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ORIGINAL ARTICLE

Safety and efficacy of Trans-warmer mattress for preterm neonates: results of a randomized controlled trial

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Objective: To compare the admission temperatures, incidence of hypothermia and discharge outcomes of preterm neonates managed with Trans-warmer mattress (TWM) initiated in the delivery room (DR) and controls.

Study Design: A prospective quasi-randomized controlled trial was performed between January and November 2009 on preterm neonates <32 weeks gestation. Infants in the intervention group were resuscitated and transported to neonatal intensive care unit (NICU) on a TWM, in addition to other measures recommended by the Neonatal Resuscitation Program.

Result: The mean (s.d.) gestational age 28.7 (3) vs 28.7 (2.4) weeks and birth weight 1151 (407) vs 1175 (413) g) were comparable in the intervention ($n = 53$) and control ($n = 49$) groups. Temperature of the DR, maternal temperature, 5 min Apgar score, mode of delivery, cord pH and need for resuscitation were similar in both groups. Temperature of neonates in the DR (36.3 vs 36.0 °C) was also similar. Admission temperature in the NICU was significantly higher 36.2 °C (0.8) vs 35.7 °C (0.8) and incidence of hypothermia (temperatures <36 °C) lower in the intervention group (34 vs 57%, $P<0.05$). TWM use was not associated with any adverse effects. On logistic regression, low birth weight, lack of use of TWM and low DR temperature were independently associated with admission hypothermia.

Conclusion: In this quasi-randomized controlled trial, the admission temperatures of preterm neonates on whom TWM was used were significantly higher compared to controls with a reduction in the incidence of hypothermia. A TWM initiated in the DR may be a simple efficacious method of reducing hypothermia in preterm neonates.
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Introduction

Maintenance of normal body temperature in preterm neonates immediately after birth remains a clinical concern, despite advancement in techniques of heat loss prevention. In the first 10 to 20 min, the newborn infant, who is not adequately thermally protected, may lose enough heat for the body temperature to fall by 2 to 4 °C (3.6 to 7.2°F), with even greater falls in the following hours.[1] The preterm infant is particularly vulnerable to cold stress because of the relatively large body surface area, thin skin, scanty subcutaneous tissue, inability to shiver and a less active metabolic tissue mass.[2]

World Health Organization has classified hypothermia in neonates as mild hypothermia or cold stress (temperatures 36 to 36.5 °C), moderate (temperatures 32 to 36 °C) and severe hypothermia (temperatures <32 °C).[3] Among 5277 preterm infants (birth weights <1500 g) admitted to the National Institute of Child Health and Development Neonatal Research Network centers during 2002 and 2003, 14.3% infants had an admission temperature <35 °C, 32.6% between 35 °C and 35.9 °C, 42.3% between 36 and 36.9 °C and 10.8% had temperatures ⩾37 °C.[4] Similarly, the EPICURE study involving 811 preterm infants (20 to 25 weeks gestation) noted admission hypothermia (<35 °C) in as much as 40% of the study cohort.[5] In another audit following the introduction of polyethylene bags, the incidence of hypothermia fell from 25 to 16%, but the main reduction in hypothermia was seen in infants born above 28 weeks gestation (19.4 vs 3.9%, $P = 0.017$). There was no significant effect in infants born before 28 weeks (29.3 vs 24.8%, $P = 0.58$).[6]

Periods of cold stress have been associated with short-term as well as long-term morbidities, including respiratory distress,[7] hypoglycemia,[8] metabolic acidosis, increased oxygen consumption,[9] coagulation defects, cerebral hemorrhage,[10] lower arterial oxygen tension,[11] late onset sepsis,[4] mortality[4,5,10] and increased oxygen dependency in survivors born at less than 26 weeks gestation.[5]

Neonatal Resuscitation Program (NRP) recommends raising the temperature of delivery room (DR), pre-heat the radiant warmer, place a portable warming pad on the resuscitation table and transport the neonate in a pre-warmed transport incubator.[12] In addition, it also recommends the use of polyethylene bag for neonates born at less than 28 weeks gestation. NRP states that

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'simultaneous use of all these strategies for maintaining temperature control has not been studied'. Further, it is important to ascertain safety of these techniques as cases of overheating have been reported with some of the strategies.[13]

Our primary objective, in the current quasi-randomized study, was to compare admission temperatures and the incidence of moderate admission hypothermia (<36 °C) in preterm neonates resuscitated in the DR and transported to the neonatal intensive care unit (NICU) on a Trans-warmer mattress (TWM) in addition to routine measures compared with those who received routine thermal care, which included hats, radiant warmers, polyethylene bags and pre-warmed transport isolettes.

