WILDERNESS & ENVIRONMENTAL MEDICINE, I, III-III (IIII)

ORIGINAL RESEARCH

A Novel Cooling Method and Comparison of Active Rewarming of Mildly Hypothermic Subjects

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Objective.—To compare the effectiveness of arteriovenous anastomosis (AVA) vs heated intravenous fluid (IVF) rewarming in hypothermic subjects. Additionally, we sought to develop a novel method of hypothermia induction.

Methods.—Eight subjects underwent 3 cooling trials each to a mean core temperature of 34.8 ± 0.6 (32.7 to 36.3° C) by 14° C water immersion for 30 minutes, followed by walking on a treadmill for 5 minutes. Core temperatures (Δ tes) and rates of cooling (°C/h) were measured. Participants were then rewarmed by 1) control: shivering only in a sleeping bag; 2) IVF: shivering in sleeping bag and infusion of 2 L normal saline warmed to 42° C at 77 mL/min; and 3) AVA: shivering in sleeping bag and circulation of 45° C warmed fluid through neoprene pads affixed to the palms and soles of the feet.

Results.—Cold water immersion resulted in a decrease of $0.5\pm0.5^{\circ}$ C Δ tes and $1\pm0.3^{\circ}$ C with exercise (P < .01); with an immersion cooling rate of $0.9\pm0.8^{\circ}$ C/h vs $12.6\pm3.2^{\circ}$ C/h with exercise (P < .001). Temperature nadir reached $35.0\pm0.5^{\circ}$ C. There were no significant differences in rewarming rates between the 3 conditions (shivering: $1.3\pm0.7^{\circ}$ C/h, $R^2 = 0.683$; IVF $1.3\pm0.7^{\circ}$ C/h, $R^2 = 0.863$; and AVA $1.4\pm0.6^{\circ}$ C/h, $R^2 = 0.853$; P = .58). Shivering inhibition was greater with AVA but was not significantly different (P = .07).

Conclusions.—This study developed a novel and efficient model of hypothermia induction through exercise-induced convective afterdrop. Although there was not a clear benefit in either of the 2 active rewarming methods, AVA rewarming showed a nonsignificant trend toward greater shivering inhibition, which may be optimized by an improved interface.

Keywords: hypothermia, rewarming, glabrous skin, arteriovenous anastomosis, afterdrop

Introduction

Accidental hypothermia, an involuntary drop in core body temperature $\leq 35^{\circ}$ C (95°F),^{1,2} is a potentially lethal condition that accounts for approximately 600 deaths in the United States each year and commonly complicates trauma or illness as a secondary condition.³ There is a 7

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Submitted for publication August, 2016.

Accepted for publication February, 2017.

to 23% mortality rate associated with mild to moderate hypothermia on emergency room and intensive care unit admission that doubles the odds of mortality compared to normothermic patients.^{2,4} Hypothermia often occurs far from definitive medical care, where invasive rewarming techniques are unavailable, necessitating external rewarming methods that have been found to have rates similar to shivering alone^{5–10} because the increase in skin temperature from exogenous heat suppresses the peripheral shivering stimulus and subsequent heat production.^{7,11} However, shivering suppression has the theoretical advantage of increased comfort, decreased physiologic strain, and conservation of energy stores.¹¹

Peripheral vasoconstriction is the body's initial response to cooling.¹² This vasomotor reaction limits

Presented at the Word Congress of Wilderness Medicine, Telluride, CO, August 2, 2016, and the SAEM Annual Meeting, New Orleans, LA, May 10–13, 2016.

the transfer of heat from the body's skin to the body's core. It is well recognized that exercise after cold water immersion causes a drop in temperature (afterdrop) as warm central blood perfuses cold extremities and this muscle-driven cold peripheral blood redistributes or convectively transfers cold back to the core. This convective cooling has been found to be 3 times greater than passive cooling¹³; however, this phenomenon has not been tested for hypothermia induction in translational research.

