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Diagnosis and management of temperature abnormality in ICUs: a EUROBACT investigators' survey

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Abstract

Introduction: Although fever and hypothermia are common abnormal physical signs observed in patients admitted to intensive care units (ICU), little data exist on their optimal management. The objective of this study was to describe contemporary practices and determinants of management of temperature abnormalities among patients admitted to ICUs.

Methods: Site leaders of the multi-national EUROBACT study were surveyed regarding diagnosis and management of temperature abnormalities among patients admitted to their ICUs.

Results: Of the 162 ICUs originally included in EUROBACT, responses were received from 139 (86%) centers in 23 countries in Europe (117), South America (8), Asia (5), North America (4), Australia (3) and Africa (2). A total of 117 (84%) respondents reported use of a specific temperature threshold in their ICU to define fever. A total of 14 different discrete levels were reported with a median of 38.2°C (inter-quartile range, IQR, 38.0°C to 38.5°C). The use of thermometers was protocolized in 91 (65%) ICUs and a wide range of methods were reportedly used, with axillary, tympanic and urinary bladder sites as the most common as primary modalities. Only 31 (22%) of respondents indicated that there was a formal written protocol for temperature control among febrile patients in their ICUs. In most or all cases practice was to control temperature, to use acetaminophen, and to perform a full septic workup in febrile patients and that this was usually directed by physician order. While reported practice was to treat nearly all patients with neurological impairment and most patients with acute coronary syndromes and infections, severe sepsis and septic shock, this was not the case for most patients with liver failure and fever.

Conclusions: A wide range of definitions and management practices were reported regarding temperature abnormalities in the critically ill. Documenting temperature abnormality management practices, including variability in clinical care, is important to inform planning of future studies designed to optimize infection and temperature management strategies in the critically ill.

Keywords: Fever, hypothermia, intensive care unit, sepsis, septic shock, bacteremia

Introduction

Temperature abnormalities occur in approximately 50% of patients admitted to adult intensive care units (ICUs) and are associated with increased mortality in select groups of patients [1-8]. Although strong theoretical arguments exist both for and against the treatment of

pyrexia, the current literature does not support an outcome benefit from a particular temperature control strategy in patients without acute neurological injury [9-15]. Those against fever control argue that pharmacologic anti-pyresis with non-steroidal anti-inflammatory drugs and/or acetaminophen is potentially toxic [16,17], and physical cooling may cause shivering which increases metabolic demand and patient discomfort. On the other hand, advocates for fever control argue for increased patient comfort and a decrease in the risk of

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multi-system organ failure. Hypothermia is associated with adverse outcome in patients admitted to ICUs and increases the risk for nosocomial infection [8,18].

A number of small clinical trials have investigated temperature control strategies in febrile critically ill patients [11-14,19]. Due to the limited guidance provided by these studies, temperature control in febrile patients remains inconsistent and further trials are needed. However, in order to inform the planning of future trials an appraisal of current attitudes and practices is needed. We therefore conducted a survey of investigators in the EUROBACT study [20], a large observational study investigating hospital acquired bacteremia in ICUs, in order to describe contemporary temperature treatment practices in an international context.

Materials and methods

A survey exploring fever management practices was developed specifically for this study (Additional file 1). Questions in English surrounding treatment thresholds, temperature measurement modalities, treatment strategies, the presence of written treatment protocols, and treatment of selected patients were included. The survey was pre-tested by sequential administration to a number of non-participating unit directors and intensivists and was revised progressively for clarity. The survey was then administered to all site leads participating in the EUROBACT study [20] using a web-based form. Respondents were asked to answer based on the expected or average practice within their respective units. Initial non-respondents were sent email reminders to complete the survey at approximately two- and four-weeks post-initiation and after were contacted directly to request participation. Data on ICU characteristics were available for all units and was obtained from the unit-based survey component of the EUROBACT study. This study involved a voluntary survey of the EUROBACT study investigators. The EUROBACT study was approved by the Institutional Review Board at Paris-Saint Joseph and each participating center in EUROBACT complied with their local ethical institutional review board approval standards.

All analyses were conducted using Stata 11.2 (StataCorp, College Station, TX, USA). Analyses were primarily descriptive. Non-normally distributed (skewed) continuous data were reported as medians with interquartile ranges (IQR) and groups were compared using the Mann-Whitney test. Grouped categorical data were compared using the Fisher's exact test or χ^2 for multiple categories. A *P*-value less than 0.05 was considered to represent statistical significance.