Secondary objectives were to compare mortality and morbidities before discharge from the hospital in two groups and to compare adverse effects (hyperthermia and skin reaction) and care-giver acceptance between groups.

Materials and methods

A quasi-randomized trial was performed between January and November 2009 on preterm neonates <32 weeks gestation born at Hutzel Women's Hospital (Detroit, MI, USA). Neonates with major congenital anomalies and pre-viable neonates were excluded. Neonates with maternal fever (temperature more than 38.2 °C) just before delivery were also excluded to reduce the risk of hyperthermia in neonates.

Trans-warmer infant transport mattress was used for pre-determined 12 h of the day, either from 0800 to 2000 hours or 2000 to 0800 hours on alternate months. All patients received routine thermal care, including hats, radiant warmers and were transported to the NICU in pre-warmed incubators with temperatures set at 37 °C. Plastic bags were used in accordance with NRP guidelines, that is, infants less than 28 weeks gestation were placed in a re-closable plastic bag below the neck without first drying the skin. TWM was activated before delivery. Trans-warmer infant transport mattress is a gel-filled disposable thermal mattress. Once activated, it reaches a maximum temperature of 40 °C within 60 s with the effect lasting up to 2 h. During the intervention period, an activated TWM covered with a blanket was placed on the resuscitation warmer and the infant received on it. TWM was used from the DR until the time of the first temperature in the NICU. All neonatal fellows were trained on the appropriate use of a TWM before study initiation. The study was not blinded due to nature of intervention.

Axillary temperature was measured in DR just before shifting the infant on to the transport isolette and on arrival in the NICU by digital thermometer (Temp-Plus II). All deliveries were attended by a neonatal fellow along with at least two pediatric residents and a respiratory therapist. Some deliveries were attended in addition by a neonatal nurse or nurse practitioner. The delivery suites and operating area are separated from the NICU by an enclosed bridge, which takes 1 to 3 min for the clinical team to traverse.

Maternal records were reviewed for maternal age, race, prolonged rupture of membranes (>18 h), chorioamnionitis based on placental pathology reports, antenatal steroid administration, mode of delivery, cord blood gas and maternal temperature before and after delivery. DR ambient temperature and use of plastic bag, hats and pre-warmed blankets in DR were recorded.

Neonatal charts were reviewed for birth weight, gestational age, Apgar scores, mortality, need of DR resuscitation, hypoglycemia (initial blood glucose <40 mg/dl), metabolic acidosis (pH <7.15 with base excess ⩾10 on initial blood gas), presence of necrotizing enterocolitis (defined as ⩾Stage II by modified Bell's staging),[14] grade 3 or 4 intracranial hemorrhage by Papille classification,[15] bronchopulmonary dysplasia (defined as oxygen need at 36 weeks postmenstrual age), sepsis (defined as positive culture from sterile site such as blood or spinal fluid and intention to treat with antibiotics for ⩾7 days), cystic periventricular leucomalacia on head ultrasound and duration of oxygen administration, ventilator need and hospital stay. We also recorded any adverse effects including hyperthermia (>37.5 °C), local skin reaction as noted by the research personnel or the bedside nurse soon after removal of the TWM and interference with resuscitation. Interference with resuscitation was assessed by a member of the DR resuscitation team, following each delivery as a Yes/No response to a questionnaire.

The study was approved by the Wayne State University Institutional Review Board, which allowed enrollment of subjects without previous informed parental consent due to many emergent and unanticipated preterm deliveries, need for the intervention immediately after delivery and the perceived minimal risk of the intervention. Parents were given an information sheet about the study soon after delivery and further data collection from medical records was performed only if the parents gave their verbal consent.

