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ORIGINAL ARTICLE

Assessing neonatal heat balance and physiological strain in newborn infants nursed under radiant warmers in intensive care with fentanyl sedation

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Abstract

Purpose To assess heat balance status of newborn infants nursed under radiant warmers (RWs) during intensive care.

Methods Heat balance, thermal status and primary indicators of physiological strain were concurrently measured in 14 newborns nursed under RWs for 105 min. Metabolic heat production (M), evaporative heat loss (E), convective (C) and conductive heat flow (K), rectal temperature (T_{re}) and mean skin temperatures (T_{sk}) were measured continuously. The rate of radiant heat required for heat balance (R_{req}) and the rate of radiant heat provided (R_{prov}) were derived. The rate of body heat storage (S) was calculated using a two-compartment model of 'core' (T_{re}) and 'shell' (T_{sk}) temperatures.

Results Mean M, E, C and K were 10.5 ± 2.7 W, 5.8 ± 1.1 W, 6.2 ± 0.8 W and 0.1 ± 0.1 W, respectively. Mean R_{prov} (1.7 ± 2.6 W) and R_{req} (1.7 ± 2.7 W) were similar ($p > 0.05$). However, while the resultant mean change in body heat content after 105 min was negligible (–0.1 ± 3.7 kJ), acute time-dependent changes in S were evidenced by a mean positive heat storage component of +6.4 ± 2.6 kJ and a mean negative heat storage component of –6.5 ± 3.7 kJ. Accordingly, large fluctuations in both T_{re} and T_{sk} occurred that were actively induced by changes in RW output. Nonetheless, no active physiological responses (heart rate, breathing frequency and mean arterial pressure) to these bouts of heating and cooling were observed.

Conclusions RWs maintain net heat balance over a prolonged period, but actively induce acute bouts of heat imbalance that cause rapid changes in T_{re} and T_{sk}. Transient bouts of heat storage do not exacerbate physiological strain, but could in the longer term.

Keywords Radiant warmer · Neonate · Heat balance · Thermoregulation

Abbreviations

A_k	Surface area of the back (m^2)
BSA	Body surface area (m^2)
C	Convective heat exchange (W or kJ min^{-1})
C_{sp}	Specific heat capacity of human tissue (kJ °C^{-1} kg^{-1})
E	Evaporative heat loss (W or kJ min^{-1})
E_C	Caloric equivalent of carbohydrates (kJ LO$_2{}^{-1}$)

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E_F	Caloric equivalent of lipids (kJ $LO_2{}^{-1}$)
F_iO_2	Fraction of inspired oxygen (%)
F_iCO_2	Fraction of inspired carbon dioxide (%)
HR	Heart rate (bpm)
K	Conductive heat exchange (W or kJ min^{-1})
M	Metabolic heat production (W or kJ min^{-1})
MAP	Mean arterial blood pressure (mmHg)
NICU	Neonatal intensive care unit
P_{bar}	Barometric pressure (mmHg)
$P_{ET}CO_2$	End-tidal CO_2 (mmHg)
R	Radiant heat exchange (W or kJ min^{-1})
RER	Respiratory exchange ratio
RH	Relative humidity (%)
R_{prov}	Radiant heat provided (W or kJ min^{-1})
R_{req}	Radiant heat required for heat balance (W or kJ min^{-1})
RR	Respiratory rate (bpm)
RW	Radiant warmer
RW_{output}	Radiant warmer output (%)
S	Heat storage (W or kJ min^{-1})
TEWL	Transepidermal water loss (g h^{-1})
T_a	Ambient air temperature (°C)
T_{re}	Rectal temperature (°C)
T_{sk}	Mean skin temperature (°C)
$T_{feedback}$	Radiant warmer servo-control feedback temperature (°C)
V	Air velocity (m s^{-1})
V_e	Minute ventilation (L min^{-1})
VCO_2	Carbon dioxide production (L min^{-1} or ml $(kg\ min)^{-1}$)
VO_2	Oxygen consumption (L min^{-1} or ml $(kg\ min)^{-1}$)
V_t	Tidal volume (L)

Introduction

For newborns admitted to the neonatal intensive care unit (NICU), providing an optimal thermal environment is a priority to ensure survival, recovery and growth (Silverman et al. 1958; World Health Organization 1997; Sherman et al. 2006). By virtue of their immature thermoregulatory system and a morphological susceptibility to excessive heat dissipation, newborn infants are predisposed to deleterious reductions in core body temperature (Bolton et al. 1996; Baumgart 2008). Mortality rates are markedly increased when premature newborns are nursed in an environment with a ‘low’ (28.9 °C) relative to a ‘normal’ (31.7 °C) ambient temperature in the first 5 days of life (Silverman et al. 1958). Accordingly, providing a thermal environment that ensures stable normothermic body temperatures by way of passive heat exchange rather than an active response is essential (Hey and Katz 1970; Tourneux et al. 2009), but providing these conditions remains a challenge even in modern NICUs (Witt 2010; Lyon and Freer 2011).

Both radiant warmers (RWs) and incubators are commonly used in NICUs. Though standard convection-warmed incubators have been investigated extensively (Magnarelli 2006), little scientific information exists regarding the efficacy of RWs. These open beds are equipped with a radiant heat source placed above the neonate to provide external thermal support while allowing nurses ease of access and visibility to the patient (Hazan et al. 1991). Typically, the radiant heat source output is servo-controlled by a single local skin temperature measurement under the axilla (Sinclair 2002). While these devices have been shown to maintain a stable rectal temperature in term newborns (Meyer et al. 2001), many authors suggest that several critical issues still exist (LeBlanc 1982; Sherman et al. 2006; Lyon and Freer 2011; Trevisanuto et al. 2011). First, a feedback mechanism relying on a single measure of skin temperature that is not directly indicative of whole-body thermal status increases the risk of passive over/underheating (Molgat-Seon et al. 2013). Secondly, the RW does not directly or indirectly account for the rate of radiant heat needed for the patient to achieve heat balance between internal production and net dissipation to the surrounding environment, but responds to acute changes in local skin temperature regulated around a set-point temperature (Baumgart et al. 1980; Wheldon and Rutter 1982). The variation in radiant heat output could elicit transient periods of heat storage and heat debt that are approximately equal over time, but lead to oscillations in core and skin temperature that subsequently induce metabolic, cardiovascular and respiratory strain. While some contemporary studies have conducted heat balance investigations of the thermal environment of newborns under RWs (Bell et al. 1980; Wheldon and Rutter 1982; Baumgart 1985; Seguin and Vieth 1996; Ginalski et al. 2008), few have been conducted in vivo, and, to our knowledge, no study has quantified time-dependent changes in heat balance components while concurrently measuring thermal and physiological strain.