Results

Of the 162 ICUs originally included in EUROBACT, responses were received from 139 (86%) centers in 23

countries in Europe (117), South America (8), Asia (5), North America (4), Australia (3) and Africa (2). There were no statistically significant differences among responders and non-responders with regard to reported average ICU case-fatality rate, ICU specialty type, university-affiliation or public/private ICU. However, non-respondents had significantly larger ICUs (median 18 beds, IQR, 11 to 25 versus 12 beds, IQR, 9 to 18; *P* = 0.018) and were more likely to be from non-European centers (11/33; 33% vs 12/129; 9%; *P* = 0.001).

Among the 139 respondents, 117 (84%) reported use of a specific temperature threshold in their ICU to define fever. A total of 14 different discrete levels were reported to define fever ranging from 37.0°C to 40.0°C with a median of 38.2°C (IQR, 38.0°C to 38.5°C). The use of thermometers was protocolized in 91 (65%) ICUs. A wide range of temperature measurement methods were used, with axilla, pulmonary artery catheter, and rectal thermometry the most commonly reported modalities (Table 1). Axillary, tympanic and urinary bladder catheter thermometry were reported as the most common primary means of measurement (Table 1).

When asked about new fever and the ordering of blood cultures, 83 (60%) reported these were only done by specific physician order, 25 (18%) stated these were routinely performed by nurses unless requested otherwise, 24 (17%) routinely performed these per protocol based on a predefined temperature threshold, and 7 (5%) indicated use of other approaches. When asked to report a usual threshold of hypothermia that would trigger the ordering of blood cultures, 129 (93%) responses were received. Fourteen different discrete levels were reported which ranged from 34°C to 38.3°C with a median of 36.0°C (IQR, 35.2°C to 36.0°C). In the event of hypothermia, 104 (75%) performed cultures only with specific physician order, 21 (15%) routinely cultured per protocol based on a specific temperature threshold, 10 (7%) routinely cultured blood as performed by nurses

Table 1 Temperature measurement modalities used in EUROBACT intensive care units

Thermometer type/location	ICUs reporting usage	Primary measure
Axillary	102	58
Pulmonary artery catheter	78	1
Rectal	73	12
Tympanic	64	30
PICCO	59	2
Esophageal	51	4
Urinary bladder	50	16
Temporal	14	9
Oral	12	2
Other	8	1

unless requested otherwise, and 4 (3%) indicated other approaches.

When asked specifically about ordering blood cultures in response to new fever or hypothermia, 136 (98%) indicated systematic use of aerobic culture bottles, 113 (81%) systematic use of anaerobic bottles, 37 (27%) systematic use of bottles for fungi, and 42 (30%) indicated that the type of bottles were specifically defined by physician order.

In the management of patients, only 31 (22%) respondents indicated that there was a formal written protocol in place for temperature control among febrile patients in their ICUs. In most or all cases the practice was to control temperature, to use acetaminophen and to perform a septic workup in febrile patients and that this was usually directed by physician order as shown in Table 2. While reported practice was to treat nearly all (median score 5 = always) patients with neurological impairment and most (median score 4 = most) patients with acute coronary syndromes and infections, severe sepsis and septic shock, this was not the case for many (median score 3 = sometimes) patients with liver failure as shown in Table 3. The responses for management (Tables 2 and 3) were similar among European and non-European respondents with two exceptions. Europeans were more likely to report either most of the time or always controlling fever (99/117; 85% vs 14/22; 64%; $P = 0.034$) and were more likely to use acetaminophen for fever control (82/117; 70% vs. 7/22; 32%; $P = 0.001$).

An exploratory analysis was conducted by comparing survey results with clinical variables obtained in the original EUROBACT study. No significant relationships were found between reported temperature thresholds in the survey for defining fever and median time to adequate therapy, case-fatality rate or the proportion of patients with fever in the original study. In addition, participating ICUs were dichotomized into those that

had case-fatality rates of 30% or less (low) and those that were greater than 30% (high) for hospital acquired bloodstream infection requiring ICU admission. No relationship between any of the survey variables and high or low case-fatality rate was observed.

Discussion

This study documents major variability in reported practices in the diagnosis and management of temperature abnormalities in critically ill patients worldwide. A total of 14 different discrete thresholds for fever were reported in this study confirming that there is not widespread accepted levels or consensus for the diagnosis of fever. Furthermore, the modalities used to measure temperature varied widely across study centers (Table 1). Although a consensus panel representing the American College of Critical Care Medicine and the Infectious Diseases Society of America recommended use of a temperature of 38.3°C or higher to represent fever, the results of this survey indicate that this definition has not been widely adopted [3]. Adoption of standard definitions and methods of measurement are needed for studies defining the determinants and outcomes of temperature abnormalities in the critically ill.

