ประสิทธิผลของการใช้ถุงพลาสติกห่อตัวทารกทันทีหลังคลอดเพื่อป้องกันภาวะอุณหภูมิกายต่ำในทารกคลอดก่อนกำหนด

นายสันติ ปุณณะหิตานนท์

สถาบันวิทยบริการ
จุฬาลงกรณ์มหาวิทยาลัย

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาวิทยาศาสตรมหาบัณฑิต
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EFFICACY OF POLYETHYLENE PLASTIC WRAP FOR THE PREVENTION OF HYPOTHERMIA DURING IMMEDIATE POSTNATAL PERIOD IN PREMATURE INFANTS: A RANDOMIZED CONTROLLED TRIAL

Mr. Santi Punnahitananda

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Thesis Title	EFFICACY OF POLYETHYLENE PLASTIC WRAP FOR THE PREVENTION OF HYPOTHERMIA DURING IMMEDIATE POSTNATAL PERIOD IN PRETERM INFANTS: A RANDOMIZED CONTROLLED TRIAL
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สันติ ปุณณะหิตานนท์: ประสิทธิผลของการใช้ถุงพลาสติกห่อตัวทารกทันทีหลังคลอดเพื่อป้องกันภาวะอุณหภูมิกายต่ำในทารกคลอดก่อนกำหนด (EFFICACY OF POLYETHYLENE PLASTIC WRAP FOR THE PREVENTION OF HYPOTHERMIA DURING IMMEDIATE POSTNATAL PERIOD IN PREMATURE INFANTS: A RANDOMIZED CONTROLLED TRIAL) อ. ที่ปรึกษา: รศ.นพ.สังคม จงพิพัฒน์วิชย์, อ.ที่ปรึกษาร่วม: รศ.นพ.สมพนธ์ ทัศนิยม, 60 หน้า.

วัตถุประสงค์:เพื่อเปรียบเทียบประสิทธิผลของประสิทธิผลของการใช้ถุงพลาสติกห่อตัวทารกทันทีหลังคลอดในการป้องกันภาวะอุณหภูมิกายต่ำในทารกคลอดก่อนกำหนด

รูปแบบการศึกษา: การศึกษาแบบสุ่มเปรียบเทียบ

สถานที่ทำการวิจัย: โรงพยาบาลจุฬาลงกรณ์ สภากาชาดไทย

วิธีการศึกษา: ทารกคลอดก่อนกำหนดอายุครรภ์น้อยกว่าหรือเท่ากับ 34 สัปดาห์ เข้าร่วมการศึกษาโดยถูกสุ่มออกเป็น 2 กลุ่ม กลุ่มแรกใช้ถุงพลาสติกชนิด polyethylene ห่อตัวทั้งตัวจนถึงลำคอทันทีหลังคลอด เป็นเวลา 3 ชั่วโมง กลุ่มที่สองได้รับการเช็ดตัวให้แห้งทันทีหลังคลอด ทารกทุกคนได้รับการดูแลอยู่ใต้เตียงให้ความอบอุ่น ทำการวัดอุณหภูมิกายทางทวารหนักเมื่อแรกรับที่ห้องเด็กและต่อไปทุกชั่วโมงอีก 3 ครั้ง

ผลการศึกษา: มีทารก 130 คนร่วมในการศึกษา ในจำนวนนี้มี 122 คนอยู่ในการศึกษาจนสิ้นสุด (กลุ่มละ 61 คน) ทารกกลุ่มที่ถูกห่อตัวด้วยถุงพลาสติกมีอุบัติการณ์ของภาวะอุณหภูมิกายต่ำเมื่อแรกรับ ต่ำกว่าทารกในกลุ่มควบคุม อย่างมีนัยสำคัญทางสถิติ (ร้อยละ26. 2 และ50 , p=0.007, OR 0.36; 95%CI 0.17, 0.76) และมีอุบัติการณ์ของภาวะอุณหภูมิกายต่ำภายใน 3 ชั่วโมงหลังคลอดต่ำกว่าทารกในกลุ่มควบคุมอย่างมีนัยสำคัญทางสถิติ (ร้อยละ44.3 และ70.5, p=0.003, OR 0.33; 95%CI, 0.16 ,0.70) ทารกกลุ่มที่ถูกห่อตัวมีอุณหภูมิกายเฉลี่ยแรกรับ (36.7 $\pm$ 0.54 °C) และที่1 ชั่วโมงหลังจากนั้น(36.6 $\pm$ 0.46 °C) สูงกว่ากลุ่มควบคุม (36.3 $\pm$ 0.66 และ 36.4 $\pm$ 0.46 °C) อย่างมีนัยสำคัญทางสถิติเช่นกัน (p= 0.002 และ 0.032 ตามลำดับ) เมื่อนำปัจจัยน้ำหนักตัวแรกคลอด, ภาวะตัวเล็กกว่าอายุครรภ์, คะแนนแอพการ์ที่1 นาทีน้อยกว่า4, และการใส่สายสวนหลอดเลือดสะดือ ซึ่งอาจมีผลต่ออุณหภูมิกายมาคำนวณในสมการ logistic regression พบว่าการห่อตัวทารกด้วยถุงพลาสติกมีผลช่วยป้องกันอุณหภูมิกายต่ำอย่างมีนัยสำคัญทางสถิติ (adjusted OR 0.39; 95%CI, 0.17, 0.87) การวิเคราะห์กลุ่มย่อยพบความแตกต่างอย่างมีนัยสำคัญทางสถิติของอุบัติการณ์ของภาวะอุณหภูมิกายต่ำเมื่อแรกรับและภายใน 3 ชั่วโมงหลังคลอด รวมทั้งอุณหภูมิกายเฉลี่ยแรกรับในทารกกลุ่มที่อายุครรภ์ต่ำกว่า 31 สัปดาห์ (อุณหภูมิกายเฉลี่ยแรกรับสูงกว่ากลุ่มควบคุม 0.62 °C; 95% CI, 0.18 to 1.05)

สรุป: การใช้ถุงพลาสติกชนิด polyethylene ห่อตัวทารกทันทีหลังคลอดมีประสิทธิผลช่วยป้องกันภาวะอุณหภูมิกายต่ำในทารกคลอดก่อนกำหนดได้

สาขาวิชา การพัฒนาสุขภาพ..... ลายมือชื่อนิสิต.....สันติ ปุณณะหิตานนท์

ปีการศึกษา 2549..... ลายมือชื่ออาจารย์ที่ปรึกษา.....

ลายมือชื่ออาจารย์ที่ปรึกษาร่วม.....

4775006030 : MAJOR HEALTH DEVELOPMENT

KEY WORD : POLYETHYLENE PLASTIC / WRAP/ HYPOTHERMIA/ PREMATURE INFANT

SANTI PUNNAHITANANDA: EFFICACY OF POLYETHYLENE PLASTIC WRAP FOR THE PREVENTION OF HYPOTHERMIA DURING IMMEDIATE POSTNATAL PERIOD IN PREMATURE INFANTS: A RANDOMIZED CONTROLLED TRIAL. THESIS ADVISOR: ASSOC. PROF. SUNGKOM JONGPIPUTVANICH, THESIS CO-ADVISOR: ASSOC. PROF. SOMPON TASSNIYOM, 60 PAGES.

Objective: To assess the efficacy of occlusive body wrapping with polyethylene plastic bag to prevent hypothermia in premature infants during immediate postnatal period.

Design: Randomized controlled trial

Setting: King Chulalongkorn Memorial Hospital, Thai Red Cross Society

Methods: Premature infant of 34 weeks gestation or less were randomized to study or control group. Study infants were placed in polyethylene plastic bags immediately after birth in delivery room, leaving only the head uncovered and were kept in plastic bags for 3 hours. Any resuscitation or treatment was done with the bags covering the bodies. Control infants were dried and resuscitated per standard protocol before transferred to nursery. All infants were stabilized under radiant warmers. Rectal temperature was taken on nursery admission and hourly thereafter for 3 hours by a digital thermometer.

Results: Of 130 randomized infants, 122 completed the study (61 in each group). The infants in wrap group had lower incidence of hypothermia on admission (26.2 vs 50%, p=0.007, OR 0.36; 95%CI, 0.17 to 0.76) as well as hypothermia during the 3 hours study period (44.3 vs 70.5%, p=0.003; OR 0.33, 95%CI, 0.16 to 0.70). Wrapped infants also had higher rectal temperature on admission (36.7 $\pm$ 0.54 vs 36.3 $\pm$ 0.66 °C, p= 0.002) and at 1 hour after admission (36.6 $\pm$ 0.46 vs 36.4 $\pm$ 0.46 °C, p= 0.032). The effects of wrapping on prevention of hypothermia was still significant after adjustment for birth weight, small for date, low 1-minute Apgar score, and umbilical catheterization (adjusted OR 0.39, 95%CI, 0.17 to 0.87). Subgroup analysis showed significant higher admission rectal temperature and lower incidence of hypothermia on admission and throughout the study period in infants of less than 31 weeks' gestation (difference in mean rectal temperature = 0.62 °C, 95% CI, 0.18 to 1.05) but not in infants of 31 to 34 weeks' gestation.

