A Randomized Trial of Exothermic Mattresses for Preterm Newborns in Polyethylene Bags

WHAT’S KNOWN ON THIS SUBJECT: Wrapping very preterm newborns in polyethylene bags in the delivery room reduces hypothermia on admission to the NICU, but many infants remain cold despite their use. Placing polyethylene-wrapped infants on exothermic mattresses may reduce hypothermia but increase hyperthermia.

WHAT THIS STUDY ADDS: Placing polyethylene-wrapped very preterm infants on exothermic mattresses in the delivery room results in more infants with abnormal temperature and more hyperthermia on admission to the NICU.

abstract

BACKGROUND AND OBJECTIVE: Hypothermia on admission to the NICU is associated with increased mortality in preterm infants. Many newborns are hypothermic on admission despite using polyethylene bags (PBs). Using exothermic mattresses (EMs) in addition to PBs may reduce hypothermia but increase hyperthermia. We wished to determine whether placing preterm newborns in PBs on EMs in the DR results in more infants with rectal temperature outside the range 36.5 to 37.5°C on NICU admission.

METHODS: Infants <31 weeks were randomly assigned before birth to treatment with or without an EM. All infants were placed in a PB and under radiant heat immediately after birth and brought to NICU in a transport incubator. Infants randomly assigned to EM were placed on a mattress immediately after delivery and remained on it until admission. Randomization was stratified by gestational age. Rectal temperature was measured with a digital thermometer on NICU admission.

RESULTS: The data safety monitoring committee recommended stopping for efficacy after analyzing data from half the planned sample. We report data for 72 infants enrolled at this time. Fewer infants in PBs on EMs had temperatures within the target range (15/37 [41%] vs 27/35 [77%], P = .002) and more had temperatures >37.5°C (17/37 [46%] vs 6/35 [17%], P = .009).

CONCLUSIONS: In very preterm newborns, using EMs in addition to PBs in the DR resulted in more infants with temperatures outside the normal range and more hyperthermia on NICU admission. Pediatrics 2013;132:e135–e141
Newborn infants lose heat rapidly after birth. Measures to prevent heat loss are taken for all infants in the delivery room (DR). Placing newborns under radiant heat and drying them with towels appears insufficient for very preterm infants; hypothermia is common on admission to the NICU and is associated with increased morbidity and mortality. Additional techniques aimed at preventing heat loss in very preterm infants in the DR have been studied. These have included increasing the DR temperature, occlusive wrapping, and polyethylene caps. In clinical trials, each of these interventions increased mean admission temperature compared with conventional care, but many infants had admission temperatures outside the normal range despite these measures. To date no single approach has been entirely successful at maintaining normothermia in very preterm infants in the DR.

Placing newborns without drying in polyethylene bags (PBs) or wraps after birth reduces evaporative and radiant heat loss while allowing heat from the radiant warmer to pass through. This technique has been shown by Vohra et al to significantly increase rectal temperature on NICU admission in 2 randomized trials. Although PBs improved mean temperature, many infants placed in a PB in both studies had temperatures <36.5°C (30% and 33%), and a small number (1 infant and 2 infants) had temperatures >37.5°C on admission. Exothermic mattresses (EMs) are also used in the DR to prevent hypothermia in preterm infants. Snapping the metal disc contained within the sodium acetate gel. After activation, the gel crystallizes to produce heat.

In practice, the activated EM acts as an external heat source so that when infants are placed on a warm EM, they absorb heat by conduction through the surface of their skin in contact with the EM. In 2 retrospective studies, less hypothermia was observed when infants in PBs were placed on EMs in the DR compared with previous cohorts when EMs were not used (23% vs 3% and 69% vs 26%). In both studies, the rate of hyperthermia increased with the addition of the EM (50% and 28%). Recent randomized trials suggest that placing preterm infants on EM in the DR significantly increases axillary temperature when used instead of PB (36.5 vs 36.1°C) and when combined with routine thermal care including PB for infants <28 weeks (36.2°C vs 35.7°C).

