Temperature management of non-elective intensive care patients without neurological abnormalities: a point prevalence study of practice in Australia and New Zealand

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The use of pharmacological and physical measures to treat fever is common in critically ill patients. In patients with acute neurological abnormalities, maintenance of normothermia is recommended by guidelines and is regarded as standard care,[1-3] but in patients with sepsis or other inflammatory abnormalities there is clinical uncertainty about how aggressively to treat fever.

Treatment of fever may relieve discomfort and reduce metabolic expense,[4-7] but there is a sound rationale for the hypothesis that the treatment of fever may be harmful in patients with infection.[8-10] Recent data from a retrospective study of 636 051 patients showed that fever in the first 24 hours in the intensive care unit is associated with decreased inhospital mortality in patients with an infection, but associated with an increased risk of mortality in those without infection.[11] Despite this, data from randomised controlled trials are of insufficient quality to make recommendations on the treatment of fever in critically ill patients with sepsis,[12] and there is uncertainty about how best to manage fever in critically ill patients with both sepsis and other inflammatory abnormalities.[8,13]

Observational data on the frequency of use of pharmacological and physical cooling interventions in critically ill patients with sepsis[14] and other inflammatory abnormalities are limited. With this in mind, the primary aim of our binational prospective point prevalence study was to identify the frequency of use of physical and pharmacological antipyretic therapies in non-elective ICU admissions with sepsis and other inflammatory abnormalities but without neurological abnormalities. The secondary aims were to determine the indications for administration of antipyretics, the specification of target temperatures, the sites used to measure temperature, and the mean peak temperatures recorded on the study day. These data will help us understand baseline practices and may aid in the design of future interventional studies investigating the effect of fever management in non-elective critically ill patients with sepsis and other inflammatory abnormalities.

ABSTRACT

Objective: To determine the frequency of pharmacological and physical cooling in non-elective general intensive care unit patients without neurological abnormalities in Australia and New Zealand, and to establish the indications for antipyretics, the prevalence of fever, and the methods of temperature measurement.

Design, setting and participants: A point prevalence study conducted on two days in 2010, in 38 ICUs in Australia and New Zealand, examining non-elective (emergency) patients admitted with sepsis and other inflammatory abnormalities but without neurological abnormalities.

Results: Of 506 general ICU patients surveyed on the study days, 311 had sepsis or other inflammatory abnormalities and no neurological abnormalities. These patients had a mean peak temperature of 37.3°C (SD, 0.8°C). In 100 patients (32.2%), the peak temperature was above 38°C. Paracetamol was the most common antipyretic used (152/311; 48.9%) and was administered for pain in 92/152 patients (60.5%), for pain and fever in 26/152 patients (17.1%), and for fever alone in 14/152 patients (9.2%). Patients who received paracetamol for fever had a mean peak recorded temperature of 38.3°C (SD, 0.8°C). Temperature measurements were mainly non-core (251/311; 81%) with axillary (116/311; 37%) and tympanic (110/311; 35%) measurements the most common.

Conclusion: Pharmacological antipyretics are used regularly for pain management rather than fever management, with paracetamol the most common antipyretic therapy. The use of NSAIDS and physical cooling is rare. Non-core temperature measurements were common.

Methods

Our point prevalence study was conducted on either 17 November or 15 December 2010 in 38 ICUs across Australia

Table 1. Patient demographics and outcome (*n* = 311)

Characteristic	*n* (%)*
Mean age, years (SD)	59.1 (17)
Sex (male)	201 (64.3)
Mean APACHE II severity of illness score (SD)	18.2 (7.4)
Readmitted to ICU	28 (9.1)
Source of admission to ICU	
Operating theatre (elective or emergency)	70 (22.5)
Accident and emergency	106 (34.1)
Hospital floor	92 (29.6)
Another ICU or hospital	43 (13.8)
Most common major diagnostic categories	
Trauma	33 (11)
Sepsis	97 (31.4)
Respiratory (total number)	44
ARDS	17 (5.6)
ALI	27 (9.1)
28-day status (alive)	246 (85.7)

APACHE = Acute Physiology and Chronic Health Evaluation.
ICU = intensive care unit. ARDS = acute respiratory distress syndrome.
ALI = acute lung injury. * Unless otherwise stated.

and New Zealand. Two single days were selected to allow flexibility for sites to participate. Data were collected over the previous 24-hour period in all patients occupying beds at 10 am on the day of the study. Human research ethics committee approval was obtained at each participating hospital and the need for individual patient consent was waived at all sites.