Conclusion: Occlusive body wrapping with polyethylene plastic bag in delivery room is efficacious in the prevention of hypothermia in premature infants during immediate postnatal period.

Field of study Health Development..... Student's signature..... Santi Punnahitananda

Academic Year 2006..... Advisor's signature..... Sungkom Jongpiputvanich

Co-advisor's signature..... Sompon Tassniyom

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CHAPTER I

RATIONALE AND BACKGROUND

Hypothermia is a common major problem for premature infants during immediate postnatal period. If present, it leads to multiple deleterious complications including hypoglycemia [1], respiratory distress [2], hypoxia, metabolic acidosis [3] , coagulation defects [4] , delayed adaptation from fetal to newborn circulation [5], acute renal failure, necrotizing enterocolitis, failure to gain weight or weight loss [6] and even, death in extreme cases [1].

Risk factors of hypothermia include prematurity, small for gestational age [7,8], asphyxia, certain congenital anomalies with opening defects such as gastroschisis, damage to central nervous system [9], low room temperature, and inadequate control of thermal environment. Significant heat loss can occur rapidly soon after birth in very low-birth-weight and/or premature infants. During the first few minutes after birth, deep body and skin temperature can drop at a rate of approximately 0.1°C and 0.3°C per minute respectively unless precautions are taken. This is equivalent to a heat loss of 200 calories per kg per minute and it has been deduced that even if heat production per unit body weight was twice that of an adult man the body temperature of the newborn would still fall [10]. This rapid drop in body temperature (2-3°C) is attributable to a combination of the physical characteristics of preterm infants and the environmental factors. Mechanisms of heat loss from the body include conduction, convection, radiation and evaporation. Newborn infants have a larger surface area in relation to body weight and a thinner layer of insulating fat. As such, body heat can be lost to the surrounding environment easily from the moment of birth [11]. The major mechanism for rapid heat loss at birth is evaporation of amniotic fluid from body surface when the wet newborn moves from the consistently warm environment of the uterus into a cooler, drier delivery room [12]. As much as 560 calories of heat are lost for each milliliter of water evaporating from the skin [13]. Premature infants have decreased fat storage for heat production and insulation, decreased glycogen stores, an underdeveloped skin which increases water loss and poor vascular control. They therefore experience higher evaporative heat loss than term infants during the first day of life, especially at low

relative ambient humidity [14]. The extent of total heat loss and the mode of heat exchange are influenced by ambient air temperature, speed of circulation, atmospheric pressure, relative humidity, and the temperature of surrounding surfaces [15, 16]. External (skin-environment) temperature gradient is also a major influencing factor for the infant's response to cold. [17]

Thermoregulation is an important determinant for survival of low-birth-weight infants. Previous studies demonstrated that reducing heat losses increased survival rates of premature infants [18, 19]. Given that premature infants develop hypothermia soon after birth, early intervention in the delivery room is therefore of high priority in thermal care of small, premature infants if hypothermia is to be prevented.

Current standard thermal care for newborn infants includes providing delivery room temperature at a minimum of 25°C [20], pre-warming any surfaces that the infant will come in contact with, immediate drying the infant [21] and removing any wet linens, wrapping the infant in a pre-warmed blanket,. Additional measures include keeping the infants away from drafts, outside walls and cold surfaces [9] encouraging skin to skin contact with mother [kangaroo care], and using radiant warmers before placing infants in an incubator for transfer.

Radiant warmers have been shown to be effective in counteracting body heat losses, provided that the infant is immediately dried and placed under the pre-warmed heater [22, 23, 24]. When an infant is placed under a radiant warmer, heat is gained by radiation but there are increased heat losses through convection and evaporation. Although causing significant increased insensible water loss in small premature infants [25], radiant warmers are still mainstay in thermal care of infants in both delivery room and newborn nursery. However, the effectiveness of radiant warmers is reduced during procedures because heat is absorbed by the covering drapes and cannot penetrate to infants. Care should also be taken to avoid under-heating during procedures. As an alternative for a healthy newborn, placing the infant on the mother's chest and abdomen after the infant is thoroughly dried and a light blanket placed around them can reduce radiant and conductive heat loss and promote temperature stabilization [26]. This approach is, however, not practical for sick premature infants requiring special intensive care who are too unstable to be placed with mothers.

Despite all the efforts to maintain normal temperature, many premature infants still develop hypothermia, especially the very small ones. The incidence of neonatal hypothermia at King Chulalongkorn Memorial Hospital in the year 2003 was as high as 55% in very low-birth-weight infants. Not only at delivery or nursery admission, premature infants can develop hypothermia at any time during the first hours of life, during which they are exposed to room temperature with interrupted, and inadequate heat provided to them. Additional efforts have been tried in order to reduce heat loss in the immediate postnatal period and these measures have been investigated.

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CHAPTER II

LITERATURE REVIEW

The search strategy was performed by searching PubMed database through December 2005 to find studies that assessed the effectiveness of efforts to reduce body heat loss during immediate postnatal period. The medical subject heading terms used for the search strategy was hypothermia. There have been many studies to investigate the effectiveness of additional measures to reduce heat loss during immediate postnatal period. Most studies have been focused mainly on reducing evaporation heat loss which is the major mechanism of heat loss during post natal period. These efforts include body wraps and/or head coverings made from a variety of materials. A polyester suit lined with aluminum known as the 'silver swaddler ' was designed in the 1960s to prevent hypothermia by reducing all modes of heat transfer to the environment (figure 1). The material itself is impermeable and therefore prevents evaporation and convection. Polyester is also a poor conductor of heat, while the silver surface protects against radiant heat loss. This has proved to be effective for infants with birth weight greater than 3,000 g and no cases of overheating have been reported [27]. This method, however, is not practical for sick premature neonates and no study has been done in this population.

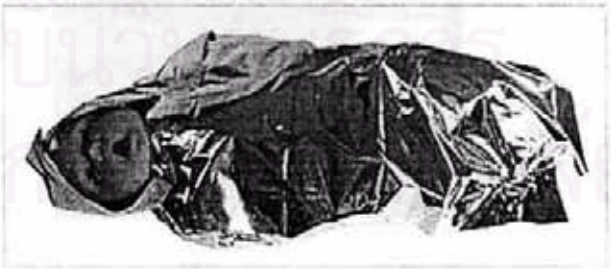


Figure 1 Silver swaddler

Other techniques have included hoods or heat shields, which are not in contact with the infant's body [28, 29]. The shields are used in addition to radiant warmers and

incubators to raise local humidity and therefore reduce evaporation [figure 2]. Although these techniques are effective they cannot be applied early during stabilization in delivery room. Furthermore, heat shields have to be removed during procedures such as intubation and umbilical line placement. Thus, the use of heat shields is not practical for sick, unstable premature infants.

Figure 2 Plastic heat shield

Barrier creams, waxes or protective films such as Aquaphor ® (Figure 3) have also been utilized to reduce heat losses in immature infants [30] but are not normally applied within the first 1 or 2 hours of birth. Furthermore, the application of ointment on premature skin may increase the risk of bacterial and fungal infection in extremely low birth weight infants [31,32].

Figure 3 Skin protective ointment (Aquaphor)

Semi-permeable membranes such as Opsite® or Tegaderm ® (Figure 4) have been studied and found to decrease excessive transepidermal water loss associated with prematurity [33,34,35] . For this reason it may decrease evaporative heat loss.

However, these occlusive membranes do not cover all parts of the body surface, leaving many areas exposed to room environment. Most studies about the occlusive dressing focused on the transepidermal water loss and there were no clinical studies investigating the direct effects of semi-permeable membranes on temperature regulation of premature infants.

Figure 4 Semi-permeable membrane occlusive dressing

Although many techniques are effective in preventing heat loss from the neonate, some treatments still have not been studied in premature infants. Furthermore, most of the interventions are not feasible in delivery room and during the stabilization period because they may interfere with resuscitation or procedures.

