Use and Effectiveness of Hypothermia Blankets for Febrile Patients in the Intensive Care Unit

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We performed a prospective observational (noninterventional) study of hypothermia blanket use in a population of adult intensive care unit patients with body temperatures of ⩾102.5°F. Thirty-nine of ninety-four febrile episodes (in 83 patients) were treated with hypothermia blankets. Logistic regression revealed that the strongest independent predictors of hypothermia blanket use were a temperature of ⩾103.5°F (odds ratio [OR] = 17), mechanical ventilation (OR = 25), and acute central nervous system illness (OR = 7.5). Hospitalization in the medical intensive care unit was strongly associated with avoidance of this therapy (OR = 0.023). Treatment with a hypothermia blanket was ordered by a physician in only 15% of cases. The mean cooling rate was the same (0.028°F/h) for blanket-treated and control patients. Multivariate Cox regression and factorial and repeated measures of analysis of variance revealed that blanket treatment was not more effective than other cooling methods. However, this treatment was associated with more "zigzag" temperature fluctuations of ⩾3°F (56% of blanket-treated patients vs. 18% of control patients; $P < .001$) and rebound hypothermia (18% vs. 0; $P = .001$). Hypothermia blanket therapy is primarily a nursing decision. We conclude that in addition to being no more effective than other cooling measures, hypothermia blanket therapy was associated with more temperature fluctuations and with more episodes of rebound hypothermia.

Hypothermia ("cooling") blankets are commonly used in the treatment of fever and hyperthermia. These devices lower core body temperature by conduction. Despite the widespread use of hypothermia blankets, there have been few studies to assess their effectiveness, and the existing clinical data are insufficient for evaluating the risks and benefits associated with their use. To our knowledge, there are no published data on how patients are selected for hypothermia blanket therapy. Therefore, we conducted a prospective observational (noninterventional) study to determine epidemiological correlates of hypothermia blanket use in clinical practice; the relative effectiveness of hypothermia blankets in lowering body temperature; and the frequency of hypothermia blanket–associated temperature fluctuations, rebound hypothermia, and patient discomfort.

See editorial response by Mackowiak on pages 1214–6.

Methods

Study design and data collection. This study was conducted at Temple University Hospital, a 540-bed tertiary care center in urban North Philadelphia, Pennsylvania. A preliminary evaluation of central supply records at our hospital showed that 74% of hypothermia blankets issued during the previous year had been used in adult intensive care units (ICUs). To obtain a relatively homogeneous population of febrile and/or hyperthermic patients, we limited our study to five adult ICUs: the coronary ICU, the medical-respiratory ICU, the cardiothoracic surgical ICU, the trauma and general surgical ICU, and the neurosurgical ICU.

Between 30 June and 1 November 1993, we conducted a prospective follow-up study of patients in these ICUs who had temperatures of ⩾102.5°F. During the study period, rounds were made five times weekly through all ICUs to record each patient's maximum daily temperature. We followed up patients whose temperatures reached 102.5°F, and we recorded demographic and clinical data, patient temperatures, the antipyretic drugs that were administered, and the physical cooling measures that were undertaken. Rectal temperatures were recorded almost exclusively. Medi-Therm I and Medi-Therm II Hyper/Hypothermia Machines (Gaymar Industries, Orchard Park, NY) were used during the study period.

All patients were followed up until their temperatures were <102.5°F for 48 consecutive hours. Patients were reentered into the study if their temperatures again reached 102.5°F and at least 2 weeks had elapsed since they had had fever of this magnitude. We also studied patients in the ICU who were treated with hypothermia blankets but whose temperatures never reached 102.5°F, but these patients were included only in analyses of adverse events associated with cooling and the duration of blanket use. One of us administered a questionnaire to communicative surviving patients at the conclusion of follow-up. We assessed patients'

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recollections of fever, shivering, and the hypothermia blankets, and the patients were asked to rate their level of comfort during the episodes of fever. This study was approved by the medical center's institutional review board.

Statistical methods. ICU patients with temperatures of ⩾102.5°F comprised the population that we analyzed for factors associated with hypothermia blanket therapy. All analyses and statistical methods were planned before the collection of data. We determined univariate relative risks, and we calculated 95% confidence intervals according to the method of Greenland and Robins [1]. We examined multiple exposure levels by using the Mantel extension test for linear trend [2]. Multivariate analysis was performed with use of stepwise forward logistic regression (SYSTAT, Evanston, IL) with an F to enter of .05. We used a base model of four factors believed, a priori, to most strongly influence hypothermia blanket use (i.e., patient age, the presence of CNS disease, maximum temperature during the period before hypothermia blanket use [cases] or during fever [controls], and hospitalization in the neurosurgical ICU). We compared the results with those from a total stepwise model and from models containing all factors significant by univariate analysis. Only main effects were included.