The present study simultaneously assessed heat balance, thermal status and primary indicators of physiological strain in a cohort of NICU patients nursed under RWs throughout a 105-min period. It was hypothesized that (a) while the mean rate of radiant heat provided by the RW (R_{prov}) is similar to the mean rate of radiant heat required to attain heat balance (R_{req}) over the assessment period, alternating bouts of systematic positive and negative heat storage occur that are significantly different from zero leading to oscillations in core and skin temperature, and (b) periodic bouts of heat imbalance cause proportional increases in physiological strain as evidenced by elevations in metabolic rate, heart rate, blood pressure and breathing frequency.

Table 1 Subject characteristics

Subject	Sex	Postnatal age (days)	Gestational age (weeks+days)	Weight (g)	Height (cm)	Body surface area (m^2)	Condition
1	M	3	34 + 0	2,128	46.5	0.17	Respiratory distress syndrome
2	M	4	39 + 0	2,750	47.5	0.19	Respiratory distress syndrome
3	F	4	38 + 4	3,727	49.0	0.23	Ebstein's anomaly
4	F	4	37 + 5	3,085	47.0	0.20	Respiratory distress syndrome
5	M	6	38 + 1	1,920	44.0	0.15	Respiratory distress syndrome
6	M	4	29 + 2	3,288	52.0	0.22	Respiratory distress syndrome
7	M	30	36 + 5	1,920	43.0	0.15	Patent ductus arteriosus
8	M	29	36 + 2	2,988	51.0	0.21	Respiratory distress syndrome
9	M	5	36 + 4	3,100	45.0	0.20	Pyloric stenosis
10	M	2	36 + 2	3,389	51.0	0.22	Respiratory distress syndrome
11	F	1	36 + 0	2,120	43.0	0.16	Respiratory distress syndrome
12	M	2	34 + 5	2,995	46.0	0.20	Gastroschisis
13	M	2	34 + 5	4,380	52.0	0.25	Hydrops fetalis/ascites
14	M	8	27 + 0	1,527	41.0	0.13	Necrotizing enterocolitis
Mean		7.5	35 + 1	2,808	47.0	0.19	–
SD		9.7	3 + 4	797	3.6	0.03	–

Methods

Participants

Following approval by the Research Ethics Board of the Children's Hospital of Eastern Ontario Research Institute, 14 neonates (Table 1) admitted to a tertiary-level NICU at the Children's Hospital of Eastern Ontario in Ottawa, Canada, were enrolled in the study. Written and informed consent was obtained from the legal guardians of each participating patient. Inclusion criteria were: a postnatal age of 0−30 days; the infant had to be nursed under a radiant warmer set on 'servo-control' mode and mechanically ventilated using a standard infant ventilator. Patients were excluded if they were hemodynamically unstable, the RW was set on 'manual' mode, on high-frequency ventilation, considered immunocompromised, had any medical conditions that had confounding thermoregulatory effects (e.g., hypoxic–ischemic encephalopathy, malignant hyperthermia, neonatal sepsis, etc.) or had malformations that precluded the use of any temperature probe (e.g., gastroschisis, peripheral skin lesions, etc.).

Instrumentation

Thermometry and heat flow

Rectal temperature (T_{re}) was measured using a pediatric general-purpose thermistor probe (400 Series, Model# ER400-9, Smiths Medical, Dublin, OH, USA) inserted to a minimum depth of 3 cm past the anal sphincter, as previously reported (Buntain et al. 1977; Mayfield et al. 1984). Skin temperature (T_{sk}) was measured at seven standardized anatomical sites over the right side of the body (foot, thigh, abdomen, chest, back, arm and forehead) using adhesive thermistor probes (400 Series, Model# STS-400, Smiths Medical, Dublin, OH, USA) shielded from direct radiant heat using a reflective disc. The local rate of conductive heat flow of the back (K_{back}) was measured using 0.3-mm-diameter T-type (copper/constantan) thermocouple integrated into a heat-flow sensor (Concept Engineering, Old Saybrook, CT, USA). This sensor was attached with surgical tape routinely used within the NICU (Transpore, 3 M, St. Paul, MN, USA). The RW (Giraffe Warmer, GE Healthcare, Helsinki, Finland) was set to a set-point temperature of 36.5 °C and RW servo-control temperature ($T_{feedback}$) was measured by skin temperature over the axilla as per standard care procedures. Radiant output from the warmer (RW_{output}) and $T_{feedback}$ were recorded every minute directly from the RW.

Body mass

Before the start of data collection, patients were placed on a standard mattress under a weighing platform integrated into the RW with a precision of 0.1 g (MS12001L, Mettler Toledo, Columbus, OH, USA). This device was designed to bear no alteration to the standard care setup all the while measuring mass change over time without interfering with the functioning of the RW. After controlling for the addition of intravenous fluids and metabolic mass loss, any further mass change was attributed to evaporative water loss.

Thus, each gram of body mass lost represents a rate of heat loss equating to the latent heat of vaporization of water of 2.430 kJ g^{-1} (Wenger 1972).