Transparent plastic coverings such as bubble wrap and single layer gowns have been utilized to minimize transepidermal water loss and hence reduce heat loss by evaporation. These have been shown to be effective in infants with birth weight greater than 2,000 g [36] and more recently in infants of less than 33 weeks' gestation [37]. The underlying principle is that polyethylene plastic coverings reduce evaporative heat loss while still allowing heat gain from radiation [38]. These are particularly effective when used in conjunction with a radiant warmer [36]. Hobbs, using single layer gowns after delivery, reported that this did not result in any cases of hyperthermia [39]. This approach is simple and convenient to apply and at the same time does not interfere with resuscitation and procedures. It therefore might be of advantage help small infants maintain normal body temperature throughout the stabilization period.

To review the published literature on the use of polyethylene plastic wrap to prevent hypothermia in premature infants, a search strategy was performed by searching PubMed database through December 2005 to find studies that assessed the

effectiveness of efforts to reduce body heat loss during immediate postnatal period. The medical subject heading terms used for the search strategy were: "temperature" OR "body temperature" OR "body temperature regulation" OR "hypothermia" AND "plastics" OR "polyethylenes" OR "polyethylene" AND "infant" AND "infant, newborn" AND "humans" with limits to newborn age group. Also related articles of the relevant articles retrieved by this search strategy have been searched. There were 5 published articles on the use of plastic wrap to prevent hypothermia in newborn infants retreived [37,40,41,42,43]. These studies have been reviewed.

In 1999 Vohra et al [40] published their study that was a randomized controlled trial comparing admission temperature between premature infants who were wrapped with polyethylene bags at birth and control infants with conventional thermal care. The result showed the infants in wrap group had significantly higher admission rectal temperature than the control infants without wraps. The effect was significant in infants younger than 28 weeks gestation. There was no untoward effect of intervention observed in the treatment group. The authors concluded that wrapping premature infants with occlusive polyethylene bags was effective in maintaining normal temperature in very low-birth-weight infants. This was the first randomized controlled study showing the benefit of polyethylene bag to wrap babies at birth. However, there are a few drawbacks in research methodology. The sample size calculation was not mentioned in methodology section. Regarding the statistical consideration, the power of the study was set but was changed later during the data collection to justify the small sample size they had. In one subgroup of infants, the mean birth weight of control infants was less than that of the wrapped infants. The difference in birth weight made the comparison less conclusive because birth weight is considered a major prognostic factor for hypothermia. This cofactor might have created some biases to the outcome. Furthermore, the primary outcome, which was a one-time temperature measurement, did not represent the infants' body temperature throughout the stabilization period, during which the infants could still develop hypothermia at any point of time.

In 2000 Bjorklund [41] demonstrated in his retrospective review that occlusive skin wrapping immediately after birth was easy to implement and resulted in normal temperature on admission in the majority of very premature infants.

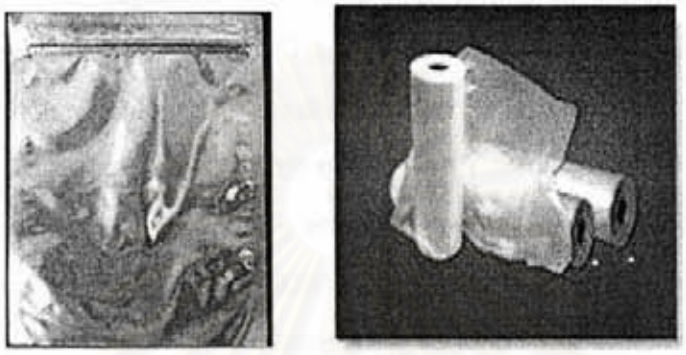
In another report by Lenclen in 2002, occlusive wrapping with a polyethylene bag at birth was shown to prevent low rectal temperature in premature infants in the immediate postnatal period [37]. This study, however, was also a retrospective, case-control study, in which many biases could not be prevented and controlled.

Knobel et al. [42] reported in their study comparing the use of polyurethane plastic bag to wrap premature infants with conventional stabilization protocol. The study was a randomized controlled trial in which the sample population was premature infants of less than 29 weeks gestation. The numbers of infants in treatment and control group were 41 and 47 respectively. The study result demonstrated that infants who were wrapped in plastic bags were less likely to develop hypothermia on admission and had significantly higher admission temperatures. In their report there was no information about randomization, and details in research methodology so the validity and reliability of the result was difficult to assess.

Recently Vohra et al. reported another randomized controlled study using the same technique to prevent hypothermia in very premature infants [less than 28 weeks gestation [43]. They demonstrated that the wrapped infants had higher mean rectal admission temperature than the control infants who were dried under radiant warmers and the temperatures at one hour after admission were comparable in both groups. There were no differences in secondary outcomes. From methodological standpoints, this study had better quality compared with their previous study in 1999. However, the incidence of hypothermia during the study in both groups was not mentioned. Looking at the temperature in the wrap group, it can be speculated that there still were some infants having hypothermia (mean admission temperature 36.5± 0.8 °C, and mean temperature at one hour after admission 36.6± 0.7 °C). Although the absolute number of temperature is considered appropriate for statistical analyses, it may not be as clinically relevant as the incidence of hypothermia in this regard.

Of the three randomized controlled trials, plastic material used to wrap infants was somewhat different. Vohra used polyethylene plastic while Wimmer used polyurethane plastic bags. All studies did not show any adverse effects associated with the use of plastic bags. Regarding the plastic material used in this trial, polyurethane bags are bags used to contain frozen or fresh food (zip lock bags, Figure 5). This kind of

plastic is thicker and harder than polyethylene bags. They are also more expensive and not available in every area. On the other hand, polyethylene bags are the most commonly used plastic bags for food and household goods. Polyethylene is high quality plastic that is easily available in and not expensive.



5A 5B

Figure 5 Polyurethane (5A) and polyethylene (5B) plastic bag

Since hypothermia is still a major problem among premature infants in Thailand. It is necessary to find an effective intervention to prevent and treat hypothermia and thus implement it to general practice. The result from previous studies on the use of polyethylene or polyurethane plastic bags is quite promising. Considering the feasibility of the technique and material used, polyethylene bags seem to be appropriate and more feasible in Thailand due to its availability and low cost. Up to the time of our review there are only a few randomized controlled studies about polyethylene wraps in small premature infants. Sample sizes of these studies were small and only one study was considered to have good quality. Moreover, none of the studies has shown the effects of temperature control throughout the first few hours of stabilization in the nursery. With the scarcity of evidence and lack of relevant additional data, a well designed randomized controlled study with appropriate methodology is needed to determine the efficacy and benefit of such technique.

CHAPTER III

RESEARCH METHODOLOGY

3.1 Research question

3.1.1 Primary research question

Is occlusive skin wrapping with polyethylene plastic bag applied immediately after birth efficacious in the prevention of postnatal hypothermia in premature infants of 34 weeks gestation or less?

3.1.2 Secondary research questions

3.1.2.1 Are there any differences in short term outcomes between premature infants receiving polyethylene wrap and those who receive routine standard thermal care?

3.1.2.2 What are the adverse effects of using polyethylene plastic bag to prevent hypothermia in preterm infants?

3.2 Research objectives

3.2.1 Primary objective

To assess the efficacy of occlusive wrapping with polyethylene bag applied immediately after birth and continued for 2 hours for the prevention of hypothermia in premature infants of 34 weeks gestation or less during immediate postnatal period compared with routine standard thermal care.

3.2.2 Secondary objective

3.2.2.1 To compare short term outcomes (hypoglycemia, metabolic acidosis, etc.) between preterm infants receiving polyethylene wrap and those who receive routine standard thermal care