We used two methods to compare the rate of temperature reduction for patients who received hypothermia blankets with that for controls: Cox regression and analysis of variance (ANOVA) (SYSTAT). For both analyses, patients whose temperatures were not recorded over an 8-hour period and patients who died within 72 hours of study entry were excluded.

For Cox regression, the probabilities of becoming afebrile were analyzed by using three temperature cutoffs (102.5°F, 102°F, and 100.5°F) below which the patient was said to be afebrile. These temperatures were chosen arbitrarily; several cutoffs were used to determine if temperature differences (or similarities) between groups were consistent when the focus of analysis switched from one temperature range to another. For the 102.5°F cutoff, patients were followed up until their temperatures remained below that cutoff for 48 hours, in conformance with the duration of follow-up prescribed by our study design.

For the other two cutoffs, patients were followed up for only 72 hours because ''late'' temperature elevations among patients treated with hypothermia blankets might be a reflection of the reason that this therapy was selected rather than of the therapy itself. For example, to avoid brain edema, a hypothermia blanket might be used to treat central fever in a neurosurgical patient; in this situation, recurrent late fevers might be expected because of the nature of central fevers. This type of confounding might also have occurred with use of the 102.5°F cutoff; however, to examine the duration of fever in a number of ways, we wished to do at least one analysis in which a more-prolonged period (the total duration of the fever episode) was examined.

For the lower two temperature cutoffs, patients were defined as afebrile if their temperatures remained below the cutoff for 24 hours; the rationale for this shorter duration of apyrexia was the same as that cited for the 72-hour observation period. Patient observations were censored if the patient's temperature never decreased below the cutoff or if the patient died before his/her temperature decreased below the cutoff. We then calculated the relative probabilities of becoming afebrile.

Patients were stratified into seven groups according to their initial temperatures: 102.5°–102.9°F, 103°–103.4°, 103.5°–103.9°, 104°–104.4°, 104.5°–104.9°, 105°–105.4°, and 105.5°–105.9°. For patients who received hypothermia blankets, the initial temperature was the temperature at the time the blanket was activated; for patients who did not receive hypothermia blankets, the initial temperature was the first temperature ⩾102.5°F. The initial temperature in the latter group was chosen to be the first temperature above a predetermined, arbitrary cutoff (102.5°F) so that there would be no particular reason (bias) why subsequent temperatures would be likely to be increasing or decreasing. On the basis of this method, for patients who did not receive blankets and who had high body temperatures, it was unlikely that their ''initial'' temperature was their highest temperature since temperatures often increase in a stepwise manner.

To compare only patients with equivalent initial temperatures, we used a generalized Cox regression model that estimates baseline hazards for each stratum of a covariate [3]. We adjusted risks for other potential confounders by using three separate models: one model for demographic factors (age, gender, and fever etiology); one model for level of illness (ventilator use, presence of coma, and an order forbidding resuscitation); and one model for other cooling measures (doses of acetaminophen and physical measures other than blankets).

We performed two types of ANOVA. In the first ANOVA, the average hourly rate of cooling during the first 72 hours after the initiation of cooling measures was calculated for each patient. This was accomplished by fitting a line through a plot of maximum temperatures for each 4-hour period vs. time (least squares method). If temperatures were not available during a 4-hour period, the maximum temperature from the prior 4-hour period was used. We compared rates of cooling for blanket-treated patients and control patients by using factorial ANOVA models. Three models, analogous to those used in Cox regression, were used to determine the effects of potential confounding factors. These models were used with and without stratification (grouping) according to initial temperature.

The second ANOVA method was a repeated-measures ANOVA. In this analysis, we calculated the probability that there was a systematic difference between patients' temperature profiles based on the use of hypothermia blankets. Potential confounding factors were handled in the same manner as in the factorial ANOVA, but patients were always stratified according to initial temperature.

Results

During the 4-month study period, there were 94 separate episodes of fever (temperature, ⩾102.5°F) in 83 ICU patients.

