

Table 1. Review of controlled trials relevant to physical antipyresis methods applied to critically ill patients.

Online-only content for "Physical Antipyresis in Critically Ill Adults" by Kiekkas and colleagues in the American Journal of Nursing, July 2008, p. 40-49.

Subjects and procedure	Main end points and results
Creechan T, et al. <i>Am J Crit Care</i> 2001;10(1):52-9.	
<p>Randomized trial of 2 physical antipyretic methods in 37 medical ICU patients with an infection-related fever.</p> <p>Group 1 was treated with an air-flow cooling blanket; Group 2 was treated with a water-flow cooling blanket. In both groups, blankets were set at 10°C and placed on top of the patient. In group 1, bed linen was placed over the blanket; in group 2, bed linen was placed between the patient's skin and the blanket.</p>	<p>End points:</p> <ul style="list-style-type: none"> • Rate of core temperature decrease (°C/hr) • Core temperature decrease to ≤ 38°C after 8 hr of treatment • Recurrence of fever <p>Results:</p> <p>Group 1:</p> <ul style="list-style-type: none"> • Significantly faster decrease in core temperature (mean, 0.377°C/hr vs. 0.163°C/hr; <i>P</i> = 0.03) • Higher percentage of patients reached goal temperature of 38°C or lower after 8 hr of cooling (75% vs. 47%; <i>P</i> = 0.08), although difference was not significant • Significantly more time from removal of blanket to recurrence of fever (mean, 22.2 vs. 6.6 hr; <i>P</i> = 0.004) • Air-flow blanket recommended for future use more often: 100% vs. 50%
Diringer MN, et al. <i>Crit Care Med</i> 2004;32(2):559-64.	
<p>Randomized validation study of an endovascular cooling method in 296 neurologic ICU patients.</p> <p>Group 1 was treated with a conventional fever management protocol (when temperature was ≥ 38°C, patients were given acetaminophen [650 mg every 4 to 6 hr PO, PR, or NG]; if fever didn't resolve within 2 hours, ibuprofen [600 mg every 4 to 6 hr PO, PR, or NG] was substituted or added; if temperature was > 38.5°C, an air-flow cooling blanket was added; if not resolved in 60 min another air-flow cooling blanket, gastric lavage, or ice packs were added); Group 2 was treated with the conventional fever management protocol plus endovascular cooling (CoolGard/Cool Line catheter system).</p>	<p>End points:</p> <ul style="list-style-type: none"> • Total fever burden during the first 72 hr of treatment (fever burden = the product of temperature elevation above 38°C and time in hours to 72 hr, in degree hr) <p>Results:</p> <p>Group 2:</p> <ul style="list-style-type: none"> • Significantly lower total fever burden (mean, 2.87°C-hr vs. 7.92°C-hr; <i>P</i> < 0.01)
Gozzoli V, et al. <i>Intern Med</i> 2001;161(1):121-3.	
<p>Randomized study examining the effect of physical antipyresis on mortality in 38 surgical ICU patients.</p> <p>Group 1 was treated with external cooling (cooling blankets, ice packs, or cloths plunged into iced water); Group 2 received no antipyretic treatment.</p>	<p>End points:</p> <ul style="list-style-type: none"> • Defervescence at 24 hr after treatment • Recurrence of fever • Patient comfort • Lengths of ICU and hospital stay • Death <p>Results:</p> <ul style="list-style-type: none"> • Mean temperature decreased significantly in both groups at 24 hr after treatment: Group 1, from 38.9 ± 0.3°C to 37.6 ± 0.5°C (<i>P</i> < 0.001); Group 2, from 38.8 ± 0.5°C to 37.7 ± 0.6°C (<i>P</i> < 0.001) • No significant differences between groups in fever recurrence, patient comfort, lengths of ICU and hospital stay, and mortality rates

PO = by mouth; PR = by rectum; NG = nasogastric tube; OG = orogastric tube.