3.2.2.2 To evaluate the adverse effects of using polyethylene plastic bag to prevent hypothermia in preterm infants

3.3 Statistical hypothesis

Null hypothesis

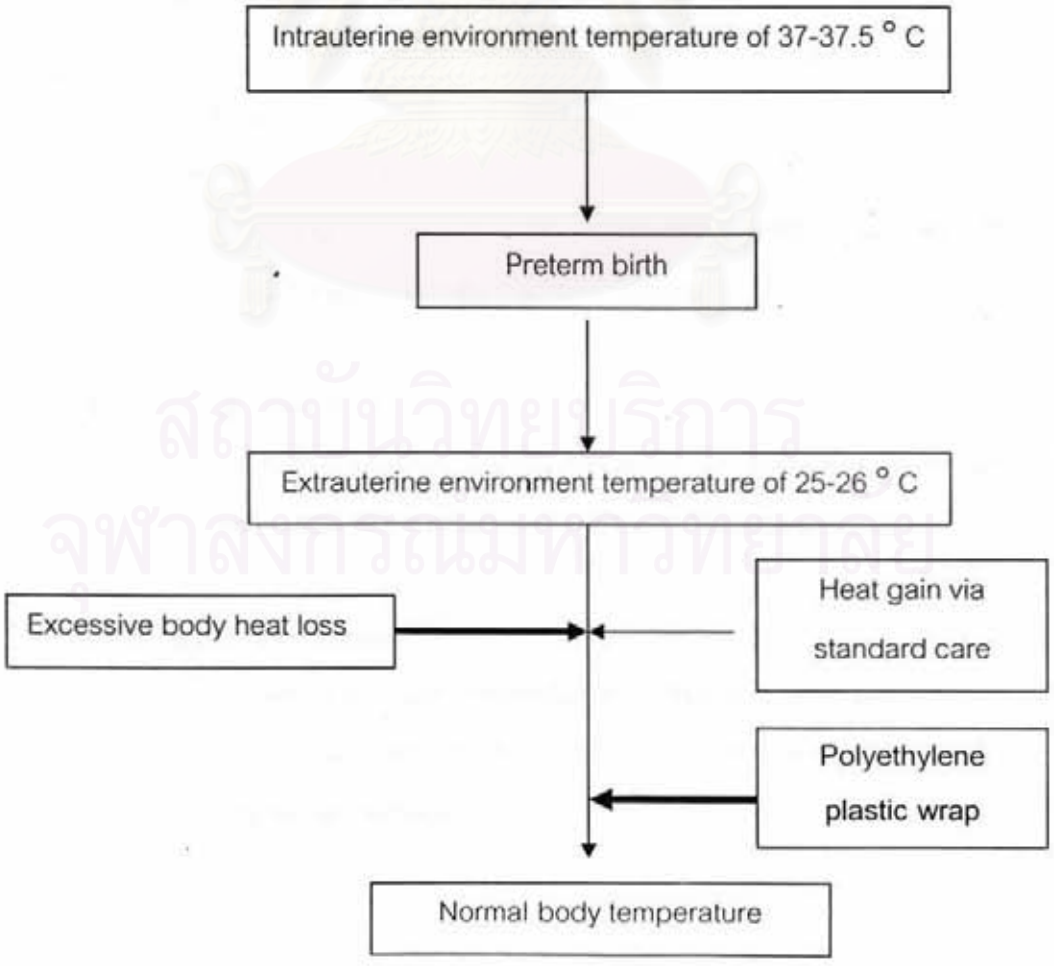
The incidence of hypothermia among preterm infants with gestational age of 34 weeks or less who are wrapped with polyethylene plastic bags immediately after birth for 2 hours does not differ from that among preterm infants receiving routine standard thermal care.

Alternative hypothesis

The incidence of hypothermia among preterm infants with gestational age of 34 weeks or less who are wrapped with polyethylene plastic bags immediately after birth for 2 hours is different from that among preterm infants receiving routine standard thermal care.

3.4 Conceptual framework

Figure 6 : Proposed conceptual framework



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3.5 Operational definitions

Hypothermia : a core body temperature of less than 36.5° C

Body temperature : core temperature measured via rectum with a digital rectal thermometer (WelchAllyn Suretemp® 986, WelchAllyn, San Diego)

Hypoglycemia : Blood glucose level using glucose oxidase strip screening test (Advantage®) or plasma glucose level less than 40 mg/dl

Metabolic acidosis : Significant metabolic acidosis requiring attention is diagnosed when Arterial or capillary blood pH is less than 7.25 or serum bicarbonate level is less than 15 meq/l or base deficit is less than 7 meq/l.

3.6 Research design

Randomized controlled trial

3.7 Research methodology

3.7.1 Population and sample

Target population

Preterm infants with gestational age of 34 weeks or less born at King Chulalongkorn Memorial Hospital

Sample population

Consecutively born preterm infants born at King Chulalongkorn Memorial Hospital who meet the inclusion criteria

3.7.2 Inclusion criteria

Gestational age less than or equal to 34 complete weeks (according to best obstetric estimate at the time of delivery)

3.7.3 Exclusion criteria

- Infants with major congenital malformations with open lesions, especially abdominal wall defects (gastroschisis, omphalocele, extrophy bladder), myelomeningocele

- Infants by whom the attending obstetrician considers pre-viable (e.g. delivery before 24 complete weeks or deliveries to which the neonatal resuscitation would not be called)
- Infants who are born 5 minutes or more before the pediatric team arrive the delivery room

3.7.4 Sample size calculation

Based on the assumption that the use of polyethylene plastic bag to wrap the infant immediately after birth and continued for the first 2 hours of life will reduce the occurrence of hypothermia in low-birth-weight, premature infants in our unit from 55 % to 20%. With the α of 0.05 and the power of 0.9 in a 2-tailed test, we calculated the sample size using the formula for 2 independent proportions as the following:

$$n = \frac{[Z_\alpha \sqrt{2\,p(1-p)} + Z_\beta \sqrt{p_2(1-p_2) + p_1(1-p_1)}]^2}{(p_2 - p_1)^2}$$

n = sample size in each group

$p = (p_1+p_2)/2$

p_1 = proportion of infants with hypothermia in control group

p_2 = proportion of infants with hypothermia in treatment group

Z_α = 1.96 for α of 0.05 (two tailed)

Z_β = 1.28 for β of 0.1 (power of 0.9)

Where p_1 = incidence of hypothermia in low birth weight infant in King Chulalongkorn Memorial Hospital = 0.55

p_2 = expected proportion of infants with hypothermia in treatment group = 0.2

The number of sample in each group calculated from the above formula is 44. With the assumption that there might be around 10% drop out rate, the adjusted sample size would be 49 in each group.

3.7.5 **Randomization and allocation concealment**

- Randomization process was done prior to the study with computer generated randomization list.
- Randomization was stratified into 2 strata according to gestational age that are: gestational age below 31 weeks and 31-34 weeks to ensure equal gestational age distribution in each group.
- The allocation was concealed and kept in separate opaque envelopes, which was sequentially numbered.
- All eligible infants were recruited and randomly assigned into either treatment (wrap) or control (none wrap) group just before delivery by responsible pediatric house staff who opened the randomization envelope and allocated the eligible infant into the group assigned.
- In case of multiple births the staff took the corresponding number of envelopes.

3.7.6 **Intervention**

Immediate thermal stabilization in the delivery room

Infants in control group received standard thermal care currently practiced at King Chulalongkorn Memorial Hospital. The protocol is recommended by the Neonatal Resuscitation Program (44). This includes

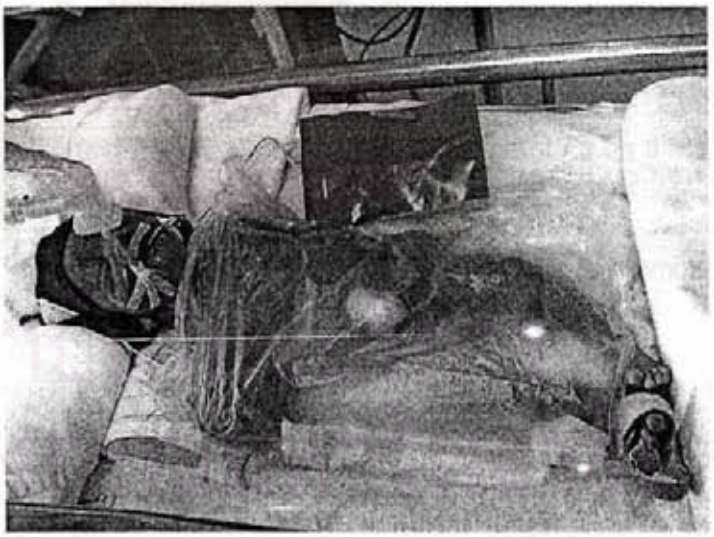
1. Pre-warming radiant warmer before delivery
2. Placing the infant under radiant warmer immediately after birth
3. Drying the infant with a warm, dry towel
4. Replacing the wet towel with another warm, dry towel to place the infant
5. All resuscitation procedures done under a pre-warmed radiant warmer

6. Swaddling the infants in a new, warm, dry towel after initial stabilization
7. Putting on a hat
8. Transferring the infant to the nursery in a pre-warmed transport incubator with incubator temperature set to 36-37 ^{0}C

The infants in wrap group received the same management, except for the drying of body. Instead of drying they received additional intervention, which included

1. Wrapping the body with a sterile, 30 x 45 cm polyethylene bag under a radiant warmer immediately after birth, leaving only the head uncovered. (Figure 7)
2. Drying the head with a warm, dry towel while the body remained in the bag without drying.
3. Assessment of the infants through the transparent plastic bag.

Figure 7 Premature infant in polyethylene plastic bag wrap



The plastic bags used in this study are commercial bags on roll used for grocery food made from low density polyethylene (LDPE).