Both the American Academy of Pediatrics (AAP) and ILCOR advise that combining these strategies may increase the risk of hyperthermia. Infants aged <31 weeks gestation born at our hospital are routinely placed in food-grade PBs after birth. Previously, infants were also placed on EMs in the DR at the discretion of the treating physician. In a prospective cohort study of infants <31 weeks gestation born at our hospital, we found that fewer infants had admission axillary temperatures within the normal range (36.5–37.5°C) when PBs were used with an EM rather than alone (9/28 [32%] vs 11/15 [73%]). Although the mean admission temperatures in the 2 groups were comparable, both hyperthermia and hypothermia occurred more frequently in infants treated with an EM and a PB in the DR. We performed this prospective randomized controlled trial to determine if placing infants in a PB on an EM in the DR resulted in more infants with temperatures outside the normal range (36.5–37.5°C) on admission to NICU.

METHODS

Setting and Participants

We conducted this randomized controlled trial at the National Maternity Hospital (NMH), Dublin, from February 2011 to February 2012. The NMH is a university maternity hospital with >9500 deliveries annually and a level 3 NICU to which ~150 infants of birth weight <1500 g are admitted each year. Infants born before 31 weeks'
gestation by best obstetric estimate (date of last menstrual period [LMP] or early dating scan) were eligible for inclusion. Infants with known congenital anomalies were excluded. The Research Ethics Committee at the NMH approved the study protocol, and written informed consent was obtained from a parent or guardian before delivery.

**Random Assignment**

Eligible infants were randomly assigned to placement on an EM or not in a 1:1 ratio. Randomization was stratified according to gestational age (<28 weeks and 28–30 weeks inclusive). We generated the treatment allocation schedule in permuted blocks of 4 using a random numbers table. Cards indicating treatment allocation “Bag & Mattress” (PB+EM) or “Bag” (PB) were concealed in sequentially numbered, sealed, opaque envelopes. A member of the neonatal team brought the next envelope in sequence from the appropriate stratum to the DR. The envelope was opened in the DR just before delivery to allow for timely activation of the EM for infants assigned to that group. Infants of multiple births were randomized separately. Neither caregivers nor outcome assessors were masked to treatment allocation.

**Interventions**

The DR temperature was recorded at each delivery from a wall-mounted thermometer and maternal temperature was recorded using a digital Genius 2 Tympanic Thermometer (Covidien, Dublin, Ireland) as close to the time of delivery as possible. Infants in both groups were stabilized in the DR on a resuscitation cot (CosyCot Infant Warmer, Fisher and Paykel Healthcare, Auckland, New Zealand) with a radiant heater that was switched on and manually set to maximal output at least 5 minutes before delivery. For all infants, a cotton towel and cotton knit hat (Premier Guard International, Guangzhou Fortunique, Guangdong Province, China) were placed before delivery on the resuscitation cot to warm under the radiant heaters. A resealable food-grade PB (SuperValu sealable, food storage bag 26.5 cm × 35 cm) was prepared by cutting a hole in the bottom of the bag large enough for the infant’s head to fit through.

All infants were transferred to the resuscitationcot immediately after birth. Umbilical cord clamping was not delayed for any infants in either group. On arrival, all infants were placed, without drying, head first into the PB so that the head protruded through the hole. Once a pulse oximeter was applied to the infant’s right wrist, the PB was sealed to enclose the infant’s body. Only the head and face were dried before the head was covered with a warm hat. All infants were placed supine, and stabilization was carried out by the neonatal resuscitation team as clinically indicated and in accordance with ILCOR recommendations.15 Infants in the PB+EM group were placed on top of an activated EM (TransWarmer, Cooper Surgical, Trumbull CT) in the DR. The EM was activated at least 3 minutes before birth10 and placed transparent side down under the warm towel on the resuscitaire before the infants were placed on top. Infants in the PB group were placed on warm towels on preheated resuscitaires in the same way as infants in the EM group. Respiratory support was given to infants in both groups with a T-piece resuscitator that delivered blended oxygen and air that was neither heated nor humidified. After stabilization in the DR, all infants were lifted off their towel and wrapped in 3 warm blankets before transfer to the NICU in a transport incubator (Air-Shields TI-100, Soma Technology, Bloomfield, CT) set to the maximum air temperature (35–37°C). All infants remained in the PB for transfer and infants in the PB+EM group remained on the EM for transfer. Once the primary outcome had been determined on arrival to the NICU, infants were placed in warm incubators, and the PB and EM were removed.