None of these patients had malignant hyperthermia induced by anesthetic agents, neuroleptics, or other causes, and none had hyperthermia caused by increased ambient temperature. During thirty nine (41%) of these episodes, patients were placed on hypothermia blankets. The median maximum temperature prior to study entry was 103.1°F (range, 102.5°–106.5°F). In 76% of febrile episodes, patients had maximum temperatures of <104°F; 64% of patients treated with hypothermia blankets had maximum temperatures of <104°F. Fifty-six (68%) of the 83 patients were male, and the median age was 50 years (range, 17–92 years).

The distribution of febrile episodes among the clinical services was as follows: internal medicine, 30% of febrile episodes; general and vascular surgery, 28%; cardiothoracic surgery, 19%; neurosurgery, 15%; and other services, 8%. The median duration of hospitalization before study entry was 5 days, and the median duration of intensive care was 3 days. In 72 febrile episodes (77%), the patients were receiving mechanical ventilation at the time of study entry. The primary causes of fever were infection, 64% of febrile episodes; central fever, 7%; drug fever, 3%; tumor fever, 1%; undetermined, 21%; and other causes, 3%. The following infections were detected: bacteremia, 20% of patients; fungemia, 2%; pneumonia, 33%; abdominal infection, 11%; urinary tract infections, 7%; sinusitis, 6%; wound infection, 5%; meningitis, 4%; tracheobronchitis, 3%; mediastinitis, 2%; and empyema, necrotizing fasciitis, and tuberculosis, 1% each. Six additional patients whose temperatures never reached 102.5°F were treated with hypothermia blankets.

With use of multivariate logistic regression, we found that a maximum temperature of ⩾103.5°F (OR = 17; 95% CI = 3.2–88), mechanical ventilation (OR = 25; 95% CI = 3.2–190), and acute CNS disease (OR = 7.5; CI = 1.4–40) were the strongest independent predictors of hypothermia blanket use; hospitalization in the medical ICU was strongly associated with avoidance of this therapy (OR = 0.023; CI = 0.003–0.18), even after controlling for height of fever and other clinical factors.

The length of time that hypothermia blankets were used for 45 patients is shown in figure 1. Blankets were used on consecutive days for most of these patients. Sixty percent of patients remained on blankets for ⩽72 hours, and 80% received this therapy for <1 week. For surviving patients, the duration of blanket use did not correlate with the patients' maximum temperatures before study entry (Spearman's Rank Correlation; $P > .507$ $r = -0.065$; $P = .35$) or with temperatures at the time that the blankets were activated ($r = 0.007$; $P > .50$). Therapy with a hypothermia blanket was ordered by a physician for only seven patients (15%); the blanket was ordered by the nursing staff for the remaining patients. Despite the fact that we made a concerted effort to read the nursing notes, with the exception of the initiation of blanket therapy, it was almost impossible to determine exactly when blankets were turned on and off; this lack of information made temperature fluctuations difficult to interpret. Shivering was almost never recorded.

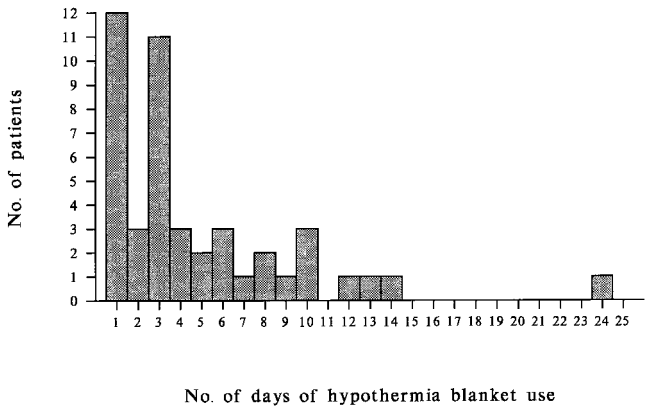

Figure 1. Distribution of durations of hypothermia blanket therapy among febrile patients in intensive care units.

Blankets were placed exclusively over the body for 29% of patients, under the body for 38%, and alternatively over and under the body for 13%; the position of the blanket could not be determined with certainty for 20%. Blankets could be set in a manual mode (the water temperature in the blanket could be adjusted by the nursing staff) or in an automatic mode (the nursing staff could set the desired patient temperature, and the machine adjusted the blanket-water temperature). The manual mode was chosen for 42% of patients, the automatic mode was chosen for 11%, alternating modes were chosen for 7%, and the mode was uncertain for 40%. A sheet was placed between the blanket and the body for 73% of patients.