Thermal stabilization in the nursery

Upon reaching the nursery, the infants were placed under a pre-warmed radiant warmer with a skin temperature probe placed on the infant's skin. Admission rectal temperature was recorded. All infants were cared under radiant warmers until all necessary procedures were performed (stabilization, intubation, surfactant application, umbilical catheterization, x-ray, etc.) and were placed in pre-warmed incubators thereafter. Infants in the control group were dried again and wet linen removed, leaving the whole body exposed under the warmer while the infants in wrap group were kept in polyethylene bags for at least 3 hours or until the infants were moved into pre-warmed incubators and the plastic bags were removed. During the procedure, a small area on the bag was cut to create a hole for the exposure of the body part. Hourly rectal and skin temperature measurement was recorded during the first 3 hours after admission.

Other treatment during the study period will be provided for the infants according to the standard protocols or practice guidelines used in the neonatal intensive care unit.

The warming equipment

- Delivery room radiant warmers were pre-warmed and set to manual control with maximum heat output. The target temperature on the surface of the bed is 36-37 ℃.

- The transport incubator were pre-warmed and set temperature to 36-37°C.

- The radiant warmers in the nursery were pre-heated with a roll of linen used as a phantom. They were set to manual control mode to obtain the phantom temperature of 36.5 ° C.

- The incubators were pre-set to air control mode. The set temperature range for infants weighing less than or equal to 1,000 grams was 36-37°C, and for infants weighing more than 1,000 grams was 34-35°C. Temperature control mode was switched to servo-control mode after the infants' temperature was stable to keep the infants' skin temperature in the range of 36.0-36.5 ° C.

Temperature measurements

- The infant's rectal temperature was recorded on nursery admission.
- Subsequent rectal temperature was then recorded hourly for 3 hours.
- Later temperature measurement was done per routine protocol.
- Rectal temperature was measured with a digital rectal thermometer (Welch Allyn Suretemp® 986, Welch Allyn, San Diego, USA). The thermometer was calibrated according to the manufacturer's protocol and by immersion in a water bath of known temperature to verify the instrument's accuracy. The calibration procedure was done regularly every week. The method of temperature measurement was as in the manufacturer's instruction.
- Measurement of rectal temperature was done by the responsible pediatric resident who performed measurement at every time point for the particular infant. The method of measurement was done in accordance with the manufacturer's instruction which was standardized.
- Rectal temperature was accepted as core body temperature and taken for statistical analyses. Where multiple temperatures were recorded within 1-hour interval, the lowest temperature recorded was taken priority.
- Measurement of environmental temperature was done with a digital thermometer used to monitor the temperature in both nursery and delivery room. The temperature was recorded at the same time of the infants' temperature recording by the responsible pediatric resident.

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3.7.7 Outcome measurement

Primary outcome measures:

- The proportion of infants who develop hypothermia on admission to nursery

-The proportion of infants who develop hypothermia during the 3 hours after nursery admission.

- Core (Rectal) body temperature on admission

A core body temperature of less than 36.5°C indicates the presence of hypothermia according to the guideline recommended by WHO in 1997. [20]

Secondary outcome measures:

- Changes of body temperatures during the study period
- Morbidity or adverse events during the study period. Which include
    - Hypoglycemia
    - Severe metabolic acidosis within 6 hours of life
    - Intraventricular hemorrhage as defined according to the criteria of Papile et al from head ultrasound performed before 7 days of life.[45]
    - Hyperthermia as defined by an admission temperature to NICU or within two hours of birth of greater than or equal to 38°C
    - Skin damage
    - Interference with resuscitation and other practices (e.g. umbilical catheter placement, intubation)
    - Fluid problems within 48 hours of life such as dehydration or fluid overload, electrolyte imbalance such as hypernatremia (serum sodium >150mmol/L) or hyponatremia (serum sodium <130mmol/L)
    - Death in the first 72 hours of life
    - Any other unexplained adverse outcome attributed to the intervention within 7 days of birth

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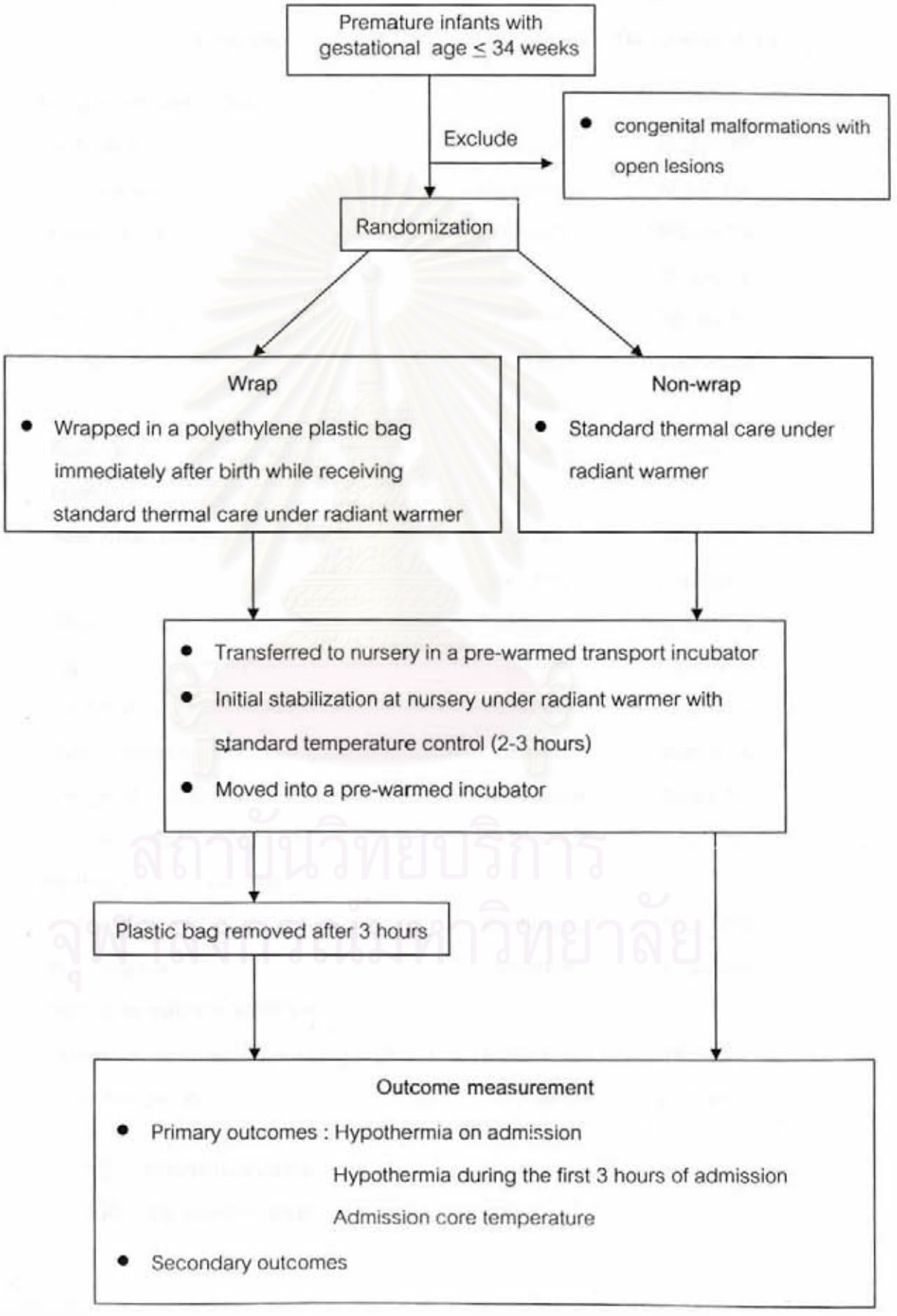
Figure 8 Research administration scheme



All of the data being measured are summarized in table 1

Table 1 : Summary of measurements

Variables	Type of data	Description of data
Baseline characteristics		
Gestational age	Continuous	Mean, SD
Birth weight	Continuous	Mean, SD
Apgar score	Discrete	Median, IQR
Sex	Binary	frequency
Maternal fever	Discrete	frequency
Mode of delivery	Discrete	frequency
Chorioamnionitis	Discrete	frequency
Prolonged premature rupture of the membranes (PPROM)	Discrete	frequency
Respiratory distress syndrome	Discrete	frequency
Sepsis	Discrete	frequency
Shock	Discrete	frequency
Type of ventilatory support	Discrete	frequency
Umbilical vessel catheterization	Discrete	frequency
Skin breakdown	Discrete	frequency
Length of time before arrival to nursery	Continuous	Mean, SD
Environmental temperature	Continuous	Mean, SD
Primary outcome variable		
Rectal temperature	Continuous	Mean, SD
Hypothermia	Discrete	frequency
Secondary outcome variables		
Temperature change during study period	Continuous	Mean, SD
Adverse events	Discrete	Frequency

SD = standard deviation

IQR = interquartile range

3.7.8 Data collection

The following data were recorded

1. Baseline characteristics :
   - Infant's demographic data : birth weight, gestational age, sex
   - Prenatal and delivery data : mode of delivery, Apgar score, maternal infection and treatment, maternal fever
   - Duration of delivery room stabilization,
   - Length of time before arrival to nursery
   - Infant's initial diagnosis and concurrent illness
   - Environmental temperatures: temperature of delivery room, transport incubator and nursery
2. Outcomes :

   Primary outcome data:
   - The occurrence of hypothermia during the 3 hours of study
   - Admission core temperature

   Secondary outcome data :
   - Changes in body temperature during 3 hours period of stabilization in nursery
   - Adverse events during the study period eg: hyperthermia, metabolic acidosis, electrolyte imbalance, skin breakdown, death

3.7.9 Data analysis

- All data were analyzed by statistical program (SPSS version 11.5). The statistical analysis was focused on the detection of significant differences between two groups with respect to occurrence of hypothermia and admission core body temperature.

