Safety and Health at Work 6 (2015) 256–262

Contents lists available at ScienceDirect

Safety and Health at Work

journal homepage: www.e-shaw.org

Original Article

Effects of Low-Dose Aspirin Therapy on Thermoregulation in Firefighters

Serina J. McEntire [1,2,*], Steven E. Reis [2,3], Oscar E. Suman [4], David Hostler [2,5]

[1] Department of Exercise Physiology College of Nursing and Health Sciences, Valdosta State University, Valdosta, GA, USA
[2] Department of Emergency Medicine, University of Pittsburgh, Pittsburgh, PA, USA
[3] Department of Medicine, University of Pittsburgh, Pittsburgh, PA, USA
[4] Department of Surgery, University of Texas Medical Branch, Galveston, TX, USA
[5] Department of Exercise and Nutrition Sciences, University of Buffalo, Buffalo, NY, USA

ARTICLE INFO

Article history:
Received 30 December 2014
Received in revised form
11 June 2015
Accepted 12 June 2015
Available online 26 June 2015

Keywords:
aspirin
exertion
firefighter
heat stress
skin blood flow

ABSTRACT

Background: Heart attack is the most common cause of line-of-duty death in the fire service. Daily aspirin therapy is a preventative measure used to reduce the morbidity of heart attacks but may decrease the ability to dissipate heat by reducing skin blood flow.
Methods: In this double-blind, placebo-controlled, crossover study, firefighters were randomized to receive 14 days of therapy (81-mg aspirin or placebo) before performing treadmill exercise in thermal-protective clothing in a hot room [38.8 ± 2.1°C, 24.9 ± 9.1% relative humidity (RH)]. Three weeks without therapy was provided before crossing to the other arm. Firefighters completed a baseline skin blood-flow assessment via laser Doppler flowmetry; skin was heated to 44°C to achieve maximal cutaneous vasodilation. Skin blood flow was measured before and after exercise in a hot room, and at 0 minutes, 10 minutes, 20 minutes, and 30 minutes of recovery under temperature conditions (25.3 ± 1.2°C, 40.3 ± 13.7% RH). Platelet clotting time was assessed before drug administration, and before and after exercise.
Results: Fifteen firefighters completed the study. Aspirin increased clotting time before and after exercise compared with placebo ($p = 0.003$). There were no differences in absolute skin blood flow between groups ($p = 0.35$). Following exercise, cutaneous vascular conductance (CVC) was 85 ± 42% of maximum in the aspirin and 76 ± 37% in the placebo groups. The percentage of maximal CVC did not differ by treatment before or after recovery. Neither maximal core body temperature nor heart rate responses to exercise differed between trials.
Conclusion: There were no differences in skin blood flow during uncompensable heat stress following exercise after aspirin or placebo therapy.

1. Introduction

Firefighters have the highest occurrence of line-of-duty death in the United States [1]. Over half of these deaths are cardiovascular events directly related to fire-suppression activities [2–4]. Continuous heavy work in thermal-protective clothing and repetitive upper body tool use characteristic of structural fire suppression impose significant cardiovascular strain by increasing myocardial oxygen demand and decreasing myocardial oxygen supply [5,6]. The physical strain combined with uncompensable heat stress provides triggers for ischemic events (i.e., myocardial infarction, stroke) [7–9].

Heart rate and core body temperature rise rapidly in response to increased physical work and environmental heat stress, which activates coagulation and causes vasoconstriction and endothelial dysfunction [7–9]. In addition, shift work, lifestyle factors, and exposure to smoke and chemicals during fire suppression may further predispose firefighters to earlier onset heart disease by

* Corresponding author. Department of Exercise Physiology, College of Nursing and Health Sciences, Valdosta State University, 1500 North Patterson Street, Valdosta, GA 31698, USA.
E-mail address: sjmcentire@valdosta.edu (S.J. McEntire).

2093-7911/$ – see front matter
http://dx.doi.org/10.1016/j.shaw.2015.06.003

amplifying inflammation and endothelial dysfunction, a precursor to atherosclerosis [10–13].

Our laboratory has completed a clinical trial investigating the effects of low-dose aspirin therapy on firefighter physiology, platelet activation, and vascular function during and following uncompensable heat stress (clinicaltrials.gov NCT01066923). Aspirin has been shown to reduce cardiac events in individuals of the general population who have cardiovascular disease (CVD) risk factors [14] and may decrease the overall prothrombotic state resulting from exertional heat stress during fire suppression. Data from our laboratory have demonstrated that aspirin therapy blunts heat-induced platelet activation and did not adversely affect core body temperature during work in an uncompensable heat stress environment [15]. However, other reports have suggested that systemic platelet inhibition by aspirin with standard therapeutic doses subsequently inhibited reflex cutaneous vasodilation [16–18]. Specifically, anticoagulation therapy inhibits the release of vasodilator substances from activated platelets [19–21], decreases the shear stimulus on the cutaneous microvasculature [17], and/or alters the internal temperature threshold for heat dissipation [16,17], eventually resulting in decreased dry heat loss capacity and increased thermal strain.