**Outcomes**

The primary outcome was rectal temperature on admission to NICU. This was measured with a digital thermometer (Vicks SmartTemp Digital Thermometer, Procter & Gamble, Cincinnati, OH) on arrival to the NICU while the infants were still in the transport incubator. The infants’ axillary temperature on admission was also recorded. Other variables including time from birth to NICU admission, history of suspected maternal chorioamnionitis, maternal temperature, maternal anesthesia, DR temperature, duration and type of respiratory support were also recorded for each infant.

**Sample Size**

Before this study, >50% of infants <31 weeks gestation treated with EM and PB in the DR at our hospital had admission temperatures outside the range of 36.5 to 37.5°C.17 To demonstrate a reduction in the proportion of infants with abnormal admission temperatures from 50% to 25% (ie, a relative reduction of 50%) by using PB alone with a 2-tailed type 1 error rate of 0.05 and 80% power, we estimated that we would need to recruit 116 infants.

**Statistics**

Data were analyzed by using SPSS version 18.0 (IBM Corporation, Armonk, NY). The primary outcome data and other dichotomous secondary outcomes were expressed as numbers and proportions and were compared by using Pearson χ² test. Continuous outcome variables with a normal distribution were expressed as mean (SD) and were compared by using a 2-tailed
t test. We considered $P$ values $<.05$ to be statistically significant.

**RESULTS**

An external data safety monitoring committee performed planned interim analysis of outcome data from the first 58 infants enrolled. The committee recommended stopping recruitment as they had identified a significant difference in the primary outcome between the groups. We report data for the 72 infants enrolled before this recommendation.

**Participants**

Ninety-three infants $<31$ weeks gestation were born at the NMH during the study period. Twenty-one infants were not enrolled. Of the 72 infants who were randomized, 37 were assigned to PBs and EMs and 35 to PBs alone (Fig 2). One infant who delivered precipitously vaginally and was randomized to the PB+EM group was not placed on an activated EM until 2 minutes after birth. This infant had an admission temperature of 37.7°C and was analyzed in her assigned group. All infants were followed from randomization to death or discharge. Infants in both groups were well matched for demographic characteristics; however, the time from birth to NICU admission was significantly longer for infants in the PB + EM group (24 vs 19 min, $P = .008$; Table 1). DR temperature, maternal temperature, and the proportion of infants with febrile mothers were similar between the 2 groups.

**Outcomes**

Significantly fewer infants in the PB+EM group had a rectal temperature of 36.5 to 37.5°C on NICU admission (15/37 [41%] vs 27/35 [77%], $P = .002$; Fig 2). The mean rectal temperature on admission was within the normal range for both groups but was higher in the PB+EM group (37.4 vs 37.0°C, $P = .017$). The mean axillary temperature was also higher in the PB+EM group (37.3 vs 36.9°C, $P = .011$). More infants treated with a PB+EM had admission temperatures $>37.5$°C (17/37 [46%] vs 6/35 [17%], $P = .009$). There was no significant difference in the incidence of hypothermia between the 2 groups (Table 2). There were no differences in the secondary outcomes measured (Table 2).

Eight infants died before discharge, 3 in the PB+EM group and 5 in the PB group. Although none of these infants were hypothermic on admission, 4 had admission temperatures $>37.5$°C. Our study was not adequately powered to detect differences in subgroups; however, the primary outcome was significantly different for both gestational age strata (PB+EM vs PB: $<28$ weeks’ gestation, 7/15 [47%] vs 13/14 [93%], $P = .007$; 28–30 weeks’ gestation, 8/22 [36%] vs 14/21 [67%], $P = .047$). Almost half of infants in the PB+EM group in both age strata had admission temperatures $>37.5$°C (7/15 [47%] and 10/22 [45%] respectively; Table 3).

We performed a regression analysis to explore the relationship between time to admission and admission temperature. It showed that there was some evidence of a positive correlation between time to admission and rectal temperature in both groups ($P = .007$), but the association is weak ($R^2 = .098$) and does not significantly account for the increase in admission temperature. Multiple regression analyses of other potential confounders revealed that there is some evidence that maternal and transport incubator temperature had an effect on infant’s temperature and the presence of hyperthermia but neither association were significant enough to explain the difference in temperature between groups. We found no association among DR temperature, gender, DR location, mode of delivery, antenatal antibiotics, maternal anesthetic, or time of mattress activation and hyperthermia.