Ventilatory parameters

Due to their underlying medical conditions, the infants included in the study had previously been intubated with an endotracheal tube and mechanically ventilated using a standard infant ventilator (Dräger Babylog VN500, Dräger Medical, Lübeck, Germany). As per standard care procedures, the infants were sedated via intravenous administration of fentanyl (0.5–2 µg/kg h^{-1}) based on their pain score, which was measured continuously. During data collection respiratory rate (RR), tidal volume (V_T), minute ventilation (V_e), fraction of inspired oxygen (F_iO_2), fraction of inspired carbon dioxide (F_iCO_2) and the partial pressure of end-tidal carbon dioxide ($P_{ET}CO_2$) were measured and recorded every minute.

Cardiovascular parameters

Heart rate (HR) was measured using a three-lead ECG at a precision of ±2 bpm. Mean arterial pressure (MAP) was calculated based on measures of systolic and diastolic blood pressure, measured non-invasively using an automatic blood pressure cuff set to measure at fixed 1-min intervals.

Environmental parameters

Ambient air temperature (T_a) and relative humidity (RH) were measured with a precision of ±0.5 °C and ±5 % RH using a temperature and humidity monitor (DIGI, Minnetonka, MN, USA). Air velocity (v) in m/s was measured using a hot wire anemometer (Model HHF2005HW, Omega Canada, Laval, QC). The spectrum of radiant heat flux density in W/m^2 across the complete range of settings on the RW was measured retrospectively using a pyranometer (Model CMP-3, Kipp & Zonen, Delft, Netherlands).

Calculations

Body surface area (BSA) in m^2 was calculated based on infant body mass in kg and length in cm (Haycock et al. 1978) as:

$$\mathrm{BSA} = \left[\left(\mathrm{mass}^{0.5378}\right)\left(\mathrm{length}^{0.3964}\right)\right] \times 0.024265\ \mathrm{m}^2 \tag{1}$$

Mean skin temperature (T_{sk}) was calculated from local skin temperatures and weighted according to the relative surface area of each segment (forehead 21 %, trunk 32 %, arm 17 %, thigh 26 % and foot 4 %) (Museux et al. 2008). Trunk temperature was represented by the average of back, chest and abdomen temperatures.

Human heat balance

A conceptual heat balance model was employed including metabolic energy expenditure (M) and the separate heat transfer avenues of conduction (K), radiation (R), convection (C) and evaporation (E), all in kJ/min (Parsons 2002; Tourneux et al. 2009). Any resultant imbalance between M and the sum of K, R, C and E provides body heat storage (S):

$$S = M - (K \pm C \pm R + E)\ \mathrm{kJ/min}. \tag{2}$$

M in kJ/min was estimated using indirect calorimetry and was derived using:

$$M = \dot{\mathrm{V}}\mathrm{O}_2\left[\left(\frac{(\mathrm{RER}-0.7)}{0.3}\right) \times E_\mathrm{C}\right] + \left[\left(\frac{(1-\mathrm{RER})}{0.3}\right) \times E_\mathrm{F}\right]\ \mathrm{kJ/min} \tag{3}$$

where E_C is the caloric equivalent per liter of oxygen for the oxidation of carbohydrates (21.13 kJ), E_F is the caloric equivalent per liter of oxygen for the oxidation of fat (19.62 kJ) and VO_2 is oxygen consumption in L/min, estimated using:

$$\dot{\mathrm{V}}\mathrm{O}_2 = \frac{\dot{\mathrm{V}}\mathrm{CO}_2}{\mathrm{RER}}\mathrm{L/min} \tag{4}$$

where RER was assumed to be 1.00 as previously reported in parenterally fed, ventilator-dependent newborns under RWs (LeBlanc 1982; Forsyth and Crighton 1995; Steward and Pridham 2001). VCO_2 is carbon dioxide production in L/min measured using:

$$\mathrm{VCO}_2 = V_\mathrm{E}\left[\frac{(P_\mathrm{i}\mathrm{CO}_2 - P_\mathrm{ET}\mathrm{CO}_2)}{P_\mathrm{Bar}}\right]\ \mathrm{L/min} \tag{5}$$

where $P_{ET}CO_2$ is the partial pressure of end-tidal CO_2 in mmHg, P_iCO_2 is the partial pressure of inspired CO_2 in mmHg, V_E is minute ventilation in L/min and P_{bar} is barometric pressure in mmHg:

Conductive heat loss (K) was calculated using:

$$K = \left[\frac{(A_\mathrm{k} - K_\mathrm{back})}{1000}\right] \times 60\ \mathrm{kJ/min} \tag{6}$$

where A_k is the body surface area in contact with the mattress in m^2, estimated using a percentage of BSA previously reported (7.3 % of BSA) (Agourram et al. 2010).

Convective heat loss (C) was calculated using:

$$C = \left[\frac{(h_\mathrm{c}(T_\mathrm{sk} - T_\mathrm{air}) \times A_\mathrm{c})}{1000}\right] \times 60\ \mathrm{kJ/min} \tag{7}$$

where h_c is the convective heat transfer coefficient (3.1 W m^{-2} K^{-1} for air velocities <0.2 m s^{-1}), T_{sk} is mean skin temperature in °C, T_a is ambient air temperature in °C, and A_c is the body surface area available for convective heat transfer in m^2 after subtracting the surface covering the infant's diaper.

Evaporative heat loss (E) was estimated using:

$$E = \left[\frac{\left(\frac{\Delta \text{mass}}{t}\right) \times 2.430}{1000} \right] \times 60 \text{ kJ/min} \quad (8)$$

where Δmass/t is the rate of change in body mass in kg min^{-1} after adjusting for the mass gained from intravenous fluid injection and metabolic mass loss. Mass from intravenous fluids was obtained by dividing the total mass of the solution (in grams) by its total volume (in mL) and multiplying the result by the rate of infusion (g/min). Evaporative water loss from the respiratory tract was assumed to be zero since patients were ventilated with inspired gas that was heated to 37 °C and humidified to 100 % relative humidity. Metabolic mass loss was estimated using:

$$\text{Metabolic mass loss} = t \left[\frac{\text{VO}_2(44\text{RER} - 32)}{22.4} \right] \text{kJ/min} \quad (9)$$

where VO_2 is the rate of oxygen consumption (L min^{-1}), RER is the respiratory exchange ratio, and t is the time (min). The resultant difference between total mass loss, metabolic mass loss and intravenous fluid infusion was assumed to be transepidermal water loss (TEWL).