Patients were included in the non-elective cohort if they were 16 years or older on the study day. Patients were excluded if they were within 48 hours of elective surgery (because of the anticipated almost universal use of paracetamol as an analgesic in this group); had an acute brain injury (stroke or traumatic brain injury, hypoxic ischaemic encephalopathy, meningitis or other neurological infection); had a suspected or proven hyperthermia syndrome (neuroleptic malignant syndrome, malignant hyperthermia, heat stroke, serotonin syndrome or hyperthermia after an overdose); or were being treated with therapeutic hypothermia (after a cardiac arrest or traumatic brain injury when the temperature target was less than 36°C).

Data were collected prospectively on admitted patients and included general patient demographics as well as specific information on temperature management in the cohort of patients with sepsis or inflammation. Demographic data included age, sex, Acute Physiology and Chronic Health Evaluation (APACHE) II data, ICU length of stay, admission diagnosis and 28-day mortality after the study day. Questions relating specifically to temperature measurement included the highest temperature measured on the study day, and the measurement technique. Information on the use of antipyretics included the drug used (paracetamol, non-steroidal anti-inflammatory drugs [NSAIDs] or cyclooxygenase-2 [COX-2] inhibitors), the dose administered, how the medication was prescribed, and the route and indication for administration. Data were also collected on the physical cooling modalities employed, including ice packs, cooling blanket, intravenous (IV) cooling catheters, refrigerated IV fluids and body cavity lavage.

The statistical analysis was carried out at the George Institute for Global Health using SAS 9.2 for Windows (SAS Institute). Descriptive statistics were used for all clinical and demographic data. Where appropriate, differences in proportions were compared by χ^2 tests. No assumptions were made for missing data.
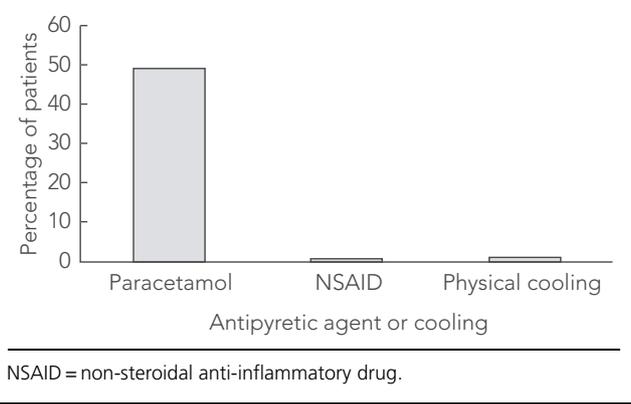
Results

A total of 38 hospitals participated in the point prevalence survey, with 506 patients screened. Of these, 311 patients met the inclusion criteria. The main diagnostic categories of the cohort were sepsis (31.4% [97/309; two missing from the data]); trauma (11.0% [33/301; 10 missing]); acute lung injury (9.1% [27/297; 14 missing]); and acute respiratory distress syndrome (5.6% [17/306; five missing]). The cohort had a mean age of 59 years (SD, 17 years); 64.6% were male; the mean APACHE II score was 18 (SD, 7.4); the 28-day mortality was 14.3%; and 80.1% were categorised as unplanned ICU admissions (Table 1). The mean peak temperature of the 311 patients was 37.3°C (SD, 0.8°C; six missing), and 20.3% (62/305; six missing) had a mean peak temperature ⩾ 38°C.

Paracetamol was used 49.5% of the time in the study population (152/307; four missing), NSAIDs 0.7% (2/306 [used with paracetamol]; five missing) and physical cooling 1% (3/300; 11 missing) (Figure 1). The indications for paracetamol and/or NSAID use were pain (64.3% [92/143; nine missing]), a combination of pain and fever (18.2% [26/143; nine missing]) and fever alone (9.8% [14/143; nine missing]). For 7.7% (11/143; nine missing) no indication for paracetamol administration was recorded (Figure 2).