Subjects and procedure	Main end points and results
Gozzoli V, et al. <i>Intensive Care Med</i> 2004;30(3):401-7.	
<p>Randomized study comparing 2 pharmacologic methods and 1 physical antipyretic method in 30 surgical ICU patients.</p> <p>Group 1 received IV propacetamol (30 mg/kg body weight); Group 2 received IV metamizol (16 mg/kg body weight); Group 3 was treated with an air-flow cooling blanket, cloths plunged into iced water, or ice packs applied on most of the body surface.</p>	<p>End points:</p> <ul style="list-style-type: none"> • Core temperature decrease after 4 hr of treatment • Energy expenditure index • Hemodynamic parameters • Urine output • Plasma cytokine concentration <p>Results:</p> <ul style="list-style-type: none"> • No significant differences among groups in core temperature decrease, heart rate, and plasma cytokine concentration • Energy expenditure index alteration per 1°C of temperature: Group 1, 8% decrease; Group 2, 7% decrease; Group 3, 5% increase (this increase was nonsignificant) • Mean arterial blood pressure alterations: Group 2, significant decrease (from 71 ± 16 mmHg at baseline to 62 ± 13 mmHg at 2 hr of treatment; P = 0.008), then returned to baseline at 4 hr of treatment. The Group 2 mean remained significantly lower than the Group 3 mean at all time points after baseline. "The longitudinal effect of external cooling on blood pressure differed significantly" from that of either drug: compared with Group 3, the mean difference was -4.8 mmHg (-7.8 to -1.8) in Group 1, and -7.8 mmHg (-11.5 to -4.1) in Group 2 • Urine output alterations: Groups 1 and 3, nonsignificant; Group 2, significant decrease (mean, from 55 ± 42 to 25 ± 19 mL/hr; P < 0.05)
Henker R, et al. <i>Am J Crit Care</i> 2001;10(4):276-80.	
<p>Study comparing 1 pharmacologic method, 1 physical method, and 1 combination antipyretic method in 14 liver-transplantation ICU patients. Only patients able to receive acetaminophen were randomized; those not so able were assigned to the physical antipyretic group.</p> <p>Group 1 was given acetaminophen (650 mg every 4 hr, PO or NG); Group 2 was treated with a water-flow cooling blanket set at 18°C; Group 3 was given acetaminophen (650 mg every 4 hr, PO or NG) plus an air-flow cooling blanket set at 18°C.</p>	<p>End points:</p> <ul style="list-style-type: none"> • Core temperature decrease after 3 hr of treatment • Incidence of shivering • Hemodynamic parameters <p>Results:</p> <ul style="list-style-type: none"> • No significant differences among groups in core temperature decrease; incidence of shivering; or alterations of heart rate, arterial blood pressure, cardiac index, and systemic vascular resistance index
Keller E, et al. <i>Intensive Care Med</i> 2003;29(6):939-43.	
<p>Validation study of an endovascular cooling method in 20 normothermic neurologic ICU patients in whom hypothermia was induced.</p> <p>Group 1 was treated with an air- or water-flow cooling blanket and ice packs; Group 2 received endovascular cooling (CoolGard/Cool Line catheter system).</p>	<p>End points:</p> <ul style="list-style-type: none"> • Time to reach target core temperature (33°C to 34°C) • Glasgow Outcome Score <p>Results:</p> <p>Group 2:</p> <ul style="list-style-type: none"> • Significantly shorter time to reach target core temperature (mean, 190 ± 110 vs. 370 ± 220 min; P = 0.023) • Higher median Glasgow Outcome Score (4.5 vs. 2.5)

PO = by mouth; PR = by rectum; NG = nasogastric tube; OG = orogastric tube.

Subjects and procedure	Main end points and results
Loke AY, et al. <i>Nurs Crit Care</i> 2005;10(5):247-54.	
<p>Randomized study comparing 2 physical antipyretic methods in 27 general ICU patients.</p> <p>Group 1 was treated with an air-flow cooling blanket; Group 2 was treated with a water-flow cooling blanket. In both groups, blankets were set at $13 \pm 1^{\circ}\text{C}$ and placed on top of the patient.</p>	<p>End points:</p> <ul style="list-style-type: none"> • Core temperature decrease to $< 38^{\circ}\text{C}$ within 8 hr of treatment • Mean time needed for core temperature to decrease to $< 38^{\circ}\text{C}$ <p>Results:</p> <p>Group 1:</p> <ul style="list-style-type: none"> • Significantly higher percentage of patients with core temperature decreasing to $< 38^{\circ}\text{C}$ within 8 hr of treatment (94% vs. 60%, $P = 0.047$) • Significantly less time needed for core temperature to decrease to $< 38^{\circ}\text{C}$ (mean, 3.1 ± 0.8 vs. 5.7 ± 1.2 hr; $P < 0.001$)
Mayer SA, et al. <i>Neurology</i> 2001;56(3):292-8.	
<p>Randomized study comparing 1 pharmacologic method and 1 combination antipyretic method in 220 neurologic ICU patients.</p> <p>Group 1 received acetaminophen (650 mg every 4 hr, PO or PR); Group 2 received acetaminophen (650 mg every 4 hr, PO or PR) plus an air-flow cooling blanket set at 10°C.</p>	<p>End points:</p> <ul style="list-style-type: none"> • Treatment success: core temperature decrease to $\leq 37.2^{\circ}\text{C}$ within 24 hr of treatment • Treatment failure: core temperature $> 38.3^{\circ}\text{C}$ within 1 hr of treatment <p>Results:</p> <ul style="list-style-type: none"> • No significant difference between groups regarding treatment success or failure
Mayer SA, et al. <i>Crit Care Med</i> 2004;32(12):2508-15.	
<p>Randomized validation study of hydrogel-coated, water-circulating energy-transfer pads in 47 neurologic ICU patients.</p> <p>Group 1 was treated with hydrogel-coated, water-circulating energy-transfer pads (Arctic Sun Temperature Management System); Group 2 was treated with a water-flow cooling blanket set at 4°C.</p>	<p>End points:</p> <ul style="list-style-type: none"> • Fever burden (the product of temperature elevation above 37.2°C and time in hours to 24 hr) • Percentage of time patients remained febrile • Time needed to attain normothermia ($\leq 37.2^{\circ}\text{C}$) • Incidence of shivering <p>Results:</p> <p>Group 1:</p> <ul style="list-style-type: none"> • Significantly lower fever burden (median, $4.1^{\circ}\text{C}\cdot\text{hr}$ vs. $16.1^{\circ}\text{C}\cdot\text{hr}$; $P < 0.001$) • Significantly smaller percentage of study time (24 hr) remaining febrile (8% vs. 42%; $P < 0.001$) • Significantly less time needed to reach normothermia (median, 142 vs. 532 min; $P < 0.008$) • Significantly higher incidence of shivering (39% vs. 8%; $P = 0.013$)
Morgan SP. <i>J Neurosci Nurs</i> 1990;22(1):19-24.	
<p>Randomized study comparing 1 pharmacologic and 2 combination antipyretic methods in 21 neurologic ICU patients.</p> <p>Group 1 received acetaminophen (650 mg PO or PR); Group 2 received acetaminophen plus sponging of the trunk and extremities with tepid water (every 30 min); Group 3 received acetaminophen plus a water-flow cooling blanket.</p>	<p>End points:</p> <ul style="list-style-type: none"> • Time needed for core temperature to decrease to $< 37.8^{\circ}\text{C}$ • Incidence of shivering <p>Results:</p> <ul style="list-style-type: none"> • No significant difference among groups in time needed for core temperature to decrease to $< 37.8^{\circ}\text{C}$ • Group 3: Significantly higher incidence of shivering (57%, vs. 0% in both other groups; $P < 0.0071$)