- The data were analyzed on an intention-to-treat (ITT) basis. This analysis included all randomized patients who started treatment and who lost to follow up. Tests

of hypotheses were conducted at the two-sided, 0.05 level of significance and confidence intervals of 95%.

Baseline characteristics

All baseline characteristics were presented and analyzed with descriptive statistics. Continuous variables were expressed as mean and standard deviation. The data included birth weight, gestational age, duration of delivery room stabilization, length of time before arrival to nursery, delivery room temperature, nursery temperature, transport incubator temperature.

Categorical and nominal variables were expressed as percentage (sex, proportion of subjects with specific diagnosis, i.e. infection, respiratory distress syndrome.

Ordinal variables were expressed as median and inter-quartile range (Apgar score).

Outcome analysis

Primary outcome:

The proportion of infants with hypothermia on admission and during the first 3 hours of life was presented as percentage. Comparison between the two groups was done with chi-square test, odds ratio and 95% confidence interval.

Admission core body temperature is continuous variable. The data was compared by unpaired student t test.

Subsequent analysis with logistic regression model was performed to determine effects of potentially important baseline variables

Secondary outcomes:

Comparison of serial body temperature during stabilization period between 2 groups were performed by Analysis of Variance with Repeated Measures.

Adverse events or morbidity variables which are categorical data. The variables include hypoglycemia, metabolic acidosis, electrolyte imbalance, death, interference with procedural technique, hyperthermia, and skin breakdown. Comparison of these proportions were done with chi square or Fisher exact test where appropriate.

All of the data being analyzed are summarized in table 2

Table 2 : Summary of statistical analysis

Dependent variables	Type of data	Statistics
Primary outcome variable		
Hypothermia on admission	Categorical	Chi-square test, Odds ratio and 95%CI
Hypothermia during 3 hours study period	Categorical	Chi-square test, Odds ratio and 95%CI
Rectal temperature on admission	Continuous	Unpaired student t test
Secondary outcome variables		
Serial rectal temperature during study period	Continuous	ANOVA with repeated measures if appropriate
Adverse events	Categorical	Chi-square or Fisher's exact test

3.7.10 Ethical consideration

The researchers submitted the documents required by the regulations according to Ethics Committee and obtained their opinion in writing. This study protocol had already approved by the Ethics Committee of the Faculty of Medicine, Chulalongkorn University. Patients could not be included until the approval of the Ethics Committee had been received. Informed consent was obtained from the parents in all cases.

The trial was conducted in accordance with ICH guidelines for Good Clinical Practice. Parents of all eligible infants received detail of the study protocol and the researcher explained the protocol thoroughly. All parents gave written informed consent before enrollment or soon after enrollment in case of emergency. The patient's right to confidentiality was maintained during data collection and processing.

The study was conducted in the Division of Neonatology, King Chulalongkorn Memorial Hospital under the supervision of the attending neonatologist.

The study protocol did not pose any increased risk for infants in control group because thermal stabilization provided for all infants was the standard routine thermal care.

Regarding the safety of the intervention, based on the results of previous studies, the use of polyethylene plastic bags in premature infants was well tolerated and no serious adverse effects were observed. (36, 37, 39, 40, 41, 42, 43) Had any infants had any adverse events attributable to the intervention, they would be treated without delay and be automatically taken out of the study.

The duration of warming under radiant warmers depended on the necessity to resuscitate the baby, and the time required for the procedures. All infants were transferred into pre-warmed incubators as soon as all procedures were finished. This is the usual routine practice for critically ill premature infants.

3.7.11 Limitation

A major limitation of this study was failure to enroll the infants in delivery room due to emergency deliveries when the pediatric team was notified and arrived the delivery room late after the infant was born. Another limitation was violation of protocol, especially in treatment group.

3.7.12 Implication

If the study results show the benefit of wrapping the small premature infant with polyethylene plastic bag to prevent hypothermia, we would recommend the use of this intervention to decrease heat loss without compromising accessibility of the infant during resuscitation and stabilization period, when the infants are most susceptible to develop hypothermia, thus improving the outcome of this high risk population.

CHAPTER IV

RESULTS

4.1 Baseline characteristics of patients

There were 140 infants screened just prior to delivery. 130 infants were enrolled in the study, 65 were randomly allocated into wrap group and 65 into control group. Figure 9 summarizes the flow of participants through the screening stage, enrollment, and completion of the study protocol.

A total of 122 infants completed the study. 6 infants (4.6%) were withdrawn from the study due to incorrect gestational age assessment at randomization. Gestational age assessment with Ballard score at nursery admission was done on these infants and showed gestational age beyond 34 weeks. Two infants had incomplete or lost temperature record, 1 from wrap group and 1 from control group. One infant who was randomly assigned to the wrap group was unwrapped during the study in error but analyzed according to the intended treatment.

Table 3 shows the baseline characteristics of the infants and their mothers. Infants in both groups were comparable in all demographic data and other initial characteristics. The mean gestational age of the infants was 30.8 weeks in both groups. The numbers of infants in each gestational age stratum in both groups were well matched. Mean birth weight was 1,569.4 and 1,419.5 g in wrap and control group respectively. The distribution of sex and proportion of small for gestational age babies were not different between the two groups. At study entry, there were no statistically significant differences between the two groups regarding route of delivery, maternal history of prolonged premature rupture of membranes, chorioamnionitis, fever and antibiotic treatment.

The infants' initial conditions and their treatment during the study period are summarized in Table 4. Also the two groups were comparable in terms of Apgar score at 1 and 5 minutes after birth, initial illnesses and treatment, including respiratory support and umbilical vessel catheterization.

Table 5 shows environmental factors affecting temperature control during immediate postnatal period. Environmental temperature was recorded in delivery room,

transport incubator, and in the nursery. All temperature records were comparable between the two groups except nursery temperature (26.1±1.2 in wrap group versus 26.8 ±1.8 C in control group, p=0.021). However the temperature difference was not considered clinical significance and the nursery temperature in both groups was within standard temperature range. Time factors included duration before admission to nursery and time under radiant warmer which were not statistically different between the two groups. The average time before nursery admission was 20 and 19 minutes in wrap and control group respectively.

Figure 9. Flow of participants through screening stage, enrollment, and completion of the study protocol