**DISCUSSION**

In this randomized controlled trial, we found that more newborns of $<31$ weeks’ gestation have normal admission temperature when PBs were used alone rather than in combination with EMs in the DR and that hyperthermia
occurred more frequently when both techniques were used. We stratified our randomization according to gestational age because we suspected that more immature infants would be at greater risk of hypothermia and might benefit most from a combination of warming strategies. However, we found that the risk of hyperthermia when both a PB and EM were used was higher than the risk of hypothermia when a PB alone was used for these infants (Fig 3).

The greatest limitation of our study was that caregivers were not masked to treatment allocation. For infants in the PB+EM group, the mattress was activated by a member of the resuscitation team, placed on the resuscitation table before delivery, and transferred with the infant to the NICU. We speculate that the unblinded nature of this study may have contributed to the difference in time to admission between the 2 groups. It is possible that caregivers consciously or subconsciously hurried infants in the PB group out of the DR more quickly than those on an EM because they were concerned that they were at greater risk of hypothermia. We observed a similar difference in time to admission in our earlier prospective cohort study. In this nonrandomized study, we assumed that the reason

infants treated with a PB+EM spent an average of 5 minutes longer in the DR was because they were smaller, more immature, and received more respiratory support and therefore may have required more time for stabilization in the DR. These demographic differences were not present in this trial. On further analysis of data from this study, we observed a positive linear relationship between the length of time from birth to admission and hyperthermia; that is, the longer an infant spent in the DR, the greater the likelihood of hyperthermia in both groups. However, the correlation is weak, and the relationship cannot be explained by time alone. Because this has been observed in both studies, we believe that this association is unlikely to be due to chance and must be due to other unidentified confounding factors.

The rate of hyperthermia among infants wrapped in PB in our study (2/35, 6%) is markedly lower than the rates reported in other studies (31%-68%).5-9 We do not know why the rate of admission hyperthermia at our hospital is comparatively low. The mean DR temperature, maternal temperature, incidence of suspected chorioamnionitis, cesarean delivery rate, and use of antenatal steroids are similar, but we differ from some other studies in that we report rectal rather than axillary temperature. Although correlation between rectal and axillary temperature in preterm infants is poorly studied, axillary temperature is considered to be less than rectal temperature by up to 0.5°C.18 For this reason, studies reporting axillary temperature may have overestimated the occurrence of hypothermia. In this trial, mean rectal temperature was 0.1°C higher than axillary temperature. However, only 17% of the control group had an axillary temperature <36.5°C on admission, considerably less than other trials.
Hypothermia is an independent risk factor for mortality in very preterm infants but less is known about the acute and long-term impact of transient hyperthermia after birth. Maternal pyrexia in labor is associated with adverse neurologic outcome in term and preterm infants (eg, neonatal seizures, encephalopathy, cerebral palsy, and mortality). It is unclear whether hyperthermia itself causes brain injury or whether other factors (eg, infection, systemic inflammation) cause both a raised temperature and brain injury. In term animals, hyperthermia appears to increase neuronal cell damage in those at risk for perinatal hypoxia-ischemia. In addition, hyperthermia during ventilation of preterm newborn lambs exacerbates lung injury. In the absence of human data, guidelines emphasize the importance of maintaining normothermia and avoiding iatrogenic hyperthermia.

Wrapping very preterm newborns in PB after birth did not present many problems for the neonatal team at our hospital. Once the infants were placed in the PB, the bag was sealed and remained sealed until arrival in the NICU. Pulse oximeters were used in all cases and the infant’s HR was auscultated through the bag without reported difficulty. Although other interventions (eg, chest compressions, umbilical line insertion, thoracocentesis) were not carried out on any infants in this trial, it is our experience that these procedures can be easily performed through an incision made in the bag. In addition to improving admission temperature, there are significant cost implications associated with using PB alone in the DR (cost per PB ∼ 10 cents [$0.13] each compared with the TransWarmer mattress ∼ €35 [$46.50] each).

Maintaining normothermia in preterm infants after birth is difficult. To date preventing hyperthermia has been the greatest challenge. Although placing preterm infants in a PB on an EM increases mean admission temperature, when used in combination, infants are at greater risk of hyperthermia. Additional research is needed to understand the consequences of transient hyperthermia in newborn preterm infants and to explore the role of continuous temperature monitoring in the DR.

