Moreira[a,b,g]

[a] Basic and Clinical Immunology, Department of Pathology, Faculty of Medicine, University of Porto, Portugal
[b] Serviço de Imunoalergologia, Centro Hospitalar São João, EPE, Porto, Portugal
[c] Faculty of Nutrition and Food Sciences University of Porto, Portugal
[d] Research Centre in Physical Activity, Health and Leisure - Faculty of Sports, Porto, Portugal
[e] Department of International Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, USA
[f] School of Public Health, University of Chile, Chile
[g] EPIUnit – Institute of Public Health, University of Porto, Porto, Portugal
[h] Department of Environmental Health, Portuguese National Institute of Health, Portugal

ARTICLE INFO

Keywords:
Allostatic load
Physical inactivity
Meal
Exercise challenge

ABSTRACT

Background: The effect of a pre-exercise meal as countermeasure to exercise induced immunodepression is poorly known. Also, sedentary behavior is associated with increased cardiometabolic risk but studies on immune changes are lacking. Therefore, we aimed to assess: 1) the impact of a pre-exercise Mediterranean meal (MdM) compared with a fast-food type meal (FFM) on exercise-induced immunological changes and 2) the impact of an induced acute period of sedentary behavior on neuro-immune-endocrine status.

Methods: /Design: This is a two steps clinical trial including: (a) randomized crossover clinical trial, comparing the effect a high-fat/low-nutrient dense meal, FFM, with an isoenergetic similar high-nutrient dense meal, MdM, in the immune response to an exercise challenge (EC) and (b) a pilot trial assessing the neuro-immune-endocrine change induced by acute decreasing by half the usual physical activity level.

Results: A total of 46 participants (26 females), median aged 25 years were included. Of those 39-completed protocol, including overweight, physical active and inactive and participants with asthma. There were no differences in the EC between interventions. Dietary factors and physical activity were closely monitored during interventions and kept similar. During physical inactivity induction, 31% reached the target of 50% reduction in mean step number and 77% reached a 30% reduction.

Conclusion: The use of a pre-exercise meal to modulate immune response and the understanding of the immunological impact of physical inactivity might help to establish future recommendations on how to practice exercise in a safer way and to recognize the potential impact of inactivity.

1. Introduction

Exercise modulates the inflammatory and immune response. Very high and no or low training loads have been associated with higher risk of illness [1]. Lymphocyte proliferation is suppressed by acute and repeated bouts of strenuous exercise [2]. A reduction in peripheral blood Th1 cell number and production of interferon γ occurs in parallel with an increase in blood Th2 and regulatory T-cells with prolonged and exhaustive exercise [3]. Physical inactivity has been associated with an increased low grade inflammation [4] and longer periods to immunodepression [5]. Therefore, a J-shaped relationship has been proposed between absolute training load and illness, however this is not applicable to all populations [1].

Response to a stressor, like strenuous exercise [6], depends on several individual non-modifiable determinants such as genetic, gender, physiologic and psychological history and changeable ones related with individual fitness and nutritional status [7–10]. The dynamic process of adjusting to perturbations of homeostasis is referred to as allostasis.

* Corresponding author. Basic and Clinical Immunology, Department of Pathology, Faculty of Medicine, University of Porto, Al. Prof. Hernâni Monteiro 4200-309 Porto, Portugal.
E-mail address: disolha@gmail.com (D. Silva).

https://doi.org/10.1016/j.conctc.2018.05.010
Received 18 December 2017; Received in revised form 13 April 2018; Accepted 3 May 2018
Available online 09 May 2018

Allostatic load is a complex clinical construct that takes in consideration the repeated stress and *wear-and-tear* on the body and brain [11,12]. Although much effort has been devoted to examining responses to physical activity changes, no holistic metric to measure sedentarism related immune dysfunction has been widely applied within exercise physiology.

Nutritional strategies have been implemented as potential countermeasures to exercise-induced immunodepression [7]. Dietary supplements, namely carbohydrate ingestion have been associated with a blunt of the inhibitory effects of exercise on T-cell proliferation and neutrophil phagocytosis/oxidative burst activity [9,13]. N-3 polyunsaturated fatty acids (PUFA) supplementation has shown conflicting results [14]. The intake of fruit and vegetables was correlated to an increase of oxidative capacity [15]. Antioxidant vitamins, have shown positive effects particularly in individuals that engage in repeated bouts of vigorous exercise [7]. However, high doses and over-supplementation might diminish body's natural antioxidant defenses [7]. Few studies have address the potential additional benefit of using whole food versus supplements in immune and health-related outcomes [16].

Mediterranean diet has antioxidant and anti-inflammatory properties [17]. Therefore, it could be used to modulate acute immune response to exercise in a favorable direction in comparison to a Western diet, which is characterized by high intake of saturated and trans fatty acids, high glycemic load foods, and has low quantities of n-3 PUFA. High glycemic and high fat meals have been correlated with postprandial lipemia and inflammation [18,19] and has been associated with acute airway neutrophilic inflammation [20]. However, these meals where never compared in their response to exercise response.