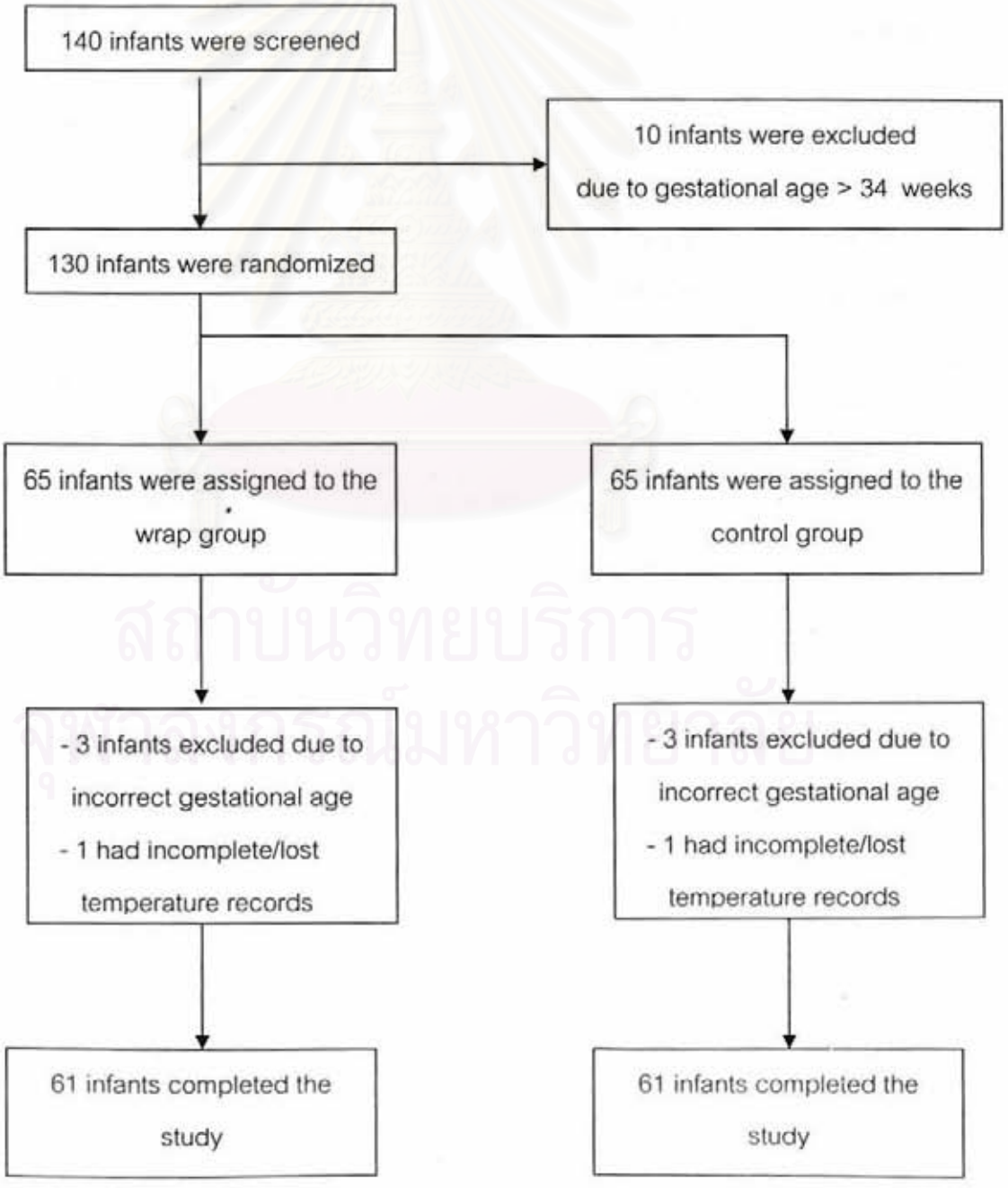


Table 3 : Baseline characteristics of infants and their mothers

	Wrap group (N=61)	Control group (N=61)
Infants		
Gestational age (weeks), mean ± SD	30.8± 2.7	30.8± 2.6
Gestational age < 31 weeks, n (%)	22(36.1)	21(34.4)
Gestational age 31-34 weeks, n (%)	39(63.9)	40(65.6)
Birth weight (g), mean ± SD	1569.4± 518.8	1419.5± 440.1
Small for gestational age (SGA), n (%)	5(8.2)	6(9.8)
Female sex, n (%)	31(50.8)	31(50.8)
Multiple birth, n (%)	14(23.0)	16(26.2)
Mothers		
Route of delivery, n (%)		
Vaginal	21(34.4)	17(27.9)
Cesarean	40(65.6)	44(72.1)
PPROM*, n (%)	20(32.8)	18 (29.5)
Chorioamnionitis, n (%)	12(20.7)	9(15.3)
Antibiotic treatment, n (%)	33(54.1)	36(60.0)
Maternal fever, n (%)	3(4.9)	2(3.3)

* Prolonged Premature Rupture of Membranes

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Table 4 : Infants' initial condition and treatment during study period

	Wrap group (N=61)	Control group (N=61)
1-minute Apgar score, median (IQR)	8 (6,8)	7 (5,8)
5- minute Apgar score, median (IQR)	9 (8,10)	9 (7,9)
Resuscitation at birth, n (%)		
Bag and mask ventilation	9 (15.0)	8 (13.6)
Intubation	8 (13.3)	10 (16.9)
Chest compression	1 (1.7)	0 (0)
RDS, n (%)	26 (42.6)	24 (40.0)
Presumed sepsis, n (%)	22 (36.1)	18 (30.5)
Shock, n (%)	1 (1.6)	3 (4.9)
Inotrope, n (%)	1 (1.6)	2 (3.3)
Initial ventilatory support, n (%)		
None	29 (47.5)	29 (47.5)
CPAP	18 (29.5)	20 (32.8)
Mechanical ventilation	14 (22.9)	12 (19.7)
Umbilical vein catheter, n (%)	17 (27.9)	17 (27.9)
Umbilical artery catheter, n (%)	23 (37.7)	23 (37.7)
Bruise/skin breakdown, n (%)	6 (9.8)	3 (4.9)

RDS = Respiratory distress syndrome

CPAP = Continuous Positive Airway Pressure

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Table 5 : Environmental factors during immediate postnatal period

	Wrap group (N=61)	Control group (N=61)
Time to admission (minute)	20.3 ± 9.5	18.9 ± 10.5
Time under radiant warmer (minute)	311.2 ± 124.8	309.5 ±217.7
Delivery room temperature (°C)	28.9 ± 3.8	28.8 ± 4.0
Transport incubator temperature (°C)	36.6 ± 0.3	36.5 ± 0.5
Nursery temperature (°C)	26.1 ± 1.2	26.9 ± 1.8*

Values are expressed as mean ± SD (standard deviation)

* p= 0.021

4.2 Primary outcome analysis

Occurrence of hypothermia and admission body temperature

Primary outcomes are shown in Table 6. Compared with the infants in the control group, the infants in wrap group were less likely to be hypothermic on admission (26.2 % vs 50 %, p= 0.007) and had significantly higher mean admission rectal temperature (36.7 °C vs 36.3 °C, p= 0.002,). Mean difference in admission temperature between the two groups was 0.35 °C, (with 95% confidence interval [0.13, 0.57]. The incidence of hypothermia within the first 3 hours of life was also significantly lower among wrapped infants as compared with controls (44.3 % vs 70.5%, p=0.003,chi-square test, table6).

In univariate analysis, the odds ratio of hypothermia on admission among the infants in the control group was 2.81, 95% CI [1.13, 6.0]. The odds ratio of hypothermia within the first 3 hours of life among the infants in control group was 3.00 , 95% CI [1.42, 6.34].

Table 6 : Assessment of temperature outcomes

	Wrap group (N=61)	Control group (N=61)	p-value
Hypothermia on admission, n (%)	16 (26.2)	30 (50.0)	0.007
Hypothermia within 3 hour period, n (%)	27 (44.3)	43 (70.5)	0.003
Admission temperature (°C),mean ± SD	36.70 ± 0.54	36.36 ± 0.66	0.002

We used logistic regression model to see effects of potentially important baseline variables on hypothermia. After adjustment for birth weight, small for gestational age, umbilical catheter placement, and low Apgar score (1- minute Apgar score < 4), the effect of body wrapping on the occurrence of hypothermia still remained significant. (p=0.015). The adjusted odds ratio of hypothermia on admission among the infants in control group was 2.69, 95% CI [1.22, 5.97]. The adjusted odds ratio of hypothermia during the first 3 hours of life among the infants in control group was 2.62, 95% CI [1.19, 5.75].

Of the covariables included in logistic regression analysis, birth weight influenced the occurrence of hypothermia on admission in univariate analysis but when taken into multiple logistic regression, the influence of birth weight was not significant (P= 0.256). Admission rectal temperature of each infant was plotted against birth weight for the two groups as shown in Figure 10