Although a wide range of temperature measurement sites and devices were reportedly employed in study ICUs, it is important to note that these vary in their accuracy in determining true core temperature. While pulmonary artery catheters are widely accepted as a gold standard for temperature measurement in critically ill patients, the use of this device in ICUs has significantly decreased in recent years [21]. Relatively few studies have directly compared other measurement techniques against this gold standard in ICU patients [22]. Erickson *et al.* compared infrared tympanometry, bladder, oral and axillary temperatures with pulmonary artery thermistor measurements in 38 patients admitted to ICU

Table 2 Management practices for patients with fever admitted to intensive care units

Item	Never	Rarely	Sometimes	Most of the time	Always	*Median (IQR)
Temperature is controlled in febrile patients	0	3 (2%)	23 (17%)	57 (41%)	56 (40%)	4 (4 to 5)
Temperature control in febrile patients is directed by physician order	3 (2%)	18 (13%)	25 (18%)	54 (39%)	38 (28%)	4 (3 to 5)
Temperature control in febrile patients is directed by nurses	15 (11%)	41 (30%)	33 (24%)	28 (20%)	21 (15%)	3 (2 to 4)
Acetaminophen (paracetamol) is used to control temperature in febrile patients	2 (1%)	13 (9%)	35 (25%)	70 (50%)	19 (14%)	4 (3 to 4)
Non-steroidal anti-inflammatory drugs (NSAIDs) are used to control temperature in febrile patients	36 (26%)	48 (35%)	41 (30%)	13 (9%)	0	2 (1 to 3)
Physical cooling methods are used to control temperature in febrile patients	1 (1%)	18 (13%)	71 (51%)	36 (26%)	13 (9%)	3 (3 to 4)
New fever triggers a full septic work-up	1 (1%)	6 (4%)	25 (18%)	82 (59%)	25 (18%)	4 (4 to 4)
Empiric antimicrobials are provided to febrile patients	1 (1%)	24 (17%)	68 (49%)	39 (28%)	7 (5%)	3 (3 to 4)

*Median score (IQR, Interquartile range) of response with 1 = Never, 2 = Rarely, 3 = Sometimes, 4 = Most of the time, and 5 = Always

Table 3 Temperature control practices in selected patient diagnostic subgroups

Item	Never	Rarely	Sometimes	Most of the time	Always	*Median (IQR)
Acute neurological injury (brain or spinal cord)	1 (1%)	3 (2%)	7 (5%)	28 (20%)	100 (72%)	5 (4 to 5)
Septic shock	4 (3%)	8 (6%)	29 (21%)	45 (32%)	53 (38%)	4 (3 to 5)
Severe sepsis without shock	6 (4%)	13 (9%)	28 (20%)	50 (36%)	42 (30%)	4 (3 to 5)
Infection without sepsis	9 (6%)	21 (15%)	32 (23%)	42 (30%)	35 (25%)	4 (3 to 5)
Acute liver failure	9 (6%)	24 (17%)	38 (27%)	38 (27%)	30 (22%)	3 (3 to 4)
Chronic liver failure	11 (8%)	30 (22%)	47 (34%)	31 (22%)	20 (14%)	3 (2 to 4)
Acute coronary syndrome	9 (6%)	12 (9%)	38 (27%)	49 (35%)	31 (22%)	4 (3 to 4)

*Median score (Interquartile range, IQR) of response with 1 = Never, 2 = Rarely, 3 = Sometimes, 4 = Most of the time, and 5 = Always

[23]. They found generally good average measurement differences among the different techniques except that axillary thermometry significantly underestimated true temperature. In addition, the accuracy of each technique varied to different extents depending on the levels of pulmonary artery temperature. Lawson *et al.* evaluated temporal artery, tympanic membrane, oral and axillary thermometers against pulmonary artery catheter temperature among 60 adults with cardiopulmonary disease admitted to ICU [24]. They found that axillary measurement typically underestimated true temperature, that oral and temporal artery measurements were the most accurate, and that tympanic measurements were the least accurate and precise. Myny *et al.* evaluated axillary and temporal artery thermometry as compared to pulmonary artery catheter in 57 mostly normothermic adult patients admitted to ICU in Belgium [25]. They found good agreement between temporal artery thermometry and pulmonary artery catheter but that axillary thermometry was biased by approximately 0.5 degrees. In another study conducted in 14 critically ill patients, Stelfox and colleagues found that while the temporal artery thermometer had good concordance at normal temperatures as compared to bladder thermometry, it was highly inaccurate at extremes of temperatures [26].