### TABLE 3

Demographics and Outcomes for Subgroups by Gestational Age

<table>
<thead>
<tr>
<th></th>
<th>PB + EM</th>
<th>PB</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infants &lt;28 wk</td>
<td>n = 15</td>
<td>n = 14</td>
<td></td>
</tr>
<tr>
<td>Gestational age (wk)*</td>
<td>25 (1.5)</td>
<td>26 (1.1)</td>
<td>.146</td>
</tr>
<tr>
<td>Birth wt (g)*</td>
<td>748 (150)</td>
<td>881 (216)</td>
<td>.059</td>
</tr>
<tr>
<td>Maternal fever</td>
<td>1 (7)</td>
<td>1 (7)</td>
<td>.987</td>
</tr>
<tr>
<td>Time to NICU admission (min)*</td>
<td>23 (7)</td>
<td>18 (4)</td>
<td>.021c</td>
</tr>
<tr>
<td>Admission rectal temperature 36.5–37.5°C*</td>
<td>7 (47)</td>
<td>13 (93)</td>
<td>.007c</td>
</tr>
<tr>
<td>Admission rectal temperature (°C)*</td>
<td>37.5 (0.9)</td>
<td>36.7 (0.4)</td>
<td>.008c</td>
</tr>
<tr>
<td>Admission rectal temperature &gt;37.5°C*</td>
<td>7 (47)</td>
<td>0 (0)</td>
<td>.004c</td>
</tr>
<tr>
<td>Admission rectal temperature &lt;36.5°C*</td>
<td>1 (7)</td>
<td>1 (7)</td>
<td>.960</td>
</tr>
<tr>
<td>Admission axillary temperature (°C)*</td>
<td>37.4 (0.8)</td>
<td>36.5 (0.5)</td>
<td>.002c</td>
</tr>
<tr>
<td>Infants ≥28 wk</td>
<td>n = 22</td>
<td>n = 21</td>
<td></td>
</tr>
<tr>
<td>Gestational age (wk)*</td>
<td>29 (0.8)</td>
<td>29 (0.7)</td>
<td>.723c</td>
</tr>
<tr>
<td>Birth wt (g)*</td>
<td>1317 (282)</td>
<td>1402 (331)</td>
<td>.354c</td>
</tr>
<tr>
<td>Maternal fever</td>
<td>3 (14)</td>
<td>4 (19)</td>
<td>.631c</td>
</tr>
<tr>
<td>Time to NICU admission (min)*</td>
<td>24 (6)</td>
<td>20 (6)</td>
<td>.118c</td>
</tr>
<tr>
<td>Admission rectal temperature 36.5–37.5 °C*</td>
<td>8 (38)</td>
<td>14 (67)</td>
<td>.047c</td>
</tr>
<tr>
<td>Admission rectal temperature (°C)*</td>
<td>37.3 (0.9)</td>
<td>37.2 (0.8)</td>
<td>.398c</td>
</tr>
<tr>
<td>Admission rectal temperature &gt;37.5°C*</td>
<td>10 (45)</td>
<td>6 (29)</td>
<td>.252c</td>
</tr>
<tr>
<td>Admission rectal temperature &lt;36.5°C*</td>
<td>4 (18)</td>
<td>1 (5)</td>
<td>.170c</td>
</tr>
<tr>
<td>Admission axillary temperature (°C)*</td>
<td>37.3 (0.9)</td>
<td>37.1 (0.6)</td>
<td>.474c</td>
</tr>
</tbody>
</table>

* Data are mean (SD).

b Data are n (%).

c Significant P value.

FIGURE 3

Rectal temperature versus birth weight on admission to the NICU.
In newborn very preterm infants, using EMs in addition to PBs in the DR results in more infants with tempering EMs in addition to PBs in the DR in newborn very preterm infants, using EMs in addition to PBs in the DR.

CONCLUSIONS

We thank Professors Peter Davis, Barbara Schmidt, and Susan Donath and Dr Louise Owen for their interim analysis of our data and Dr Gloria Crispino O’Connell at StatisticaMedica (www.statisticamedica.com) for her help with the statistical analysis of our data.

REFERENCES

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*Pediatrics* 2013;132;e135; originally published online June 17, 2013;
DOI: 10.1542/peds.2013-0279

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