The use of acetaminophen among patients treated with hypothermia blankets did not differ from that among the other febrile patients—either in the rate of use (96% for blanket-treated patients vs. 87% for those not treated with blankets; $P = .18$, Fisher's exact test) or in the number of doses administered (median number of doses over the first 72 hours, four and three, respectively; $P = .11$, Mann-Whitney U test). However, patients treated with hypothermia blankets were six times more likely to be treated with an adjunctive cooling measure (i.e., ice packs, cool baths, or alcohol rubs) than were those not treated with blankets; (36% vs. 6%, respectively; $P < .001$).

Patients with initial temperatures of ⩾102.5°F were stratified according to the initial temperatures, by 0.5°F increments, to compare rates of core temperature cooling among those who received hypothermia blankets and those who did not. Fifteen patients were excluded from these analyses: in nine cases, there was insufficient temperature data or the patients died <72 hours after blanket therapy was initiated; and six patients who received hypothermia blankets had temperatures that decreased to <102.5°F by the time the blanket was activated. Seventy-six percent of patients were placed in the first two temperature strata. The most meaningful comparison between hypothermia blanket–treated patients and controls could be made for

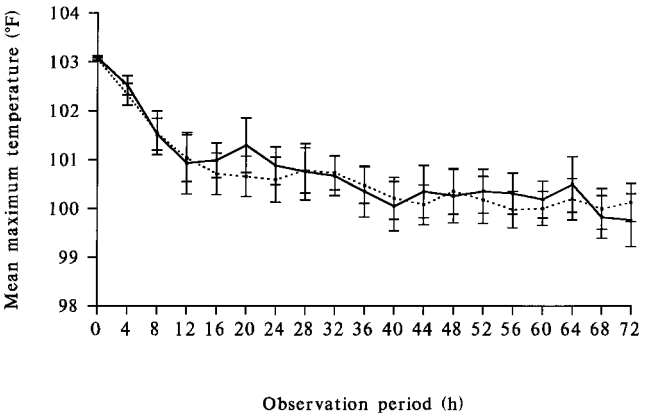

Figure 2. Mean initial temperatures (shown at time ''0'') and mean maximum temperatures for each 4-hour period (shown at all subsequent 4-hour endpoints) among intensive care unit patients with initial temperatures of 103.0°F–103.4°F. Patients who received hypothermia blankets (*solid line*) are contrasted with those who received other cooling measures (*dotted line*). Error bars indicate standard errors for each temperature. This initial temperature stratum offered the most efficient comparison between cooling methods.

patients whose initial temperatures were between 103°F and 103.4°F; 10 of these patients were in the blanket-treated group, and 15 were in the control group.

Other meaningful strata were those for initial temperatures of 102.5°F–102.9°F (4 patients and 31 patients, respectively), and those for initial temperatures of 103.5°F–103.9°F (4 patients and 2 patients, respectively). Twelve evaluable patients treated with hypothermia blankets (40% of blanket-treated patients) had initial temperatures of >103.9°F, while only one patient (2%) treated with other cooling measures had a temperature of >103.9°F. More temperatures were recorded for evaluable patients treated with hypothermia blankets in the first 72 hours than for other evaluable patients (median number of temperatures, 33 vs. 20; $P < .001$, Mann-Whitney U test). This difference persisted after controlling for the height of the initial fever.

We analyzed temperature differences between hypothermia blanket–treated patients and the other patients over the first 72 hours with use of ANOVA. All models showed a significant reduction in temperature in individual patients over the first 72 hours (mean initial temperature, 103.2°F; mean final temperature, 100.0°F; $P < .001$, multivariate Huynh-Feldt statistic). However, the mean cooling rate was 0.028°F/h for both blanket-treated and control patients. The results were unchanged in models that took into account the number of temperatures taken and possible confounding variables (the confounding factors are enumerated in the statistical methods section). The rates of temperature decline determined with use of these models were equivalent whether or not patients were stratified according to their initial temperature. A comparison of maximum temperatures over time, in one stratum, is shown in Figure 2. Temperature profiles in both patient groups were found to be equivalent when we used multivariate repeated-measures ANOVA ($P > .64$, multivariate Wilks' Lambda F statistic).