Sample size and statistical power

Data from our center over the previous year had revealed a mean (s.d.) admission temperature of preterm babies of 35.5 (1.5) °C. Assuming that an increase in mean admission temperature of 1 °C (from 35.5 to 36.5 °C) would be a clinically significant improvement, a sample size of 48 in each group was calculated to provide a power of 90% to yield a statistically significant result, with α set at 0.05, two tailed (Sample Power SPSS). Descriptive statistics included mean (s.d.) and number (percent) as appropriate. χ^2 and Student's *t*-test were used to assess differences between the intervention and control groups. Logistic regression was used to assess the association between moderate admission hypothermia (temperatures <36 °C) and clinical variables such as birth weight, randomization category, need for resuscitation in DR, maternal temperature and temperature of DR. Analysis was performed according to the intention-to-treat principle and not by actual use of TWM.

Results

Between January 2009 and November 2009, a total of 109 infants were eligible. Of these, two patients were excluded owing to parental refusal, one was excluded owing to maternal fever, three owing to the absence of neonatal fellow from delivery and one owing to the presence of congenital anomaly. Data were analyzed for 102 neonates: 53 in the TWM intervention group (TWM group) and 49 in the routine care group (routine care group). Among those randomized to TWM, five infants were not resuscitated on TWM, whereas two infants in the control group were placed on TWM for thermal care owing to oversight. There were 40 neonates in this study who received both plastic bag and TWM and 35 patients who received plastic bag without TWM. Maternal and infant baseline characteristics in the two groups were comparable, except that maternal temperatures before delivery tended to be higher in the intervention group (Table 1).

The mean time of measurement of temperature in NICU was comparable in two groups: 34 min in TWM group vs 38 min in control group ($P = 0.8$). Mean (s.d.) temperatures in the two groups in the DR, on admission to the NICU and the incidence of hypothermia, are presented in Table 2. Twenty-seven neonates did not have their temperature measured in the DR (8 neonates in TWM group, 19 neonates in control group) due to unavailability of thermometer or due to oversight. All neonates had temperature taken in NICU. Mean admission temperatures in the NICU were significantly higher in the TWM group. Incidence of moderate hypothermia (<36 °C) was significantly lower in the TWM group. DR temperatures as well as temperature of neonates in DR were comparable between groups. Figure 1 reflects the distribution of temperatures in the two groups in the DR and on admission to the NICU. In the DR, 14 (31%) patients in TWM group compared with 11 (37%) in control group had temperatures <36 °C; corresponding numbers on admission to the NICU were 18 (34%) in the TWM group and 28 (57%) among controls ($P = 0.02$). On subgroup analysis, infants <28 weeks in the TWM category ($n = 21$) had a mean (s.d.) admission temperature of 35.9 (1.0) °C compared with 35.7(0.9) °C, $P = 0.51$ in the control group ($n = 22$). Infants >28 weeks in the TWM category ($n = 32$) had a significantly higher mean (s.d.) admission temperature of 36.4 (0.7) vs 35.7 (0.7) °C, $P = 0.002$, compared with controls ($n = 27$).

Table 3 compares the rate of mortality and morbidities in the two groups of infants. There is no statistical difference in two groups, although the study was not powered to look at this. On logistic regression analysis, reduction in moderate admission hypothermia (<36 °C axillary temperature) was significantly associated with higher birth weight (odds ratio (OR) 1.002; 95% confidence interval (CI) 1.001 to 1.003; $P = 0.003$), use of TWM (OR 2.76; 95% CI 1.13 to 6.71, $P = 0.025$) and higher DR temperature (OR 1.31; 95% CI 1.07 to 1.6, $P = 0.008$). There were two patients in the intervention group with temperature >37.5 °C

Table 1 Comparison of infant and maternal characteristics in the TWM vs routine care groups

