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Nonpharmacologic approach to minimizing shivering during surface cooling: A proof of principle study☆

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Abstract

Purpose: This study had 2 objectives: (1) to quantify the metabolic response to physical cooling in febrile patients with systemic inflammatory response syndrome (SIRS) and (2) to provide proof for the hypothesis that the efficiency of external cooling and the subsequent shivering response are influenced by site and temperature of surface cooling pads.

Methods: To quantify shivering thermogenesis during surface cooling for fever, we monitored oxygen consumption (VO_2) in 6 febrile patients with SIRS during conventional cooling with cooling blankets and ice packs. To begin to determine how location and temperature of surface cooling influence shivering, we compared 5 cooling protocols for inducing mild hypothermia in 6 healthy volunteers.

Results: In the patients with SIRS, core temperature decreased 0.67°C per hour, all patients shivered, VO_2 increased 57.6%, and blood pressure increased 15% during cooling. In healthy subjects, cooling with the 10°C vest was most comfortable and removed heat most efficiently without shivering or VO_2 increase. Cooling with combined vest and thigh pads stimulated the most shivering and highest VO_2 and increased core temperature. Reducing vest temperature from 10°C to 5°C failed to increase heat removal secondary to cutaneous vasoconstriction. Capsaicin, an agonist for the transient receptor potential cation channel subfamily V member 1 (TRPV1) warm-sensing channels, partially reversed this effect in 5 subjects.

Conclusions: Our results identify the hazards of surface cooling in febrile critically ill patients and support the concept that optimization of cooling pad temperature and position may improve cooling efficiency and reduce shivering.

1. Introduction

Fever is a complex physiologic and behavioral response to infection or injury, the key feature of which is a temporary resetting of the body's thermostatic set point causing an

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increase in core temperature [1]. Clinical studies suggest that the effects of fever in sick humans depend, in part, on the severity of the underlying illness [2]. These studies demonstrate that fever shortens, and antipyretic drugs prolong, non–life-threatening illnesses, including chicken pox [3], rhinovirus [4,5], and shigellosis [6].

The influence of fever in severe sepsis is less clear. Up to 90% of patients with sepsis are febrile [7-9]. Retrospective studies of patients with invasive bacterial infections generally show fever to be associated with improved survival but less consistently so than in patients with lower acuity infections [10-14]. For example, Bryant et al [10] reported their analysis of 218 patients with gram-negative bacteremia demonstrating 2.4-fold higher survival (71% vs 29%) in patients who were febrile on the day of bacteremia (maximum daily temperature >38.3°C) compared with those who remained afebrile. In a reanalysis of published retrospective studies that we ranked based on acuity of illness, we found that fever-associated improvement in survival was lost in higher acuity disease [2]. These studies [11,15] also showed that survival decreased when fever exceeded 39.4°C, suggesting that there is an upper limit to the optimal febrile range. Fever in critically ill patients persisting for 5 days or more is associated with longer mechanical ventilation and intensive care unit stay and higher mortality [16]. Mortality was higher and neurologic outcome was worse in patients with brain injury and fever than those who remain afebrile [17,18].

Collectively, these studies suggest that suppressing fever in critically ill patients will have profound but difficult to predict consequences that depend on the clinical context and argue for rigorous prospective studies of fever suppression in well-defined illnesses. However, standard methods for fever reduction and suppression are either ineffective or unsafe in the critically ill patient population. Acetaminophen is poorly effective in critically ill patients [19,20]. Nonsteroidal anti-inflammatory agents such as ibuprofen are more effective in reducing fever [8], but the associated toxicity profile (eg, renal toxicity and platelet dysfunction) raises concerns about its use in many critically ill patients. Physical cooling methods can reduce core temperature with variable efficiency, but all methods cause shivering [21-23], increase in metabolic rate [24-26], and cause cutaneous vasoconstriction [27], which interferes with surface cooling methods. Pharmacologic methods are available to reduce the shivering response; however, these drugs have side effects that may limit their usefulness in critically ill patients [19,20,26,28-36].

This study had 2 objectives focused on the problem of fever management in critically ill patients. We first quantified the increase in oxygen consumption (VO_2) associated with shivering during conventional surface cooling in patients with systemic inflammatory response syndrome (SIRS) in whom fever persisted despite acetaminophen treatment. We then tested the hypothesis that the efficiency of external cooling and the subsequent shivering response are influenced by site and temperature of surface cooling using a precision surface cooling system to induce mild hypothermia in healthy subjects.

2. Materials and methods

2.1. Clinical protocols

All protocols were approved by the University of Maryland Institutional Review Board.

2.2. Standard surface cooling in critically ill patients with fever

We analyzed the core temperature, VO_2, and hemodynamic parameters in 6 patients with SIRS [37] during external cooling for a fever (core temperature >38.3°C). All patients were endotracheally intubated and mechanically ventilated with fraction of inspired oxygen 60% or less. After a decision by the treating intensivist to initiate surface cooling for fever, consent was obtained, and baseline measurements of hemodynamic factors and VO_2 were measured over 15 minutes. Two Cincinnati Sub-zero Blanketrol II cooling blankets (Cincinnati, OH) set to 4°C were placed, 1 above and 1 below the patient, and axillary and inguinal ice packs were applied. Oxygen consumption was measured using a Viasys (Conshohocken, PA) Vmax 229 metabolic cart connected to the exhalation port of the Siemens Maquet Servo-i ventilator (Washington, DC). Baseline hemodynamic and VO_2 values were established over the 15-minute period before initiation of cooling and were measured every 15 minutes during a 90-minute cooling period. The change in VO_2 was analyzed by calculating the maximal VO_2 increase during cooling compared with baseline levels and also by calculating the area under the VO_2 vs time curve using the trapezoidal rule [38]. Core temperature was measured from either a urinary bladder catheter or central venous catheter probe that was already present at the time of the study. Blood pressure was measured noninvasively every 15 minutes. Heart and respiratory rates were determined from the cardiac monitor and ventilator, respectively.

2.3. Optimization of cooling during induction of mild hypothermia in healthy subjects

After informed consent, 6 healthy male volunteers were subjected to the same 5 cooling protocols using the Arctic Sun™ 5000 cooling system (Medivance, Denver, Colo) and large standard cooling pad sets. The cooling pads sets consisted of a 2-piece vest that covered the back and lower abdomen and 2 thigh pads. All subjects underwent the following five 30-minute cooling protocols in the order listed: (1) vest at 10°C, (2) vest at 5°C, (3) vest and thigh pads at 10°C, (4) thigh pads at 5°C, and (5) vest at 5°C with