We calculated the probabilities of becoming afebrile by means of Cox regression with use of three temperature cutoffs: 102.5°F, 102°F, and 100.5°F. We compared hypothermia blanket–treated patients with other febrile patients only when the initial temperatures were equivalent. Multivariate models were used in an attempt to control for possible confounding factors and for the number of temperatures taken. There were no statistically significant differences between hypothermia blanket–treated patients and controls. The relative probabilities of becoming afebrile for patients treated with hypothermia blankets using temperature cutoffs of 102.5°F, 102°F, and 100.5°F were 0.69 (95% CI = 0.37–1.3), 0.83 (CI = 0.44–1.6), and 0.74 (CI = 0.28–1.9), respectively.

Patients treated with hypothermia blankets had more temperature fluctuations than did other patients. We defined a temperature ''zigzag'' to be a temperature increase and decrease (in either order) of ≥3°F within a 24-hour period. Twenty-five hypothermia blanket–treated patients (56%) had temperature zigzags, whereas 10 (18%) of 55 febrile patients treated with other cooling measures had temperature zigzags ($P < .001$, χ^2 test). This difference persisted after controlling for the total number of temperatures taken, and the height of the initial fever. Among hypothermia blanket–treated patients who had temperature fluctuations, the median number of zigzags was 1.5, and among other febrile patients who had temperature fluctuations, the median number of zigzags was one. Rebound hypothermia was defined as a decrease in temperature to <97°F after the initiation of any cooling measure. Patients treated with hypothermia blankets had more episodes of rebound hypothermia than did patients treated with other cooling methods. Eight of the study patients had 16 episodes of rebound hyperthermia; all were receiving treatment with hypothermia blankets ($P = .001$, Fisher's exact test). Two of these patients required active rewarming.

We administered a verbal questionnaire to patients to assess the discomfort associated with fever and cooling measures, but our analysis was severely limited by the inability of the patients to communicate and the presence of selective amnesia. Of the 45 patients treated with hypothermia blankets, 14 died before they could be interviewed, eight were neurologically impaired, seven could not remember the fever and the blanket, and 12 were not interviewed. Of the 55 patients treated with other cooling measures, eight died before they could be interviewed, 13 were neurologically impaired, four had amnesia, and 22 were not interviewed. Two of four hypothermia blanket–treated patients recalled shivering, and two of eight patients treated with other measures recalled shivering.

Discussion

Physical cooling methods are used to treat hospitalized patients who have hyperthermia or high fevers. Our study demon-

strated that hypothermia (cooling) blankets are frequently used to treat adult ICU patients with temperatures of ⩾102.5°F. In a previous study, we found that orders for antipyretic medications correlated most strongly with the specialty of the ordering physician; however, the actual decision to dispense antipyretics was made almost exclusively by nurses [4]. The use of hypothermia blankets also appears to be primarily a nursing decision.

Several factors were independently associated with hypothermia blanket therapy. First, the use of these blankets correlated with the height of fever. This is an understandable finding since physical cooling measures might be perceived as increasingly appropriate as a patient's temperature rises. Second, blanket use correlated with the presence of acute CNS illness. This finding may be related to knowledge that fever can increase brain edema in patients with head injuries or in those who have undergone cranial-vault neurosurgery [5]. It is of interest that when we examined acute CNS disease and residence in the neurosurgical ICU as independent variables, only the former was statistically significant, suggesting that, in this instance, it was the diagnosis rather than patient location that dictated the choice of cooling method. Third, blanket use was associated with the use of mechanical ventilation, which may have been a surrogate for a greater severity of illness. Although it was possibly more difficult to administer antipyretic medications to patients receiving mechanical ventilation, this did not appear to have influenced the decision to use a hypothermia blanket; antipyretic use did not differ between patients treated with blankets and patients treated with other measures, and blanket use was not affected by the presence of orogastric or nasogastric tubes. Last, we found that nurses in one of the ICUs were significantly less likely to use hypothermia blankets than were nurses in the other ICUs, even after controlling for patients' clinical conditions. However, we believe that this finding reflected the unit director's philosophy, since his dislike for hypothermia blankets was well known.

Hypothermia blankets were used in a variety of ways; differences included the positions of the blankets relative to the body, methods of water temperature adjustment, and use of sheets between the patient and the blanket. The manufacturer's operation manual does not recommend any specific practice except the use of sheets with all-vinyl blankets [6]. In a study by Caruso et al. [7], 89 patients treated with hypothermia blankets were randomized into four blanket-temperature groups. There were no statistically significant differences in the mean times required to reduce core temperatures to 38.9°C (102°F), but cooler blanket temperatures were associated with lower comfort scores and a greater incidence of rebound hypothermia [7]. We did not attempt to analyze the merits of any practices with respect to blanket use.