Variable mean ± s.d. or n *(%)*	*TWM group* (n = *53)*	*Routine care group* (n = *49)*	P-*value*
Maternal age (years)	25.3 ± 6	25.4 ± 5.7	0.9
Gestational age (weeks)	28.7 ± 3	28.7 ± 2.4	0.9
Birth weight (g)	1151 ± 407	1175 ± 413	0.7
Chorioamnionitis	10 (19.6%)	9 (23%)	0.4
Race (black)	46 (87%)	45 (94%)	0.4
C-section	22 (42%)	20 (41%)	0.55
Male gender	26 (49%)	23 (47%)	0.5
Any antenatal steroids	43 (84%)	31 (74%)	0.2
Cord pH	7.28 ± 0.1	7.25 ± 0.16	0.28
Apgar 5 min	6 ± 2.2	6 ± 2.2	0.9
DR resuscitation[a]	36 (67.9%)	35 (71.4%)	0.83
Maternal temp. before delivery (°C)	36.8 ± 0.5	36.6 ± 0.5	0.08
Maternal temp. post delivery (°C)	36.3 ± 0.7	36.4 ± 0.7	0.6
DR temp (°C)	21.8 ± 2.4	21.2 ± 2.6	0.2

Abbreviations: DR, delivery room; TWM, Trans-warmer mattress.
[a]DR resuscitation included endotracheal intubation, chest compression or use of epinephrine.

Table 2 Temperature profiles in the TWM and routine care groups

Variable mean ± s.d. or n *(%)*	*TWM group* (n = *53)*	*Routine care group* (n = *49)*	P-*value*
Temp in DR[a] (°C)	36.3 ± 0.8	36.0 ± 0.5	0.17
Temp in NICU (°C)	36.2 ± 0.8	35.7 ± 0.8	0.003*
Temp in DR <36 °C	14 (31.1%)	11 (36.7%)	0.39
Temp in DR <35 °C	4 (8.9%)	1 (3.3%)	0.64
NICU temperature <36 °C	18 (34%)	28 (57%)	0.02*
NICU temperature <35 °C	2 (4%)	7 (14%)	0.06

Abbreviations: DR, delivery room; NICU, neonatal intensive care unit; TWM, Trans-warmer mattress.
[a]Forty-five neonates in intervention group and 30 neonates in control group had temperature taken in delivery room. All neonates had temperature taken in NICU.
*P<0.05.

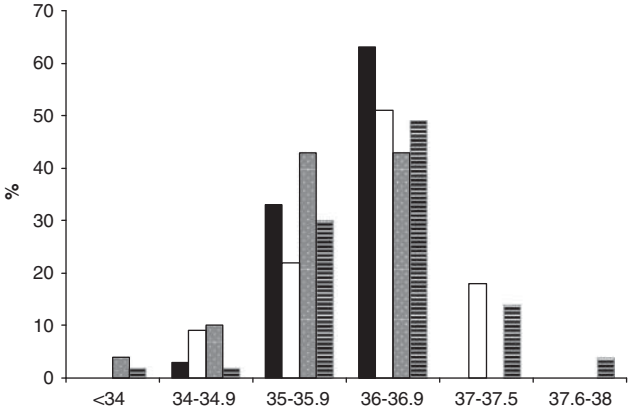

Figure 1 Temperature distribution of patients in delivery room and neonatal intensive care unit.

Table 3 Comparison of discharge outcomes in the TWM and routine care groups

Variable mean ± s.d. or n *(%)*	*TWM group* (n = *53)*	*Routine care group* (n = *49)*	P-*value*
Mortality	0 (0%)	1 (2.0%)	0.48
IVH (grade 3 or 4)	5 (9.4%)	1 (2.0%)	0.12
BPD	16 (30%)	11 (22%)	0.26
NEC	11 (21%)	16 (33%)	0.19
Sepsis	13 (25%)	13 (26%)	0.19
Cystic PVL	3 (5.7%)	2 (4.1%)	0.54
Hypoglycemia	11 (22%)	10 (22%)	0.58
Metabolic acidosis	1 (1.9%)	3 (6.1%)	0.28
Days in hospital	49 ± 30	54 ± 33	0.40
Ventilator days	12 ± 19	16 ± 25	0.38
Days on oxygen	23 ± 27	30 ± 37	0.23

Abbreviations: BPD, bronchopulmonary dysplasia; IVH, intraventricular hemorrhage; NEC, necrotizing enterocolitis; PVL, periventricular leucomalacia; TWM, Trans-warmer mattress.

($P = 0.4$) and none above 38 °C. There was no patient with any local skin reaction. Use of TWM was well received by DR personnel, with no respondent noting an interference with the resuscitation.