Of the patients who had paracetamol, 64.3% (92/143; nine missing) were prescribed it regularly and 35.7% (51/143) had a *pro re nata* (PRN; as needed) order. Most patients received paracetamol via the oral or nasogastric route (75.9% [107/141; nine missing]); 22.0% (31/141) via IV administration, and 2.1% (3/141) rectally.

Figure 1. Type of antipyretic or physical cooling used in patients on study day (*n* = 311)

NSAID = non-steroidal anti-inflammatory drug.

Figure 2. Indications for paracetamol administration (*n* = 152)
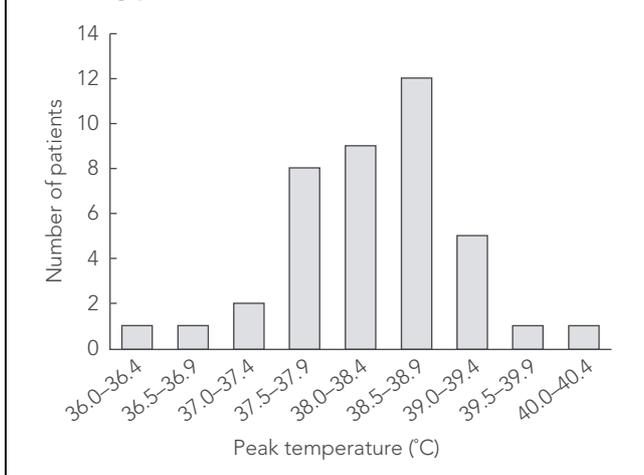

For the 40 patients who received paracetamol for fever, the mean peak temperature was 38.3°C (SD, 0.8°C; range 36.1–40.2°C) (Figure 3). For patients administered paracetamol for pain (excluding fever; *n* = 102), the mean peak temperature was 37.1°C (SD, 0.6°C; range, 35.4–39.9°C) [t(140) = −9.63; *P* < 0.001].
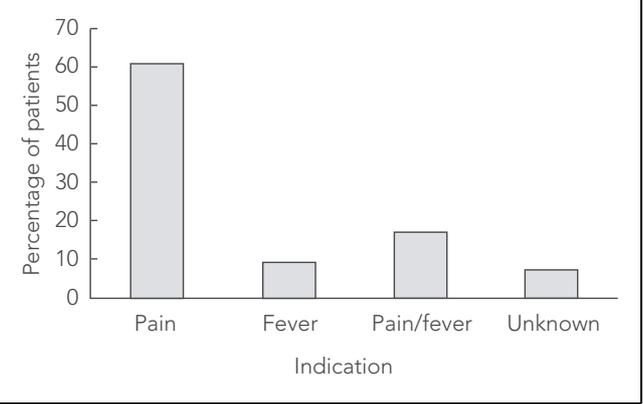
The use of physical cooling on the study day was rare, with 1% of patients receiving this form of cooling (3/300). Two patients received a cooling blanket while one had ice packs in use. The mean peak temperature for the patients receiving physical cooling was 39.2°C (SD, 0.9°C; range, 38.5–40.2°C). Patients not receiving physical cooling had a mean peak temperature of 37.3°C (SD, 0.8°C; range, 32.3–40.3°C)

Temperature measurements were mainly from non-core sites (82.6% [251/304; seven missing]), with the axilla (38.2% [116/304; seven missing]) and tympanum (36.2% [110/304; seven missing]) the most common sites. The most

frequently used core temperature measurement site was the nasopharyngeum (10.5% [32/304; seven missing]), followed by an intravascular site, measured by the use of a pulmonary arterial catheter (3%; 9/304), and the bladder (3%; 9/304) (Figure 4).

Possible confounding factors in the observed temperature data include the use of extracorporeal circuits (9.7% [30/308; three missing]) and use of steroids in the study population (18.8% [58/309; two missing]).