The most important result of the present study was that for equivalent degrees of fever, hypothermia blankets did not appear to cool patients more rapidly than did other methods, but use of these blankets was associated with greater temperature fluctuations and more rebound hypothermia. Since only one evaluable patient treated without a hypothermia blanket had an initial study temperature of >104°F, this result is applicable only to patients with temperatures of <104°F. Furthermore, all study patients had fever—not hyperthermia—and would therefore be expected to respond to treatment with antipyretic drugs. Hypothermia blankets might be a superior form of therapy for hyperthermic patients with temperatures of <104°F. It is possible that hypothermia blankets produced greater discomfort than other cooling measures, but we were unable to determine this mainly because of the patients' inability to communicate or inability to remember febrile episodes.

Hypothermia blankets promote heat loss by conduction, as do other methods such as immersion in cold water and application of ice packs. Other physical cooling methods promote heat loss by convection (e.g., fans), or evaporation (e.g., ice water or alcohol sponge baths). There are some data suggesting that evaporative methods are more effective than conductive methods, in part because conductive methods are greater inducers of shivering. In one study [8], healthy volunteers raised their rectal temperatures to 104°F by exercising at 93°F wet-bulb temperature. The rate of cooling for the subjects immersed in cold water (58°F) was slower than for those treated with water sprays (87°F), with or without blown compressed air. The immersed subjects were the only ones to shiver; some did so continuously. Studies of hyperthermia victims have yielded similar results [9].

In a study comparing evaporative methods, acetaminophen, or a combination of these treatments [10], 130 children admitted to a pediatric hospital because of fever were randomized to one of six treatment groups who received varying combinations of acetaminophen and sponging. Acetaminophen alone and sponging alone were comparably effective, but combinations of the two produced more rapid cooling. However, in a similar study of febrile children, Newman [11] found that tepid-water sponging in combination with acetaminophen therapy offered no advantage over acetaminophen therapy alone.

Data concerning the relative efficacy of hypothermia blankets are limited. In one small study [12], 21 hospitalized patients with neurological diseases whose rectal temperatures reached ⩾101°F were randomized into three treatment arms: acetaminophen-alone, acetaminophen with tepid water sponging, and acetaminophen with hypothermia blanket therapy. Only the last two groups were directly compared. The mean time required for rectal temperatures to decrease to 100°F was 100 minutes in the hypothermia blanket group and 144 minutes in the sponging group, but this difference was not statistically significant. Use of the blankets produced significantly more shivering than did the other two treatments.

Our study was observational and therefore subject to several limitations. Because patients whose temperatures reached 104°F were predominantly treated with hypothermia blankets, we were unable to determine the relative efficacy of other cooling measures in such patients. However, 64% of the

patients treated with hypothermia blankets had maximum temperatures of <104°F. Because cooling therapies were not randomly allocated, patients receiving hypothermia blankets differed in several respects from patients receiving other treatments.

We used stratification and mathematical models of several types in an attempt to compare only temperatures of like patients. While this approach has its limitations, we believe it may have some features unavailable in a randomized trial. Although clinical data are lacking, hypothermia blankets are widely used, and an observational study is arguably necessary to establish the ethical propriety of a randomized trial [13]. Hypothermia blankets can be used in a wide variety of ways, and an observational study provides data about the usefulness of this therapy as it is actually administered; protocols appropriate for a clinical trial may not always be feasible in clinical practice. Last, febrile patients in the ICU are a difficult group to enroll in randomized studies because of the unpredictable nature of their fevers, the need for rapid therapy, and the difficulty obtaining informed consent. Therefore, it is possible that patients enrolled in a trial might not be representative of the population of interest.

We believe that the superiority of hypothermia blankets over other cooling methods remains questionable. Our findings suggest that their routine use for patients with core temperatures of <104°F may not be warranted. The use of hypothermia blankets was typically initiated by nurses, often without the knowledge of physicians, which made interpretation of antibiotic effectiveness and patient progress difficult; this situation is clearly not desirable. Further research, including prospective randomized trials and studies of the cost-effectiveness of various cooling measures, is needed.

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