To our knowledge, this is the first study to comprehensively examine the effects of low-dose aspirin therapy on multiple indices of thermoregulation, inflammation, and physiological responses to exertion in the heat while wearing thermal-protective clothing. Previous studies demonstrating an attenuation in skin blood-flow responses were primarily done under passive heat stress conditions in middle-aged and older adults [16,17], with large doses of aspirin [22], or using anodal current-induced vasodilation [18,22], none of which is reflective of the environmental conditions or exertional loads that firefighters are exposed to. In addition, doing exercise in the heat leads to total body water and plasma volume losses, which further reduce blood flow to the gut [23]. Hypoperfusion of the gut leads to mucosal damage and the invasion of endotoxins into the blood. Low-dose aspirin has also been reported to damage the gut mucosa [24,25]. Elevated endotoxin levels can lead to fever, shivering, dizziness, nausea, vomiting, and diarrhea, all of which have been reported in endurance athletes [26–28]. The level of plasma tumor necrosis factor-α (TNF-α) is significantly increased in response to endotoxin [29]. Endotoxin and cytokine release may be indicative of poor thermal compensation. Understanding the impact of aspirin therapy on endotoxin release and the subsequent cytokine response is vital with regard to the safety profile of aspirin use during exertion under uncompensable heat stress conditions.

This is important given that firefighters may use daily aspirin therapy as primary prevention against heart attacks as well as to treat minor pain; therefore, information on the effect of aspirin during uncompensable heat stress is needed to make educated decisions about preventative treatment of CVD. If aspirin is detrimental to some aspect of thermoregulation, then this can guide physicians to treat the risk factors of CVD with other therapies and provide critical information about the risk/benefit ratio for aspirin therapy in firefighters whether used in an occupational context or for the management of CVD risk. This examination of the thermoregulatory, inflammatory, and physiological responses to low-dose aspirin therapy in firefighters during and following exertion under uncompensable heat stress conditions offers a more in-depth assessment of the safety of its use in this occupational cohort.

2. Materials and methods

We conducted a double-blind, placebo-controlled, crossover study to determine the additional effects of aspirin therapy on reflex cutaneous vasodilation, core body temperature, and heart rate responses under uncompensable heat stress conditions. Participants were volunteers and career firefighters from fire departments and emergency service agencies from Western Pennsylvania. All participants had no history of CVD, did not use medications expected to blunt the physiologic response to treadmill exercise or those with the known side effect of impaired thermoregulation, medications or supplements known to alter endothelial function (i.e., arginine, omega 3 fatty acids, nonsteroidal anti-inflammatory drugs, tobacco), or had no known history of platelet dysfunction, aspirin allergy/intolerance, or iodine allergy. The University of Pittsburgh Institutional Review Board approved the study and all participants provided written informed consent prior to participation.

2.1. Screening

All participants received a physical examination from a study physician including a 12-lead electrocardiogram (ECG) and a treadmill exercise stress test. Height was determined using a stadiometer, weight was recorded on a digital scale accurate to 0.5 g (KERN & SOHN GmbH, Balingen, Germany), and body fat was measured using three-site skinfold measurements [30]. Exclusion criteria included hypertension during screening and a resting ECG depicting the presence or history of CVD.

A Bruce protocol treadmill test was used to determine aerobic capacity (VO_{2max}) with open-circuit spirometry (TrueOne 2400; Parvo Medics, Sandy, UT, USA) measuring respiratory rate and maximal oxygen consumption (VO_{2peak}). Test results were interpreted by a board-certified cardiologist.

After meeting all inclusion criteria, a venous blood sample was obtained from each participant for estimating baseline platelet closure time. The sample was stored for future assay for detecting levels of endotoxin, interleukin-6 (IL-6), and TNF-α. Epinephrine-induced platelet aggregability (platelet closure time) was determined in whole-blood samples using a platelet function analyzer (PFA-100, Siemens, Malvern, PA, USA). A timeline of study visits is presented in Table 1.

2.2. Baseline skin blood flow

Following the screening visit, all participants returned to our laboratory for skin blood-flow measurements to establish baseline

Table 1
Timeline of study visits

Study visit 1	Screening	Informed consent, demographics, screening, and exercise stress test
Study visit 2	Baseline and maximal SBF, ASG	Resting LDF in heated room (37.5–40°C) Iodine paper test for sweat gland activation
Study drug No. 1 (14 d)		
Study visit 3	Protocol 1	1. Baseline measurements and preparation 2. Pre-exercise LDF, ASG 3. 45-min hot exercise 4. Postexercise LDF, ASG 5. 30-min recovery period
3-wk washout period before beginning second study medication		
Study drug No. 2 (14 d)		
Study visit 4	Protocol 2	1. Baseline measurements and preparation 2. Pre-exercise LDF, ASG 3. 45-min hot exercise 4. Postexercise LDF, ASG 5. 30-min recovery period

ASG, activated sweat gland; LDF, laser Doppler flowmetry; SBF, skin blood flow.