While a range of responses was given, most respondents indicated that they treat fever in critically ill patients most or all of the time (Table 2). Though there is generally good theoretical and clinical evidence to support lowering of temperature in febrile patients with neurological compromise, this is not the case for most other critically ill patients. Five randomized clinical trials (RCTs) have been published that have assessed the effects of anti-pyretic therapy on neurologically intact febrile patients admitted to ICUs [9,11-14,27]. Four of these studies found no difference in outcome associated with temperature lowering therapy but were limited by small sample size [9,11-13]. On the other hand, Schulman *et al.* compared a strategy of aggressive versus permissive fever control in critically ill surgical patients and found that there was a trend toward increased mortality associated with fever treatment that necessitated

stopping the trial due to safety concerns [12]. It is also important to recognize that the effect of fever control on outcomes may be dependent on whether the fever is due to an infectious etiology or not [5,6].

Despite the lack of evidence to support treatment of fever in most patients admitted to ICU, this appears to be common practice as evidenced by this study and other reports in the literature. One study from Canada found that among 100 critically ill adults without acute neurological injury, 79 received pharmacologic and/or physical anti-pyretic therapy during an episode of fever [28]. Similarly, another study conducted in Japan and Korea found that more than 50% of patients admitted to ICUs were treated with temperature lowering therapy [5]. Notably, they found a significantly increased risk for death associated with non-steroidal anti-inflammatory drug or acetaminophen therapy in patients with sepsis. Moreover, an online survey of members of the Australian and New Zealand Intensive Care Society Clinical Trials Group found that most respondents reported the use of interventions to lower temperature among febrile patients [29].

While this study provides insights into opinions and practices among a large number of centers, there are some important limitations that merit discussion. While EUROBACT does include representation from ICUs from six continents, most of the participants were European with disproportionate representation from France and Greece. Centers were not selected randomly from around the globe and as a result a significant selection bias is present. It is therefore not possible to accurately define different regional practices globally. A second limitation is that we reported responses in this study directly as entered by respondents without further validation or auditing of suspect data. As examples, one respondent reported using a remarkably high temperature of 40°C or higher to define fever and one reported that fever never triggered a septic workup (Table 2). Whether these are truly the cases or whether these are erroneous responses is not known. A third limitation is that the responses in this study were reported practices from one individual from an ICU. These may not be

reflective of what is actually done in true practice as would be revealed by a chart audit.

Conclusions

This study documents wide variability in approaches to diagnosis and management of temperature abnormalities among critically ill patients. Furthermore, despite being potentially harmful, most respondents report that they treat neurologically intact febrile patients admitted to ICU with temperature lowering interventions. This study provides support for further efforts to define and implement best practices for management of temperature abnormalities in the critically ill.

Key messages

- Temperature abnormalities, including fever and hypothermia, are common among patients admitted to ICUs.
- There is major variability among ICUs in the methods of temperature measurement and for defining temperature abnormalities.
- Broad practice variation exists among ICUs for the further investigation and management of patients with temperature abnormalities.
- Given the commonality, impact on outcome and wide practice variation in diagnosis and management of temperature abnormalities in ICUs, further investigation and consensus are warranted to establish best practices

Additional material

Additional file 1: EUROBACT Investigators Survey. This survey was sent to study participants.

Abbreviations

ICU: Intensive Care Unit; IQR: Inter-quartile range; RCTs: Randomized control trials.

Competing interests

None of the authors have financial or non-financial competing interests that would influence the conduct or reporting of this study.

Authors' contributions

DN and KL conceived and designed the study, collected data, conducted the primary analysis and drafted the manuscript. AT and AV contributed to study design, data collection and analysis. JR, DK, GD and J deW contributed to study design and collection of data. JFT participated in study conception and design, collection of data and analysis. All authors contributed to critical revision and approval of the final manuscript. The EUROBACT Study Investigators (listed by country) are Jeffrey Lipman, Department of Intensive Care Medicine, Royal Brisbane and Women's Hospital, Brisbane, Australia; Anne Leditschke, Helen Rodgers, Canberra Hospital Intensive Care Unit, Canberra Hospital, Canberra, Australia; David Milliss, Thomas Gottlieb, Intensive Care Services, Concord Hospital, NSW, Australia; Stuart Baker, Brigit Roberts, ICU, Sir Charles Gairdner Hospital, Perth, Australia; Peter Krafft, Silvia Benreiter, Intensiv 1b, Hospital Rudolfstiftung, Vienna, Austria; Pieter Depuydt, Intensieve Zorg, Universitair Ziekenhuis Gent,

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