Discussion

Statement of principal findings

In our point prevalence study, 61.5% of patients (311/506 in 38 ICUs) met our inclusion criteria of non-elective patients with no neurological abnormalities. Seventy-five

Figure 3. Peak temperature range for patients receiving paracetamol for fever (*n* = 40)

Figure 4. Temperature measurement site for patients with sepsis and inflammation (*n* = 311)
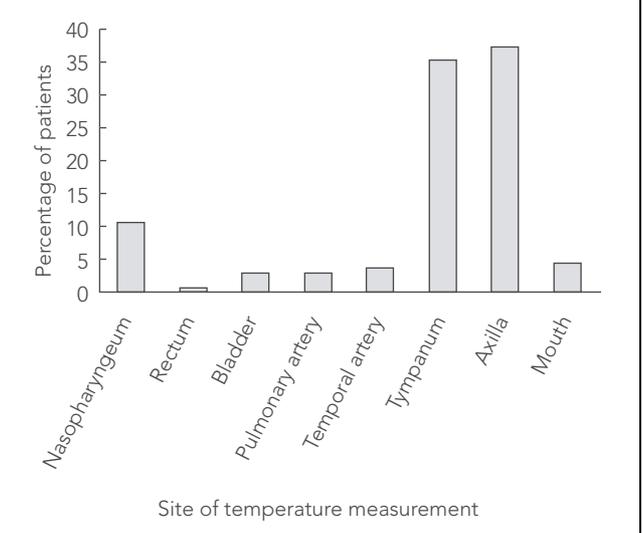
per cent of peak temperature measurements were between 36.8°C and 37.8°C, with 20.3% of readings ⩾ 38°C. Paracetamol was the most common pharmacological agent used. Although about one-quarter (28%) of patients received paracetamol for fever or fever and pain, the main indication for treating patients with paracetamol was pain (64.3%). When paracetamol was given for fever, the mean peak temperature on the study day was significantly higher than when it was given for pain exclusively (38.3°C v 37.2°C; *P* < 0.001). NSAIDs and physical cooling techniques were not often used. Finally, non-core temperature measurement sites were frequently used (82.6%) compared with core temperature sites.

Comparison with previous studies

We present prospective point prevalence data describing the incidence of fever in general mixed intensive care patients with sepsis or inflammatory abnormalities, but no acute neurological abnormalities. The patient population we studied was similar to those in international studies and other studies from Australia and New Zealand[7,14-16] also describing incidence of fever and paracetamol use. Our study reports multicentre data on measured temperature in non-elective patients without neurological abnormalities, and also details temperature management in contemporary, clinical practice.

Data from a Canadian retrospective cohort study of 24 204 patient admission episodes suggest that the mean temperature during the first 24 hours of ICU admission is 37.7°C (SD, 0.94°C) and that 24% of ICU admissions have a temperature ⩾ 38.3°C (tympanic and temporal artery measurements) within the first day of ICU admission.[7] A prospective observational study from Japan and Korea reported that 310 of 1425 patients with and without sepsis (22%) had temperatures between 38.5°C and 39.4°C at the study baseline on the first day of ICU admission (temperatures were measured in the pulmonary artery, bladder, axilla and tympanum).[17] In a Belgian study,[16] 139 of 493 patients (28%) had a temperature of ⩾ 38.3°C (temperatures were measured in the pulmonary artery, rectum, axilla or inguinal area, with the addition of 0.5°C to convert the reading to a core temperature equivalent) on ICU admission. However, Circiumaru[15] reported a higher incidence of fever using a similar definition (⩾ 38.4°C, tympanic temperature). In this study, the authors reported 61 episodes of fever during the first day of intensive care admission in a 100 patient prospective cohort study from England. In a French[18] retrospective study of 10 962 patients, 3172 (29%) had a peak temperature ⩾ 38.3°C at admission to an ICU (measurement technique not stated). Our data are broadly consistent with these studies, but these data illustrate important

issues that affect interpretation of temperature data, including variability in the definition of a raised temperature; temperature measurement technique and frequency of sampling; the concurrent use of pharmacological and physical interventions; illness severity and casemix of the described cohort, and lead-time bias.