PO = by mouth; PR = by rectum; NG = nasogastric tube; OG = orogastric tube.

Subjects and procedure	Main end points and results
Price T, et al. <i>Nurs Crit Care</i> 2003;8(1):37-45.	
<p>Randomized study comparing 4 physical antipyretic methods in 67 ICU patients with cerebral insult.</p> <p>First group allocation: <i>Group A</i> received paracetamol (1g NG or OG); <i>Group B</i> did not.</p> <p>Second group allocation, among patients whose temperature remained static or increased: <i>Group 1</i> was treated with an air-flow cooling blanket; <i>Group 2</i>, with an air-circulating fan; <i>Group 3</i>, with ice packs; <i>Group 4</i>, with cloths plunged into iced water.</p>	<p>End points:</p> <ul style="list-style-type: none"> • Core temperature decrease to $\leq 38^{\circ}\text{C}$ within 1 hr of treatment • Recurrence of fever within 24 hr • Incidence of shivering <p>Results:</p> <p><i>Group 4:</i></p> <ul style="list-style-type: none"> • Higher percentage of patients with core temperature decrease to $\leq 38^{\circ}\text{C}$ within 1 hr of treatment, but only in <i>Group A</i> patients
Poblete B, et al. <i>Br J Anaesth</i> 1997;78(2):123-7.	
<p>Nonrandomized study comparing 2 pharmacologic methods and 1 physical antipyretic method in 20 general ICU patients.</p> <p><i>Group 1</i> received IV propacetamol 1,000 mg; <i>Group 2</i> received IV metamizol 500 mg; <i>Group 3</i> was treated with cloths plunged into iced water and placed on most of the body surface.</p>	<p>End points:</p> <ul style="list-style-type: none"> • Core temperature decrease • Energy expenditure • Hemodynamic parameters <p>Results:</p> <ul style="list-style-type: none"> • Mean core temperature decrease: nonsignificant in <i>Group 1</i>; in <i>Group 2</i>, 0.4°C, $P < 0.05$; in <i>Group 3</i>, 2°C, $P < 0.0001$ • Mean energy expenditure decrease: nonsignificant in <i>Groups 1</i> and <i>2</i>; in <i>Group 3</i>, 243 kcal/day, $P = 0.004$ • Mean heart rate decrease: nonsignificant in <i>Group 1</i>, 6 beats/min in <i>Group 2</i> ($P < 0.05$), 14 beats/min in <i>Group 3</i> ($P < 0.0001$) • Mean arterial blood pressure decrease: nonsignificant in all groups
Schulman CI, et al. <i>Surg Infect</i> 2005;6(4):369-75.	
<p>Effect of pharmacologic or physical antipyretic methods (or both) on mortality rates in 82 trauma ICU patients, excluding those with cerebral injury.</p> <p><i>Group 1</i> received "aggressive" treatment: acetaminophen was given when core temperature rose above 38.5°C; use of an air-flow cooling blanket was added when temperature exceeded 39.5°C; <i>Group 2</i> received "permissive" treatment: both acetaminophen and cooling blankets were initiated when temperature exceeded 40°C.</p>	<p>End points:</p> <ul style="list-style-type: none"> • Average daily core temperature • Development of infection • Death <p>Results:</p> <ul style="list-style-type: none"> • No significant difference between groups in the development of infection <p><i>Group 1:</i></p> <ul style="list-style-type: none"> • Significantly lower daily core temperatures (mean, $36.7 \pm 0.7^{\circ}\text{C}$ vs. $37.8 \pm 0.6^{\circ}\text{C}$; $P = 0.006$) • Higher mortality (7 deaths vs. 1, $P = 0.06$)

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