Discussion

In the current quasi-randomized controlled trial, we evaluated the effects of the use of TWM in addition to other routine NRP-recommended measures of thermoregulation, starting in the DR among preterm (<32 weeks gestation) infants. The use of TWM increased the admission temperature and decreased the rates of admission hypothermia. Mortality and morbidity rates, however, were not significantly different. Use of TWM was not associated with significant risk of hyperthermia or skin reaction and was not perceived to interfere with resuscitation by the DR personnel.

Although mentioned as a thermoregulatory strategy for preterm infants in the NRP, there is paucity of data on use of TWM in the DR. The limited previous studies have all reported results very similar to ours. One randomized study involving premature neonates with birth weight <1500 g showed an improvement in temperatures in the TWM group, when compared with those who received routine care.[16] This study included a total of 24 patients and was carried out before the routine use of other measures such as plastic bag in infants with gestational age <28 weeks. In another retrospective observational study over three time periods, hypothermia was less frequent in the 'bag and mattress' group compared with the 'bag-only' and traditional care groups (26 vs 69 vs 84%, respectively) even though the median time to admission was longest in the 'bag and mattress' group (23 min). Multiple regression analysis showed that use of the mattress raised admission temperatures by 1.04 °C.[17] Another quality assurance non-randomized study on 115 very-low-birthweight infants compared those who were placed on the TWM and those treated with standard care. Hypothermia (<97.4 °F) was significantly lower in the mattress group than for controls (52.5 vs 77.3%), despite the fact that the mattress group had a lower mean gestation, a lower birth weight and a higher proportion of Apgar scores of less than 5 at 5 min compared with controls. The use of the heated gel mattress raised body temperatures by a mean of 0.7 °F per infant.[18]

To our knowledge, this is the first quasi-randomized study to evaluate the safety of a combination of measures (such as polythene bag and TWM for thermoregulation of preterm infants). The risk of hyperthermia with multiple interventions has been a concern. Hyperthermia may also be harmful and increases neuronal damage, especially in babies with ischemic insult.[19] In a recent study, Singh *et al*.[17] showed an increase in admission temperature of preterm neonates in the 'bag and mattress' group compared with 'bag' group and routine thermal care epochs, but with significantly more hyperthermia (>37.5 °C) in (28 vs 4 and 0.4%) patients. In our study, we had two (3.8%) infants with temperatures >37.5 °C (37.7 °C for both). The DR temperature in both deliveries was 24 °C and axillary temperature in DR was 37.5 and 37.1 °C before transport to NICU. We had excluded patients from the study with maternal temperature >38.2 °C. It is important to consider maternal temperature, gestational age and ambient DR temperature, which may not be routinely available, whereas using a combination of techniques including TWM for temperature maintenance. Monitoring of temperatures in the DR would also help to reduce any potential risk of hyperthermia.

Mortality and morbidity did not significantly differ between control and intervention groups. This can be ascribed to the fact that our sample size was not powered to detect a difference. Our study had certain limitations. For logistic reasons, we used a quasi-randomization strategy. Given the nature of intervention, we could not blind the care-givers to the intervention. The design of our center and the distance that infants need to traverse caused a temperature drop, which the TWM obviated. The efficacy of the TWM, therefore, may need further validation in other settings where the NICU and delivery area are in close proximity. Although about 18% of the study cohort had birth weight <750 g, we were not powered to specifically examine the safety and efficacy of the TWM in this vulnerable group. Nonetheless, this study shows the safety and efficacy of a TWM, in addition to other thermal care measures, in achieving an increase in admission temperatures and reducing hypothermia in preterm infants. Avoidance of cold stress at birth is a fundamental step in promoting cardiopulmonary transition from *in utero* to an extra-uterine existence. The results of our quasi-randomized trial may have broad implications for optimizing DR care for preterm infants.

Conclusion

In this quasi-randomized controlled trial, the admission temperatures of preterm neonates (<32 weeks) on whom TWM

was used were significantly higher compared with controls with a reduction in the incidence of hypothermia (<36 °C). Use of TWM initiated in the DR may be a simple efficacious method of reducing the incidence of hypothermia in preterm neonates.

Conflict of interest

The authors declare no conflict of interest.

Acknowledgments

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