The rate of body heat storage (S) was estimated using:

$$S = [(0.6 \times \Delta T_{re}) + (0.4 \times \Delta T_{sk})] \times \text{mass} \times C_{sp} \text{ kJ/min} \quad (10)$$

where ΔT_{sk} is the change in mean skin temperature, ΔT_{re} is the change in rectal temperature, mass is infant body mass in kg and C_{sp} is the specific heat capacity of human tissue (Agourram et al. 2010) (3.494 kJ $°C^{-1}$ kg^{-1}). The weighting coefficients for T_{re} and T_{sk} matched those previously reported in neonates (Baumgart 1985; Agourram et al. 2010).

The rate of radiant heat provided to the patient (R_{prov}) and the rate of radiant heat required to attain heat balance (R_{req}), i.e., an S value of 0, were subsequently calculated using:

$$\dot{R}_{prov} = -[(M - \{K + C + E\}) - S] \text{ kJ/min}, \quad (11)$$

$$\dot{R}_{req} = -[M - (K + C + E)] \text{ kJ/min}. \quad (12)$$

Experimental protocol

Participant characteristics (mass, length, age, gestational age, postnatal age and sex) were first recorded. Nursing staff then placed the infant onto the weighting platform integrated into the servo-controlled RW. Skin temperature sensors were then placed and a rectal thermometer was inserted by a member of the nursing staff. The NICU environmental conditions were similar for all trials (T_a: 23.5 ± 0.4 °C; RH: 34 ± 12 %; P_{bar}: 759 ± 3 mmHg). Data collection began and the patient was left undisturbed for 105 min. If medical intervention was required, data collection was immediately ceased. All data were collected using a National Instruments data acquisition module (model NI cDAQ-9172) at a sampling rate of 1 Hz. Data were simultaneously displayed and recorded using customized LabVIEW software (Version 8.6.1, National Instruments, Austin, TX).

Statistical analysis

All data are presented as mean ± standard deviations (SD). Paired sample t tests were used to compare R_{req} and R_{prov}. 95 % confidence intervals were calculated for S and observing whether these intervals including zero is equivalent to testing to the null hypothesis that S does not differ significantly from zero at the 0.05 significance level. For each subject, positive and negative components of S were separated and summed to define the cumulative positive and negative heat storage components, respectively. Similarly, mean positive and negative rates of change in T_{sk} and T_{re} were determined by separating and subsequently averaging the positive and negative components of change in T_{sk} and T_{re}. Simple regression analyses were preformed between M, HR, MAP, RR and S. An alpha of 0.05 was set for all analyses. Statistical analysis was performed using SPSS version 19.0 for Windows (SPSS Inc., Chicago, IL, USA).

Results

Heat balance

The partitioned heat balance components are presented in Fig. 1. Mean evaporative heat loss (E) was 5.8 ± 1.1 W, while convective heat loss (C) was 6.2 ± 0.8 W and conductive heat loss (K) was 0.1 ± 0.1 W. The mean rate of metabolic heat production (M) was 10.5 ± 2.7 W. To attain heat balance (i.e., an average $S = 0$), the difference between the sum of whole-body heat loss and M had to be counterbalanced by a rate of radiant heat flux (R_{req}) of 1.7 ± 2.7 W. On average, S (with 95 % confidence interval limits in parentheses) was 0.0 ± 0.5 W (+0.3, –0.4 W) and, thus, did not differ significantly from zero ($p > 0.05$). Accordingly, the mean rate of radiant heat flux actually provided by the warmer (R_{prov}) was 1.7 ± 2.6 W, which was similar to mean R_{req} for the 105-min duration of data collection

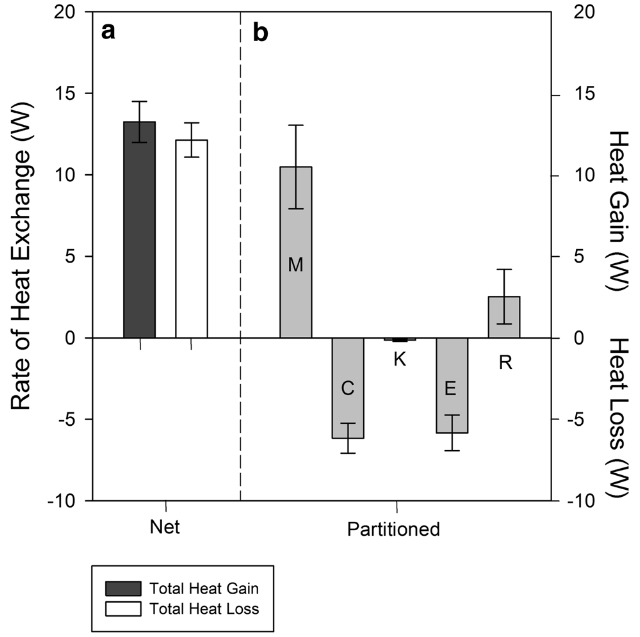

Fig. 1 **a** Comparison of the mean rates of total heat gain and total heat loss and **b** heat balance components partitioned into specific heat exchange avenues: rates of convection (*C*), conduction (*K*), evaporation (*E*) and radiation (*R*) as well as metabolic heat production (*M*)

($p = 0.876$). The relation between R_{req} and R_{prov} for each subject at each 5-min time point is illustrated in Fig. 2, with R_{prov} actually only matching R_{req} in 46.7 % of cases.

