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Immunometabolic parameters in overweight dogs during weight loss with or without an exercise program

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ABSTRACT

The influence of physical activity on metabolic health in overweight dogs is unknown. This study was conducted to evaluate biomarkers of immunometabolic health in relation to changes in physical activity and adiposity. Client-owned overweight dogs participated in a 12-wk intervention based on caloric restriction combined with a training program (fitness and diet [FD] group, n = 8), or caloric restriction alone (diet-only [DO] group, n = 8). Physical activity was monitored by accelerometry. All dogs were fed the same diet and achieved similar weight loss. Fasting blood samples were collected before and after 6- and 12-wk intervention. Insulin resistance was evaluated from plasma insulin and C-peptide as well as homeostasis model assessment. Inflammation and dyslipidemia were evaluated from circulating leptin, adiponectin, C-reactive protein (CRP), monocyte chemoattractant factor-1 (MCP-1), interleukin-8 (IL-8), and cholesterol. Accelerometer counts in both groups were high compared with previous reports of physical activity in overweight dogs. No difference in blood parameters was evident between groups, evaluated by linear mixed-effects model ($P > 0.05$). Within the groups, the following changes were significant by t-test ($P < 0.05$): leptin decreased in both groups. Within the FD group, IL-8, MCP-1, and CRP decreased at 6 wk and IL-8 and cholesterol at 12 wk. Within the DO group, C-peptide and HOMA decreased at 6 wk and C-peptide at 12 wk. We conclude that, for both groups, weight loss resulted in minor indications of improved immunometabolic health, whereas this level of physical activity did not add further benefits.

1. Introduction

Overweight dogs have a shorter life span and increased susceptibility to diseases such as hip dysplasia and arthritis compared with lean dogs [1]. In recent years, increasing evidence show that obesity affects the immunometabolic health of dogs resulting in insulin resistance, low-grade chronic inflammation, and dyslipidemia [2–5]. In humans, physical activity (PA) effectively protects against similar immunometabolic derangements and reduces the risk of obesity-related diseases [6,7]. Although many pet dogs have a sedentary lifestyle [8,9], the potential benefits of increasing PA have not been investigated in relation to the immunometabolic derangements occurring with obesity in dogs.

Adiposity in humans is associated with increased concentrations of leptin and other proinflammatory adipokines, cytokines, and acute-phase proteins, whereas the anti-inflammatory and insulin-sensitizing adipokine adiponectin is reduced [10]. This proinflammatory state

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directly influences glucose metabolism, resulting in decreased insulin sensitivity [10]. In dogs, leptin concentrations also increase with higher body fat mass [11], whereas the involvement of other inflammatory markers in canine obesity and weight loss is less clear. Recently, concentrations of interleukin-6 (IL-6) and monocyte chemoattractant protein-1 (MCP-1), but not IL-8, were found to be increased in overweight dogs [12], whereas another recent study found decreasing concentrations of IL-8 and other interleukines with weight loss in dogs [13]. C-reactive protein (CRP) and MCP-1 have been reported to decrease with weight loss in some studies but not in others [2,4,5,13]. Discrepancies are also found regarding the role of adiponectin in dogs. An increase in circulating adiponectin in response to weight loss has been reported in 2 studies [5,14], whereas others found no effect of adiposity and weight loss in dogs [2,4,13].

Physical activity is acknowledged as a predictor of immunometabolic health in humans [7], and fitness or PA is regarded a more important prognostic factor for morbidity and mortality than fatness [15]. Irrespective of weight loss, increased PA has been shown to decrease plasma concentrations of CRP and proinflammatory cytokines and improve insulin sensitivity in obese humans [16,17]. Consequently, during the last few decades, extensive research has been exploring circulating immunometabolic biomarkers in relation to time spent in sedentary behavior and the duration and intensity of PA. Accelerometers are commonly used for objective PA measurements, and this tool has recently been validated in dogs [18], where cut-points for categorizing sedentary behavior and intensities of PA have now been established [8,18].

