JOURNAL OF SURGICAL RESEARCH 190 (2014) 672–682

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.JournalofSurgicalResearch.com

Association for Academic Surgery

Short-term physical inactivity impairs vascular function

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ARTICLE INFO

Article history:
Received 16 January 2014
Received in revised form
26 January 2014
Accepted 6 February 2014
Available online 12 February 2014

Keywords:
Physical inactivity
Endothelial dysfunction
Arterial stiffness
Inflammation

ABSTRACT

Background: Sedentarism, also termed physical inactivity, is an independent risk factor for cardiovascular diseases. Mechanisms thought to be involved include insulin resistance, dyslipidemia, hypertension, and increased inflammation. It is unknown whether changes in vascular and endothelial function also contribute to this excess risk. We hypothesized that short-term exposure to inactivity would lead to endothelial dysfunction, arterial stiffening, and increased vascular inflammation.

Methods: Five healthy subjects (four men and one woman) underwent 5 d of bed rest (BR) to simulate inactivity. Measurements of vascular function (flow-mediated vasodilation to evaluate endothelial function; applanation tonometry to assess arterial resistance), inflammation, and metabolism were made before BR, daily during BR, and 2 d after BR recovery period. Subjects maintained an isocaloric diet throughout.

Results: BR led to significant decreases in brachial artery and femoral artery flow-mediated vasodilation (brachial: 11 ± 3% pre-BR *versus* 9 ± 2% end-BR, $P = 0.04$; femoral: 4 ± 1% *versus* 2 ± 1%, $P = 0.04$). The central augmentation index increased with BR (−4 ± 9% *versus* 5 ± 11%, $P = 0.03$). Diastolic blood pressure increased (58 ± 7 mm Hg *versus* 62 ± 7 mm Hg, $P = 0.02$), whereas neither systolic blood pressure nor heart rate changed. 15-Hydroxyeicosatetraenoic acid, an arachidonic acid metabolite, increased but the other inflammatory and metabolic biomarkers were unchanged.

This article was presented at ASC Annual Meeting on February 6, 2014.

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0022-4804/$ – see front matter Published by Elsevier Inc.
http://dx.doi.org/10.1016/j.jss.2014.02.001

Conclusions: Our findings show that acute exposure to sedentarism results in decreased endothelial function, arterial stiffening, increased diastolic blood pressure, and an increase in 15-hydroxyeicosatetraenoic acid. We speculate that inactivity promotes a vascular "deconditioning" state characterized by impaired endothelial function, leading to arterial stiffness and increased arterial tone. Although physiologically significant, the underlying mechanisms and clinical relevance of these findings need to be further explored.

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1. Introduction

Sedentarism, also known as habitual physical inactivity, is proposed to be an important and independent contributor to atherosclerosis and cardiovascular disease [1,2] and to other chronic conditions [3]. Sedentary behavior, by most definitions, refers to activities that do not increase energy expenditure substantially above the resting level, such as sitting, lying down, seated computer use and watching television and other variants of screen-based entertainment [4]. In 2007, less than half of US adults met the recommended physical activity standards [5]. Because prevalence of sedentary living continues to rise [6], understanding the physiological effects of physical inactivity and how it contributes to increased cardiovascular risk is crucial.

Bed rest (BR) has previously been used as a model to study the effects of sedentarism. Prior BR studies demonstrated that prolonged inactivity leads to reductions in conduit artery diameter [7], decreased reactive hyperemia (RH) [8], development of insulin resistance [9], type 2 diabetes [10], upregulation of the renin-angiotensin axis [11], and possibly vascular dysfunction [12]. Brachial artery flow–mediated dilatation (FMD) and arterial stiffness measured by arterial tonometry are used to assess vascular function, and when they are impaired, they have been independently associated with increased cardiovascular risk [13–16]. The effects of a short exposure to sedentarism on vascular function are poorly understood. Furthermore, an inflammatory response is implicated in the setting of vascular dysfunction and injury. Recent studies have shown that levels of certain proresolution lipid mediators, derived from fatty acid components of the red blood cell membrane, may suggest active resolution of inflammation [17–19]. We hypothesized that short-term exposure to sedentarism in healthy subjects leads to endothelial dysfunction, an increase in arterial stiffness, and an increase in inflammation. To test this hypothesis, we used a BR model in young healthy subjects.

2. Methods

We selected a 5-d period for BR because our intent was to understand the effects of an acute, short-term period of sedentarism on vascular function and inflammatory parameters.

2.1. Subjects

Four healthy male subjects (age 22 ± 2 y) and one healthy female subject (age 23 y) were recruited. Screening procedures included a history and physical examination, 12-lead electrocardiogram, complete blood count with differential, chemistry profile, lipid profile, toxicology screen, β-human chorionic gonadotropin (in the woman), and psychological evaluation. Subjects were nonsmokers and received no medication before the study. The exclusion criteria included documented peripheral arterial disease, vasculitis, evidence of active infection, other concurrent significant illness within 30 d of study initiation, a history or evidence of hypertension, coronary artery disease, diabetes, renal insufficiency, thyroid disease, hepatitis, anemia, current pregnancy, psychiatric disorder, obesity, hyperlipidemia, and alcohol or drug abuse. Additional exclusion criteria included known sleep disorders, shift work, and transmeridian travel within the 6 mo before starting the study. The female subject stopped taking oral or injected contraceptive agents 6 mo before beginning the experiment and was not pregnant during conduction of the studies.

2.2. Protocol

The protocol consisted of three phases: pre-BR, BR, and 2 d after BR, the recovery period (Fig. 1). Measurements of vascular function and inflammation were made at five time points: pre-BR, days 1, 3, and 5 (end-BR, last day), and 2 d after the completion of BR (recovery). The remaining variables, including metabolic biomarkers, bone density, and body composition, were measured at the pre-BR and end-BR time points. Pre-BR included an equilibration period of 55 h, during which subjects were admitted in a fasting state to the Clinical Research Center and started on an isocaloric diet containing 200 mEq of sodium, 100 mEq of potassium, 1000 mg of calcium, and 2500 mL of fluid. BR was begun after the equilibration period and lasted 5 d; during this period, subjects wore prophylactic antiembolism stockings. Sleep–wake cycles remained constant throughout BR, with each subject attaining 8 h of sleep each day between 11:30 PM and 7:30 AM. Subjects were confined to bed for the entire BR period. They were allowed to lie on their sides in a supine position on their backs or in a prone position on their abdomens. They voided and defecated in the supine position. They ate meals while lying on their sides, propped up on one elbow. Smoking, alcohol, and caffeine were not permitted during the experimental period. The end-BR phase began immediately after BR and lasted 2 d, during which time subjects resumed ambulatory activities at the Clinical Research Center, at the end of which testing took place. Various physiological measurements were assessed pre-BR, during, at the completion of BR, and 2 d after the end of BR (recovery), including blood analysis, heart rate (HR), blood pressure, brachial artery flow-mediated vasodilation ultrasound (FMD) and applanation tonometry. Dual-energy X-ray absorptiometry (DEXA) was completed during the pre-BR and again as soon as BR was completed. The study protocol was approved in advance by the Committee on