When analyzing *S* every 5 min within each 105-min trial for each subject, it was clear that heat balance (i.e., $S = 0$) was not maintained steadily throughout; rather, acute bouts of positive and negative heat storage were observed, to a varying degree, in all participants (Fig. 3). After 105 min of exposure, the mean sum of all positive heat storage positive was 6.4 ± 2.6 kJ, and the mean sum of all negative heat storage was –6.5 ± 3.7 kJ, while the net cumulative change in body heat content was –0.1 ± 3.7 kJ (Fig. 4).

Thermometry

Over the course of the experimental trials, mean T_{re} fluctuated by an average rate of 0.27 ± 0.38 °C/h. Similarly, T_{sk} fluctuated to the order of 0.70 ± 0.81 °C/h. However, it was observed that core and skin temperatures varied in an alternating pattern. As such, the average positive and negative rates of change in T_{re} were +0.65 ± 0.52 and –0.79 ± 0.67 °C/h, respectively, and the average peak positive and peak negative rates of change in T_{re} were +1.50 ± 1.10 and –1.89 ± 1.29 °C/h, respectively. The average positive and negative rates of change in T_{sk} were +3.36 ± 2.77 and –4.51 ± 2.39 °C/h, respectively, and the average peak positive and peak negative rate of change in T_{sk} were +8.12 ± 3.69 and –9.27 ± 4.98 °C/h, respectively.

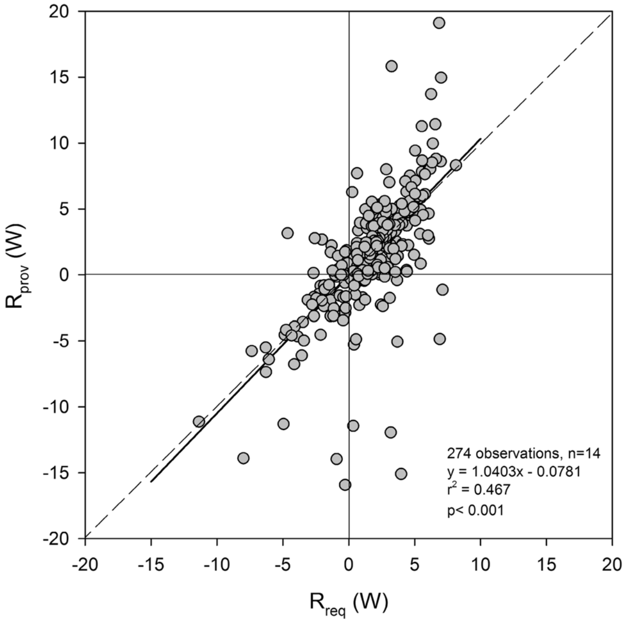

Fig. 2 A comparison between the rate of radiant heat provided (R_{prov}) and the radiant heat required to attain heat balance (R_{req}). The black line represents the regression line and the dotted line indicates line of identity (i.e., $y = x$). Adjusted R^2 statistics indicate the goodness of fit of data to the line of identity

Physiological strain

Despite the high time-dependent variability in *S* within each participant, the absolute magnitude of *S* was not associated with elevations in metabolic, cardiovascular or respiratory strain. Specifically, variability in *M* ($r = 0.05$, $p = 0.438$), HR ($r = 0.04$, $p = 0.516$), MAP ($r = 0.12$, $p = 0.208$) and RR ($r = 0.03$, $p = 0.512$) were not significantly associated with concurrent variability in *S*. This observation is further evidenced by the small average within-subject coefficient of variation (CV) for *M*, HR, RR and MAP relative to the large CV for *S* and radiant heat output (Table 2). Figure 5 shows a representative example of the changes in *M*, HR, RR, MAP, T_{re} and T_{sk} as a function of large fluctuations in RW heat output throughout the duration of an experimental trial in one subject.

Discussion

The continuous assessment of individual heat balance components coupled with thermometric measurements of body temperatures in the present study allowed for a precise evaluation of neonatal thermal status during standard NICU care under an RW. To our knowledge, no previous study has continuously measured time-dependent changes in neonatal heat balance under RWs. The main findings of the current