In this study population of diet-restricted inactive or exercised dogs, we have previously reported preservation of lean body mass [19] and changes in the gene expression relating to glucose metabolism [20] in the exercised group. For the present article, the aim was to evaluate the accelerometer data in more detail and to evaluate changes in indicators of glucose metabolism (fasting glucose, insulin, and C-peptide), cholesterol, the adipokines leptin and adiponectin, as well as inflammatory parameters (CRP, IL-2, IL-6, IL-8, IL-10, MCP-1) in response to the diet restriction with or without physical exercise. We hypothesized that a weight loss program based on physical exercise in combination with an energy-restricted diet would improve glucose homeostasis and decrease inflammatory markers more than a weight loss program based on energy restriction alone.

2. Materials and methods

2.1. Weight loss and fitness intervention

The protocol was approved by the Ethical and Administrative Committee at the Department of Veterinary Clinical and Animal Sciences, University of Copenhagen, and by the Danish Animal Experimentation Inspectorate. A signed informed owner consent was obtained for each dog before initiation of the study. Privately owned medium to large breed dogs with a sedentary lifestyle were recruited for the study. The dogs had to be overweight (body condition score [BCS] ≥6 on a 9-point scale [21]), but otherwise healthy based on clinical examination and blood profiles. A sedentary lifestyle was broadly defined as not habitually engaging in high intensity activities and daily walks being short or of mainly low intensity. Inclusion for a sedentary lifestyle was based on owner interview, clinical observation of the dog's gait and behavior off leash, and a treadmill trial run. Dogs were excluded if they were able to run comfortably at a speed >8 km/h with a 5% incline, but they had to be capable of doing light to moderate exercise (light trotting) without showing signs of musculoskeletal pain, based on clinical examination and gait evaluation by a skilled veterinary surgeon.

The study was designed as a prospective clinical trial. It was anticipated that, for many owners, it would not be possible to have their dog come in for training sessions, and therefore randomization was not instigated. Details of the interventions are described in Vitger et al [19]. In short, based on owner preference, the dogs were allocated to either the fitness and diet (FD) group or to the diet-only (DO) group. All dogs participated in a 12-wk calorie-restricted weight loss program. For the FD group, the caloric restriction was combined with an exercise program involving 1 h of treadmill exercise (land and underwater) 3 times weekly at the University Hospital for Companion Animals, Copenhagen, and the owners were asked to increase daily walks by 30 min. To measure PA, all dogs wore an accelerometer (Actigraph GT3X+, ActiGraph, Pensacola, USA) in the neck collar for 1 wk before the intervention for baseline measurement, and continuously during the 12-wk intervention period. The dogs wore the accelerometers 24 h daily, but to present values that are comparable to previous studies using similar accelerometers, results are shown for daytime recordings only (6 am–11 pm). For the same reason, data are presented as counts per min (cpm), and as time (min) spent in sedentary behavior and at 2 levels of PA intensities using cut-off points from the integrated axis previously established by Yam et al [18]: 0 to 1,351 cpm for sedentary behavior (no movement of the trunk), 1,352 to 5,695 cpm for light-moderate intensity PA (slow to moderate movement in a confined space or outdoors on a leash), and >5,696 cpm for vigorous PA (outdoors without a leash).

All dogs were fed the same dry diet (Royal Canin Satiety Support, protein 44% ME, fat 31% ME, and carbohydrate 25% ME, Royal Canin, Aimargues, France). The product is specifically made for weight loss intervention with a relatively higher protein (30% as fed) and fiber (16.5% as fed) content combined with lower fat content (9.5% as fed) compared with canine maintenance diets. To achieve a weight loss of approximately 1.5% per wk, energy allocation was calculated by use of computer software (Slimfit, Royal Canin, Aimargue, France) to meet 55% of the dog's estimated daily energy requirements (set as 132 kcal/kg target weight$^{0.73}$ for both groups). Target weight was estimated on the basis of body condition score. Based on these calculations, the mean initial energy allocation was 62 ± 2 kcal/kg target weight$^{0.75}$. The dogs were weighed every second wk, and if weight loss was <1% or >2%, their daily feeding allowance was adjusted by ±10%. For evaluation of body composition, dual-energy x-ray absorptiometry (DEXA) was performed