Immersion of arms and legs in 42 to 45°C water have resulted in rewarming rates 2 to 3 times faster than the commonly recommended external rewarming modalities.^{14,15} This is likely due to warming of the glabrous (nonhairy) skin regions that cover the soles of the feet and palms of the hands. These areas contain retia venosa, specialized densely packed subcutaneous arteriovenous anastomoses (AVA) that are under both local vasomotor and thermoregulatory control and have significant effects on thermoregulation.^{16,17} The AVA have the capacity for very high blood flow and bypass cold arterioles, capillaries, and peripheral insulating tissues to deliver blood directly to the retia venosa. The retia venosa can radiate heat if cooling is needed or rewarm large volumes of venous blood that go directly to the core. When AVA structures vasodilate, they have been shown to facilitate heat exchange more than 5 times that of nonglabrous skin during exercise.¹⁸ Hypothermic rewarming by warm water immersion, to date, has limited field applications due to logistical theoretical constraints and risk of inducing cardiovascular collapse.¹⁹ A recommended prehospital rewarming treatment used by search and rescue teams, emergency medical services, and the military is warmed administration of intravenous fluids (IVF).^{3,19–23} Prior to administration, IVF should be warmed to 38 to $42^{\circ}C$, ^{1–3} as $21^{\circ}C$ (room temperature) IVF decreases normothermic core temperatures by 0.3°C/L.²⁴ A liter of 40°C IVF provides 8 kcal of heat directly into circulating normothermic blood.4,25,26 While studies have examined the perioperative prevention of inadvertent hypothermia, the physiologic effects of warmed IVF in hypothermic individuals has not been studied.

The purpose of this study was to develop and test a novel methodology of heat distribution to induce hypothermia and then to compare active rewarming techniques vs spontaneous rewarming in mildly hypothermic participants. Our hypotheses were that use of convective cooling would be faster than immersive conductive cooling and the AVA rewarming would result in the most rapid rate of rewarming.

Methods

PARTICIPANTS

Eight healthy volunteers participated in this prospective randomized crossover trial. They were recruited via email listservs and word-of-mouth. They completed a Physical Activity Readiness Questionnaire to ensure the absence of any cardiopulmonary risk factors. No participants were excluded from the study. Written informed consent was obtained from each subject.

Anthropometric data including age, weight, height, and measurements of skinfold thickness at 4 sites (biceps, triceps, subscapularis, and suprailiac) was collected for body fat analysis (calculated from the Durnin/Womersley caliper method) prior to first cooling trial. Subjects were instructed to abstain from alcohol, medications, and any vigorous physical activity for a 24-hour period prior to each immersion trial. The study was approved by the Stanford University School of Medicine Institutional Review Board (NCT02339103).

FACILITIES AND EQUIPMENT

The trials were conducted in a $2.4 \times 3.3 \times 2.4$ m temperature-controlled environmental chamber. The trial conditions were held at an ambient temperature of 10°C and relative humidity of 20 to 35%. The treadmills (model SC7000, SCIFIT, Tulsa, OK) were housed in the experimental chamber.

Esophageal temperature (Tes) and heart rate were monitored throughout each trial. Tes was measured with a commercially available general-purpose thermocouple probe (Mon-a-therm No. 503-0028, Mallinckrodt Medical Inc., St. Louis, MO). These probes were self-inserted by the subjects through the nose to the base of the probe at a depth of 38 to 39 cm and held in place by a loop of surgical tape (Transpore, 3M Corporation, Saint Paul, MN) adhered to the skin adjacent to the naris. The probes were connected to a laptop-based thermocouple transducer/data collection system (GEC instruments, Gainesville, FL), which recorded temperature data at 1-second intervals. Heart rate monitors/data loggers (model S810, Polar Electro Oy, Kempele, Finland) were used to record and collect heart rate data at 5-second intervals. At the end of each trial, temperature data were downloaded to a central computer and transferred to a spreadsheet (Microsoft Excel) for subsequent analysis. Shivering was quantified at 5-minute intervals by the Bedside Shivering Assessment Scale, a validated quantification method for shivering.^{27,28}

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