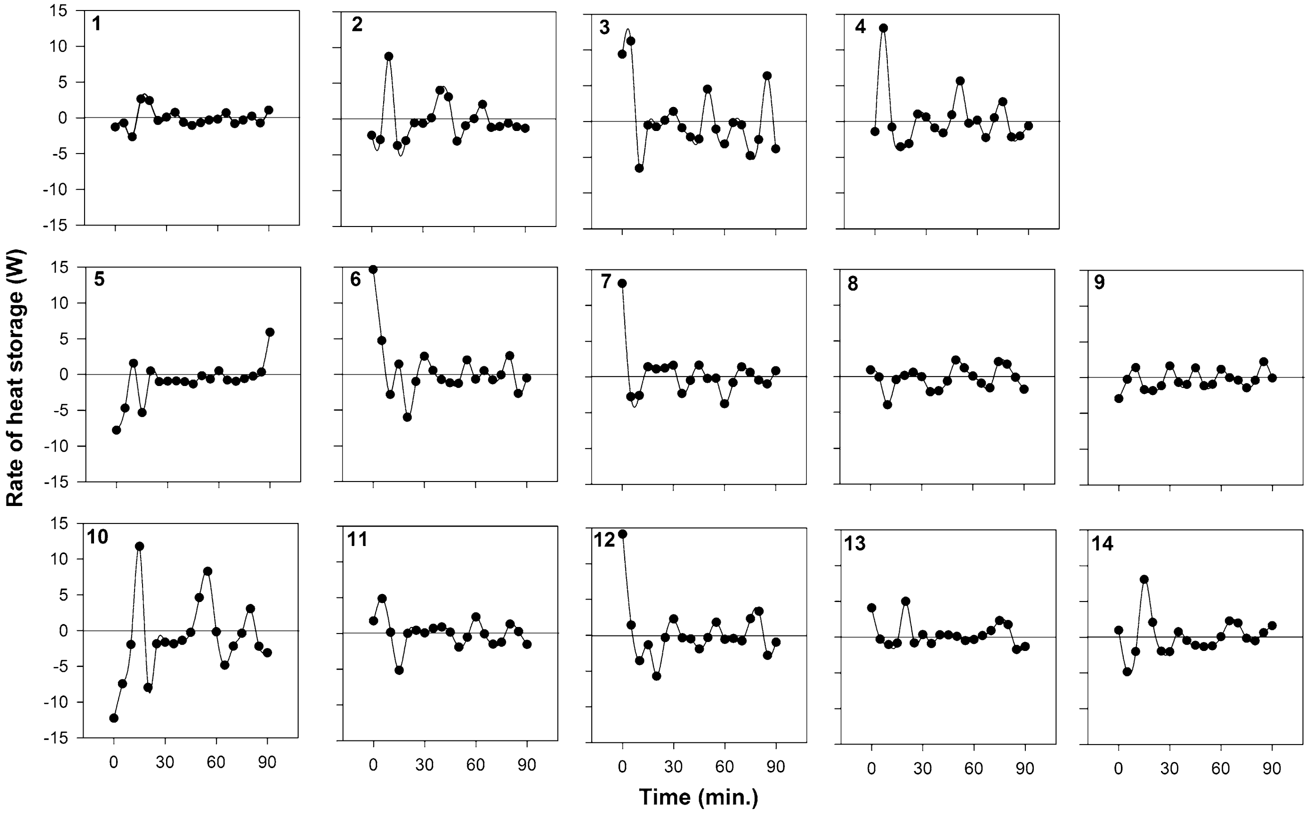

Fig. 3 Matrix plot of individual patterns of change in heat storage (S) over 105 min for each subject

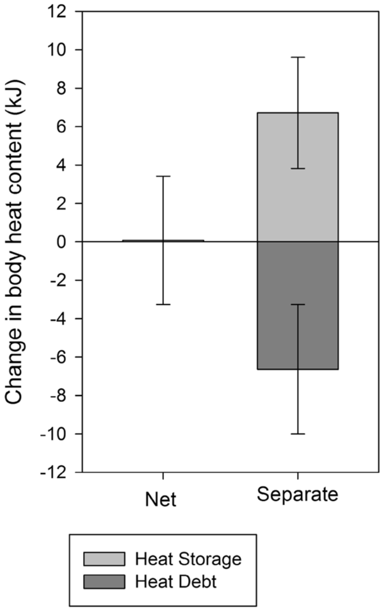

Fig. 4 Mean change in body heat content (in kJ) over 105 min presented as a global average (Net) and partitioned (Separate) into mean negative and mean positive components

study were: (1) while an RW facilitated the maintenance of net heat balance over a prolonged period, large acute variations in radiant heat output occurred that did not match the heat balance requirements of the neonate; (2) these acute variations in RW output invoked transient periods of positive and negative heat imbalance that caused oscillations in skin temperatures and, to a lesser extent, core temperature; (3) in the majority of cases, the variations in skin and core temperatures induced by the warmer were not sufficient to exacerbate physiological strain.

Heat balance

Convection (C) constituted the largest portion of whole-body heat loss at 50.8 ± 12.5 %. In contrast to incubators which regulate internal air temperature, RWs lead to a higher C as they expose the neonate to a lower ambient air temperature (Flenady and Woodgate 2003). In spite of a low ambient air velocity (<0.2 m/s), the mean gradient between T_{sk} and T_a during our study was 11.3 ± 1.3 °C, thereby increasing the drive for convective heat loss. In addition, increases in RW heat flux led to elevations in T_{sk}

Table 2 Mean, standard deviation and average within-subject coefficient of variation (CV) for *M*, HR, RR, MAP, *S* and RW heat output

	M (w)	HR (bpm)	RR (bpm)	MAP (mmHg)	S (kJ)	RW heat output (%)
Mean	10.3	135	49	43.6	0.34	30.3
SD	1.2	5	5	0.9	0.22	32.1
CV	12 %	4 %	10 %	10 %	66 %	106 %

M metabolic heat production, *HR* heart rate, *RR* respiratory rate, *S* rate of heat storage

that further exacerbated the T_{sk}–T_a gradient and thus *C*. Evaporation (*E*) accounted for 48.1 ± 11.7 % of whole-body heat loss, which is consistent with high rates of evaporation previously reported in neonates nursed under RWs (Wheldon and Rutter 1982; Kjartansson et al. 1995) and underscores the importance of adequate hydration for NICU patients under RWs. It should be noted that *E* varies considerably between individuals according to several factors including ambient humidity, gestational age, postnatal age and body surface area exposed to the ambient environment (Rutter and Hull 1979a). Indeed, a wide range of values for *E* have been reported from 0.5 W (Kjartansson et al. 1995) in term infants to 7.8 W in preterm infants (Rutter and Hull 1979b). In our study, mean *E* was relatively high at 5.8 ± 1.1 W, presumably due to the relatively low ambient humidity (0.98 kPa) leading to a high vapor pressure gradient between the skin and the ambient air. Conduction (*K*) represented the smallest heat loss avenue accounting for the remaining 1.1 ± 0.9 %. Endogenous heat production was 10.5 ± 2.7 W based on an average estimated rate of oxygen consumption of 11.3 ± 4.0 ml kg^{-1} min^{-1}. These results were similar to those observed in other studies involving term neonates nursed under RWs (Marks et al. 1980; Bauer et al. 2009; Sinclair et al. 2013). The mean rate of radiant heat required to attain heat balance (R_{req}) was consequently 1.7 ± 2.6 W. The mean rate of radiant heat provided to the patient (R_{prov}) of 1.7 ± 2.7 W was almost identical to the R_{req} ($P = 0.66$). Baumgart (1985) previously used a similar methodological approach to assess the relation between R_{req} and R_{prov} in a cohort of neonates nursed under RWs and reported a significant linear correlation between R_{prov} and R_{req} ($r = 0.68$, $p < 0.001$). However, their data merely suggested that, on average, R_{req} was matched by R_{prov} over 90 min, and the time resolution employed in their study did not permit the assessment of any transient mismatch between R_{prov} and R_{req} throughout the measurement period. In the present study, R_{req} and R_{prov} were assessed every 5 min in each patient and there was only a moderate level of agreement between R_{prov} and R_{req} ($R^2 = 0.467$, $p < 0.01$) (Fig. 2). While the correct amount of radiant heat was provided by the RW to the patient in only 46.7 % of all cases, the absolute variance in R_{prov} (20.7 W) was more than double that of R_{req} (8.9 W) indicating that the rate of radiant heat provided by the RW oscillated above and below the required rate to attain heat balance. Indeed, previous studies demonstrated that during standard care under a servo-controlled RW, large acute variations in RW heat flux frequently occur (Baumgart et al. 1980; Wheldon and Rutter 1982; Seguin and Vieth 1996). In their study, Wheldon and Rutter (1982) reported instances where variations in radiant flux density of ±25 W/m^2 occurred within 2−3 min, far exceeding the physiological requirement for heat balance.