Accordingly, we hypothesized that (1) a pre-exercise Mediterranean diet meal may induce a blunted immune and inflammatory response to exercise, and (2) an induced sedentary behavior may increase the allostatic load. Therefore, we aimed to assess in a randomized cross-over trial the effects of two isoenergetic nutrient different meals (MdM vs FFM) in the acute neuro-endocrine immune response to an exercise challenge; followed by a pilot trial assessing the impact of an induced short-term period of sedentarism on the allostatic load and immune outcomes.

2. Methods

2.1. Study design

This is a two steps clinical trial including: (a) randomized crossover clinical trial, comparing the effect a high fat micronutrient poor meal, fast-food like meal (FFM) versus a isoenergetic similar, micronutrient different, Mediterranean like meal (MdM) in the inflammatory and immune response to an exercise challenge (Fig. 1) and (b) non-randomized pilot trial assessing the impact of an induced physical activity reduction, decreasing by half the mean step numbers per day, for two weeks (Fig. 2).

A wash-out period of 7 days was performed between exercise challenges, after which participants crossed over to the alternate diet sequence. Study period length was selected in order to reach complete normalization of post prandial inflammation and plasma lipid level markers and to avoid carry-over of the exercise immune response, accordingly to previous published studies [18,21]. Baseline physical activity and diet were assessed during the 7 days washing-out period. Outcomes were evaluated before and after each meal; after exercise challenge and after physical activity reduction.

This trial was registered in clinicaltrials.gov NCT02027675.

2.2. Participants

Subjects were invited to participate through trial posters bulletin boards, newspapers, internet advertisements and during hospital visits. All those with interest to participate completed a generic online questionnaire that was linked to the online recruitment platform http://meriitproject.weebly.com/, which included contact information details and questioned age, height and weight and previous asthma reported diagnosis. The flow chart of recruitment strategy is described in Supplementary Fig. 1.

2.2.1. Inclusion and exclusion criteria

Subjects with asthma diagnosis, with excess of weight or obese, with body mass index (BMI) $\geq$25kg/m2, or healthy with normal BMI (18.5–24.9kg/m2) between 18 and 35 years old were eligible for participation after providing informed consent.

Participants were excluded if they met any of the following criteria: suffered from a respiratory disease other than asthma, except for severe asthma according to GINA guidelines; had any major systemic diseases (diabetes, cardiac arrhythmia, angina, congestive heart failure, abnormal electrocardiogram, renal or hepatic failure, mal-absorption disease, intestinal inflammatory disease, chronic infectious diseases); women who were breastfeeding, pregnant or intending to be pregnant; subjects unable to comply with the study and follow-up procedures; had dietary restrictions (ex. food allergy, vegetarians) or were on a weight losing diet during the last 3 months before the study.

2.3. Randomization, allocation and blinding

Participants were randomly assigned to the intervention order in a double-blinded fashion. A research assistant, generated the random allocation of the meals sequence and assigned the subjects to the intervention order, stratified by asthma diagnosis. This researcher was not involved in the evaluation or intervention procedures. The research nutritionist who prepared the meals was informed which meals to prepare for that day, but was unaware of participant's allocation and was not involved in the recruitment procedures or in the outcomes evaluations. The investigator that performed exercise challenge was also blinded for the intervention. The investigators that assessed the outcomes were blinded to the participant's allocation order. Participants were informed about the two different isoenergetic meals, but were unaware until the study visit of the content of each the meals or the order of the meals.

2.4. Study procedures

All participants performed a baseline visit. Then they would be submitted to (a) randomized cross over trial that included two different meals (FFM vs MdM) followed by an exercise challenges, each meal separated by a wash out period of seven days and then (b) two weeks of induced physical activity reduction. During the follow-up period they were asked to maintain their dietary habits.

On the days of both interventions participants were requested to have the same breakfast, at the same time, so that residuals from breakfast could be minimized, avoiding coffee or caffeine containing products; abstain smoking habits 12 h before the meal and during intervention and alcohol ingestion during the preceding seven days.

The evaluations for outcomes and confounding factors were performed before and after each meal and after each of the exercise challenges, during wash-out period and at the end of the physical activity reduction (Fig. 1, Table 1).

2.5. Interventions

2.5.1. Meal and exercise challenge

2.5.1.1. Fast food like and mediterranean like meal preparation and analysis. Meals were chosen to be energetically similar and respecting the Dietary Reference Intakes (DRI) for macronutrient distribution [22]. Two different meal were performed one Fast Food (FFM) and the other Mediterranean like meal (MdM). After each meal, participants were not allowed to eat or drink, and could not perform any physical