Few studies which report on the incidence of fever include details on the use of temperature thresholds for interventions and the types of interventions used.[7,15,16,18] In a multicentre observational study of 51 febrile patients with sepsis, the mean peak temperature on Day 0 was 38.6°C (95% CI, 38.4–38.7°C) with a mean paracetamol dose of 1.8 g (SD, 1.6 g) per day, with paracetamol used in 69% of patients.[19] An Australian retrospective observational study of 106 sepsis patients found that the mean peak temperature in patients who had fever (*n* = 36) was 38.5°C (SE, 0.5°C), the mean total paracetamol dose during the study was 10.5 g (SE, 7.9 g), and that paracetamol was used for peak temperatures in 56% (SE, 0.08%) of patients with sepsis and fever.[14] In an Australian and New Zealand survey of fever management in febrile ICU patients with sepsis,[20] 269 of 423 clinicians (64%) indicated that they would act to reduce the temperature at or below 38°C. Eighty-six per cent selected paracetamol as their first-line intervention, and 59% used only physical cooling for their second-line choice if fever persisted despite first-line treatment. In this survey, clinicians were asked for thresholds for fever treatment in intensive and permissive arms of a theoretical clinical trial of fever management. For the intensive arm, the threshold for treatment was 38°C, and for the permissive arm, the threshold was between 38.8°C and 39.5°C. Our data on the threshold for use of paracetamol are consistent with these studies. However, the proportion of patients receiving paracetamol in a heterogeneous cohort was lower than in the three studies that reported on use of paracetamol in patients with sepsis exclusively.[21]

Implications

Our results suggest that in a clinical trial, a treatment threshold of 38.0–38.5°C with paracetamol used as a first-line treatment is reasonable, with breakthrough treatment of physical cooling therapies at higher thresholds (eg, > 39°C). Our study suggests that Australian practice is to use paracetamol first with physical cooling used as breakthrough treatment. However, the Japanese and Korean study showed that their practice was to use physical cooling first, followed by pharmacological antipyretics in patients with sepsis.[17] This practice may have other benefits, as found in a multicentre randomised controlled trial comparing physical cooling to no physical cooling in 200 febrile patients with septic shock.[21] Patients who received physical

cooling had significant short-term reductions in vasopressor dose. Therefore, the first-line intervention for a clinical trial needs careful thought.

The fact that the dominant temperature measurement methods used were non-core measurements has implications for understanding the relationship between core and non-core temperature measurements in clinical practice and clinical trials. Traditional approaches include the use of a conversion factor of between 0.3°C and 0.5°C,[22] but a recent systematic review questioned the methodology of studies on this issue.[23] As a result, the authors suggested avoiding the use of conversion factors until more reliable estimates of the relationship are available.

Strengths and limitations

Our study has several strengths, including that it provides current, prospective, multicentre, binational data on temperature management in febrile patients in ICUs. We have described key aspects of temperature management, including peak daily temperatures, temperature measurement techniques, types of and indications for antipyretic drugs used, and physical cooling modality in general ICU patients with sepsis and inflammation.

Limitations of our study include the lack of longitudinal data. Data were collected over a 24-hour period, and therefore may not be a true representation of clinical practice. We did not collect the temperature which triggered the administration of antipyretics; we collected the highest and lowest temperature on the study day. Some of the interpretation of temperature could be confounded by the fact that about 10% of patients (30/311) were on an extracorporeal circuit and 19% (58/311) were receiving steroids; these factors can both alter body temperature. The patients included in the study were a convenience sample, and we did not account for lead-time bias, illness severity, or specific diagnosis of sepsis or inflammation, each of which may have an impact on the way fever is managed. Lastly, the main indication for antipyretic prescription was pain and fever, rather than for fever alone, with only a small number of patients actually being treated just for an indication of fever. However, our study was conceived as an exploratory observational study to facilitate the design of further observational and interventional studies of temperature management for critically ill patients with sepsis or inflammation.

Conclusion

We identified that pharmacological antipyretics are used regularly for pain management rather than fever management, with paracetamol the most common therapy used. The use of physical cooling was rare, and non-core temper-

ature measurements were common. Our results are important in understanding current temperature management practice in Australian and New Zealand ICUs. They will help define temperature thresholds for antipyretic interventions and the type of pharmacological and physical cooling intervention to be used in a clinical trial.

Competing interests

None declared.

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