The mean net change in body heat content from the beginning to the end of the 105-min assessment period in the present study was 0.1 ± 3.7 kJ. As such, no systematic under- or overheating occurred ($p > 0.05$). However, the assessment of dynamic neonatal heat balance within this period showed that oscillations in the rate of heat storage occurred to an extent in all patients. The upper left and bottom right quadrants in Fig. 2, respectively, represent cases in which the RW was on when it should have been off, and vice versa. While the latter occurred in more than twice as many cases (23) as the former (11), combined, such an absolute error only arose in 12.4 % (34) of all cases (274). The majority of data points in Fig. 2 are in the top right quadrant indicating that radiant heat was indeed provided when there was a heat balance requirement for supplemental heat; however, it is clear that in nearly all cases an incorrect amount of heat was provided (i.e., $R_{prov} \neq R_{req}$). Furthermore, radiant heat was progressively overdelivered as R_{req} became more positive.

The poor agreement between R_{req} and R_{prov} in the present study indicates that the method employed for regulating radiant heat output from the RW is suboptimal. Using a single measure of local skin temperature, or even core temperature, largely ignores the fact in situations of cold or heat stress; regional tissue temperatures change in a heterogeneous fashion, thereby increasing the risk of passive over/underheating if a single site is selected to regulate RW output. An alternative method would be to develop a model that estimates R_{req} and delivers the exact heat flux required for heat balance on a constant basis. It follows that steady-state skin and core temperatures should then be achieved. Such a model would account for between-patient variability in R_{req} based on biophysical factors that have a profound influence of heat balance and could be coupled with a continuous T_{sk} monitor with upper and lower limits that could override RW heat output, thereby alleviating the risk

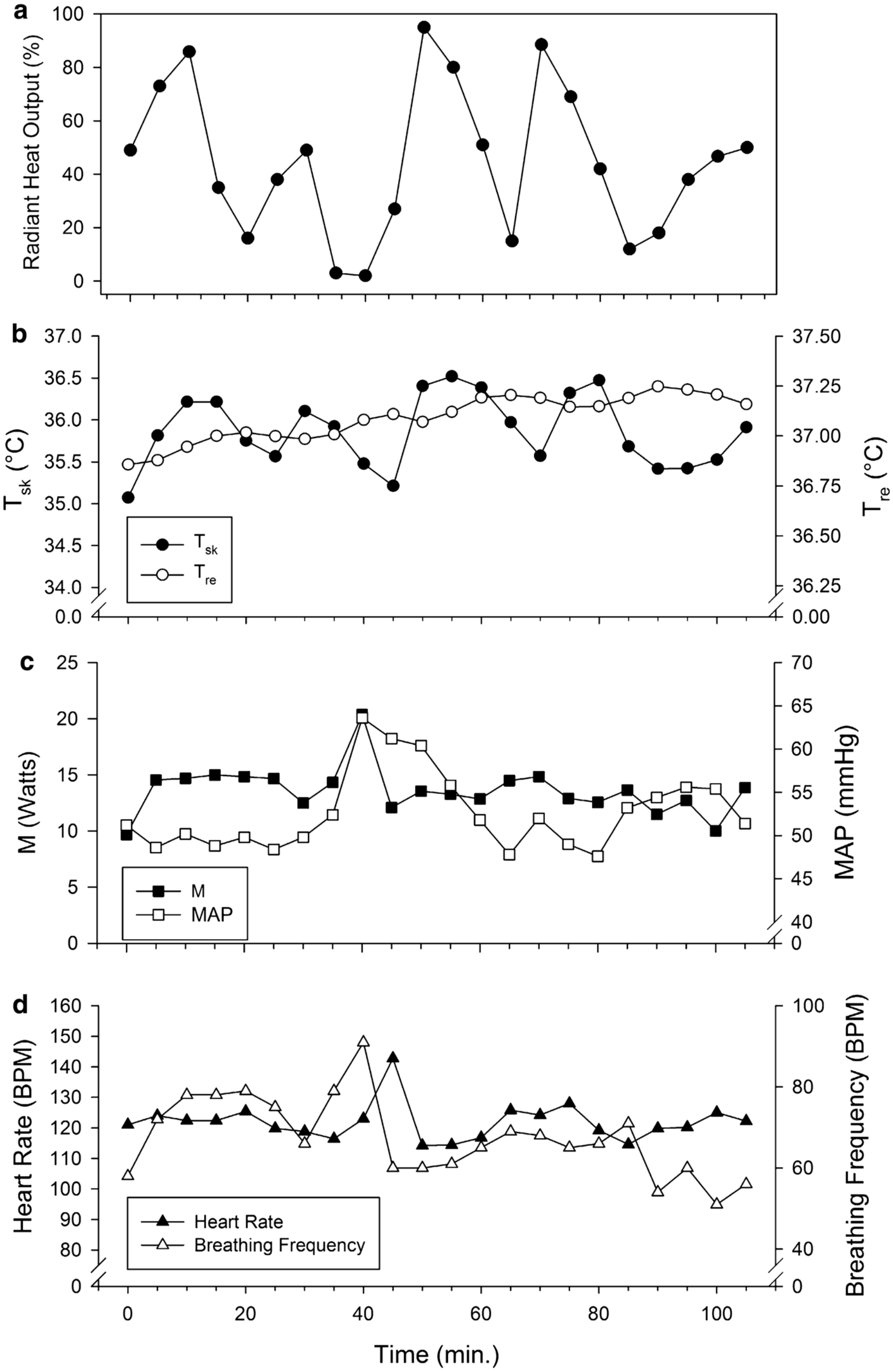

Fig. 5 Fluctuations in **a** radiant warmer (RW) heat output over time and the associated, **b** changes in rectal temperature and mean skin temperature, **c** metabolic heat production (*M*) and mean arterial pressure (MAP), and **d** heart rate (beats per minute) and breathing frequency (breaths per minute) in one representative subject

of over/underheating. Of the separate heat balance components that comprise R_{req}, according to the present data, the between-subject variability in *C* and *K* was on average very low. On the other hand, *M* and *E* varied by a greater amount between individuals and subsequently contributed most to the variability observed in R_{req}. Factors contributing to the between-subject differences in *M* likely include body mass (Hill and Rahimtulla 1965); however, developmental status also has a profound influence on *M* independently of mass, with basal metabolic rate increasing by ~35 % during the first 2 days after birth despite body mass becoming temporarily lower, and by ~50 % during the first 9 days after birth (Hill and Rahimtulla 1965). Some of the between-subject variability in *E* could be due to differences in skin barrier function and subsequently transepidermal water loss (TEWL) between patients. However, infants born at a gestational age of 30 and 32 weeks have displayed a fully functional stratum corneum and therefore normal levels of

TEWL (Kalia et al. 1998), and the mean gestational age of the patients in the present study was 35 weeks. Another contributor to the variability in E may be differences in the humidity gradient between any moisture on the skin and ambient air; while ambient air temperature was closely regulated in the NICU, ambient humidity tended to vary according to outdoor humidity (Thomas et al. 2010), which in the site of the study (Ottawa, Canada) is very low in winter but much higher in early summer.

It is noteworthy that the time course of changes in S varied substantially between subjects (Fig. 3), a fact that may be explained by the wide range of biophysical characteristics of our sample population. Indeed, weight, body surface area and gestational age were vastly different between subjects. Each of these factors has been shown to affect thermoregulatory response to environmental perturbations (Parsons 2002). Furthermore, by virtue of differences in circulating hormones, sex has been shown to be an important factor when considering thermoregulatory response (Gagnon et al. 2013; Charkoudian and Stachenfeld 2014). While sex-based differences in thermoregulatory function resulting from differences in circulating hormones are evident in adults, it stands to reason that the presence of these differences may be reduced given that newborns have lower concentrations of circulating hormones than adults (Mann et al. 2003). However, we observed no systematic effect of body morphology or sex on heat balance under RW. We conclude that our study did not have a large enough sample size to assess the individual effects of body morphology and sex on heat balance status under RW. While these are certainly salient questions, further study is required.

Acute changes in radiant heat output in the present study led to large variations in local skin temperature and to a lesser extent core temperature (Fig. 5). While excessive or insufficient radiant heat output may cause changes in both core and skin temperatures, they may only negatively affect a newborn if they are prolonged, too great in magnitude or induce chronic physiological strain. Indeed, acute changes in the thermal environment could exacerbate metabolic, cardiovascular and respiratory strain. However, we observed no systematic influence of transient positive and negative heat storage upon changes in M, HR, MAP or RR, suggesting that the induced variation in core and skin temperature remained within a physiologically acceptable range (Table 2; Fig. 5). The absence of any significant variation in the primary indicators of physiological strain in response to acute changes in S may be related to the effects of fentanyl sedation. For example, fentanyl analgesia has been shown to reduce non-shivering thermogenesis in neonates in the NICU following surgery (Okada et al. 1998). Nevertheless, the nature of the feedback system regulating the flux of heat from the RW carries inherent error due to the fact that skin temperature over the axillary artery is the only source of information to which the system responds. Although our study showed that in the vast majority of situations, the RW provided a thermal environment that succeeds in maintaining body temperatures within a safe range, there were instances where excessive heating or excessive cooling were observed. In particular, one patient showed an increase in local skin temperatures of the head, chest and abdomen above >37.8 °C in response to an increase in RW heat output in the absence of an increase in T_{feedback} (Molgat-Seon et al. 2013). This accidental bout of overheating caused sudden increases in HR, MAP and RR.

Neonatal body temperature management is complex, particularly in at-risk newborns. Though RWs provide many benefits, they must be used with caution. The results from the current study provide empirical data describing the time-dependent changes in the heat balance status of neonates nursed under RW. Our data suggest that while RWs maintain thermoneutrality over time, they induce large variations in thermal status. While these variations did not lead to an exacerbated physiological strain in the patients assessed in the present study, future research is needed to assess whether they lead to negative longer-term outcomes. Future research should also focus on determining the best method for predicting the rate of radiant heat required for heat balance in each individual patient; this will likely include accounting for between-patient variability in metabolic rate and evaporative heat loss which can be potentially estimated using biophysical parameters.

Conclusion

In conclusion, the present study shows that while mean R_{req} is similar to mean R_{prov} over 105 min, alternating bouts of positive and negative body heat storage occur, confirming our first hypothesis. Accordingly, neonates nursed under RWs experienced marked fluctuations in both core and skin temperatures. In the vast majority of cases, however, these temperature variations lie within a physiologically acceptable range, since indicators of metabolic, cardiovascular and respiratory strain were not altered by changes in S.

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