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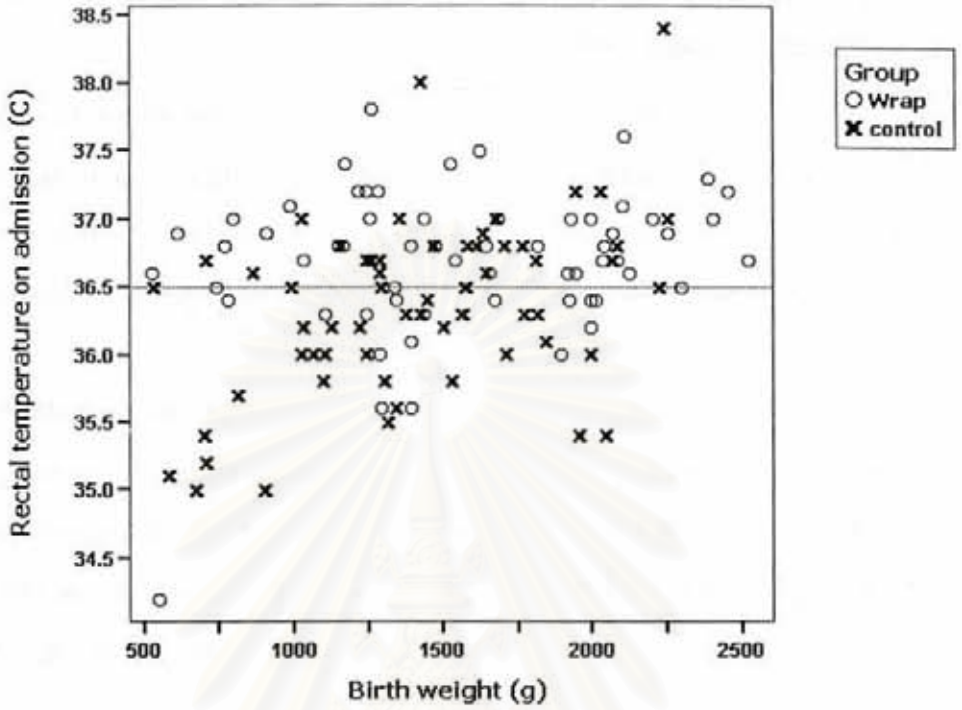
Figure 10: Admission temperature and birth weight of infants in wrap and control group



Subgroup analysis by gestational age strata

We also did subgroup analysis of primary outcomes with 2 subgroups as defined by gestational age strata we used with stratified randomization (gestational age < 31 weeks and 31-34 weeks). The results are shown in Table 7. In the subgroup of gestational age less than 31 weeks, there were statistically significant differences in temperature outcomes between the wrap and control group. The differences included the incidence of hypothermia on admission (18.2 % vs 61.9%, p=0.003), the incidence of hypothermia during 3 hours after birth (36.4 % vs 90.5%, p<0.001), and admission rectal temperature (36.75 $\pm$ 0.69 °C vs 36.14 $\pm$ 0.73 °C, p= 0.007). The mean difference in admission temperature between the two groups was 0.62 °C, with 95% confidence interval [0.18, 1.05]. The odds ratio of hypothermia on admission among the infants in the control group was 2.94, 95% CI [1.20, 7.19]. The odds ratio of hypothermia during the first 3 hours of life among the infants in control group was 2.95, 95% CI [1.60, 5.44].

While the differences were demonstrated in the more premature subgroup, comparison in the older subgroup of gestational age 31-34 weeks did not show statistically significant differences in any of the outcomes.

Table 7 : Assessment of temperature outcomes in 2 gestational age groups

	Wrap group	Control group	p-value
GA < 31 weeks (n)	22	21	
Hypothermia on admission, n (%)	4 (18.2)	13 (61.9)	0.003
Hypothermia during 3 hour period, n (%)	8 (36.4)	19 (90.5)	<0.001
Admission temperature (°C),mean ± SD	36.75 ± 0.69	36.14 ± 0.73	0.007
GA 31-34 weeks (n)	39	40	
Hypothermia on admission, n (%)	12 (30.8)	17 (43.6)	0.241
Hypothermia during 3 hour period, n (%)	19 (48.7)	24 (60.0)	0.314
Admission temperature (°C),mean ± SD	36.68 ± 0.45	36.47 ± 0.59	0.09

GA = gestational age

4.3 Secondary outcome analyses

Changes of body temperature during study period

The analysis of serial temperature measurement during the first 3 hours of nursery admission showed statistically significant difference between two groups in terms of rectal temperature at baseline (p=0.002), and at 1 hour (p=0.032). There was no statistically significant difference in body temperature taken at 2 and 3 hours after admission (p=0.151 and 0.341) as shown in Table 8 and Figure 11.

Subgroup analysis of temperature also demonstrated significant differences in rectal temperature at every time point in the subgroup of gestational age < 34 weeks (Table 9). The infants in wrap group had higher rectal temperature throughout the study period.

Table 8 : Changes in rectal temperature during study period

Rectal temperature (°C)	Wrap group (N=61)	Control group (N=61)	p-value
on admission	36.70 ± 0.54	36.36 ± 0.66	0.002
1 hour	36.61 ± 0.46	36.43 ± 0.46	0.032
2 hour	36.66 ± 0.35	36.54 ± 0.52	0.151
3 hour	36.73 ± 039	36.67 ± 0.31	0.341

Values are expressed as mean ± SD

Figure 11 : Rectal temperature at different time points after nursery admission

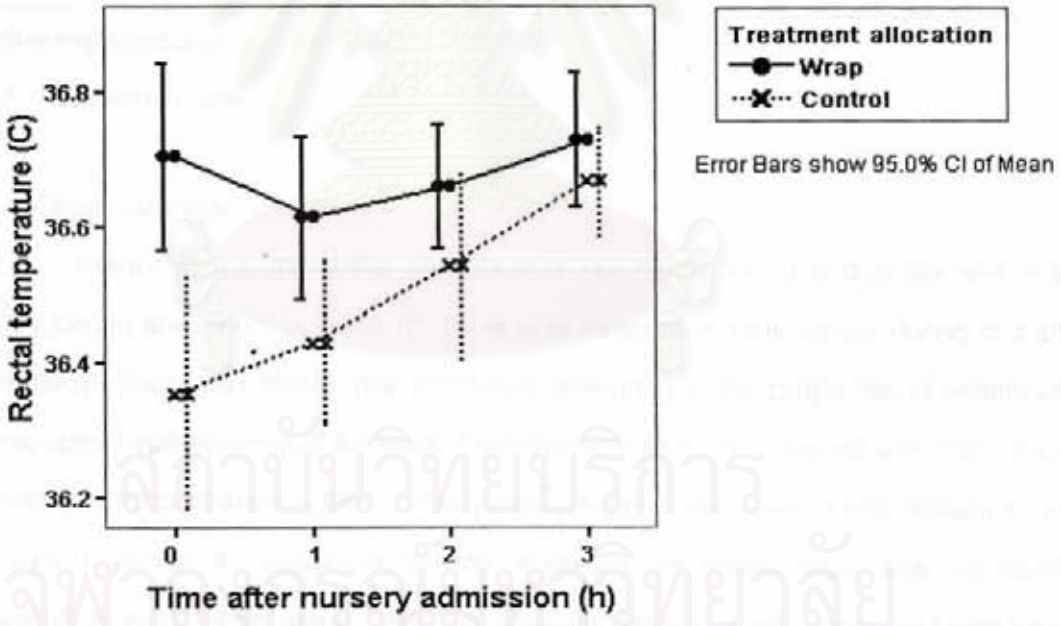


Table 9 : Changes in rectal temperature during study period in 2 gestational age subgroups

GA< 31 weeks subgroup	Wrap group (n=22)	Control group (n=21)	p-value
Rectal temperature on admission	36.75 ± 0.69	36.14 ± 0.73	0.007
Rectal temperature at 1 h	36.60 ± 0.58	36.20 ± 0.60	0.032
Rectal temperature at 2 h	36.66 ± 0.32	36.27 ± 0.68	0.020
Rectal temperature at 3 h	36.71 ± 0.25	36.50 ± 0.35	0.032
GA31-34 weeks subgroup	**Wrap group (n=39)**	**Control group (n=40)**	**p-value**
Rectal temperature on admission	36.68 ± 0.45	36.47 ± 0.59	0.09
Rectal temperature at 1 h	36.62 ± 0.40	36.55 ± 0.31	0.41
Rectal temperature at 2 h	36.65 ± 0.38	36.69 ± 0.32	0.66
Rectal temperature at 3 h	36.73 ± 0.45	36.75 ± 0.24	0.82

Value expressed as °C, mean ± SD

GA = gestational age

Other secondary outcomes

Infant's status, morbidity, and adverse outcomes during and at the end of the study period are shown in Table 10. There was no death in either group during and after the study. There was statistically significant difference in the proportion of infants who developed hypoglycemia in the control group compared with the wrap group (p=0.037). There was no difference in terms of respiratory support and oxygen requirement in both groups. However, the oxygen concentration used in the control group was significantly lower than in the wrap group, although absolute difference was small and considered not to be of clinical significance. (FiO_2 difference = 0.04, p=0.041). There was no statistically significant difference in terms of hyperthermia, metabolic acidosis, intraventricular hemorrhage and serum electrolytes.

Regarding potential hazards of using polyethylene plastic bag to wrap the infants, we did not find any significant higher rate of adverse effects such as hyperthermia and skin damage. All three infants who had hyperthermia (1 in the wrap

group and 2 in the control group) had history of maternal fever prior to delivery. All infants in the wrap group tolerated the intervention well. The use of polyethylene plastic bag was well accepted by pediatric residents and nurses. The wrap procedure did not interfere with resuscitation in delivery room.

Table 10 : Assessment of secondary outcomes

	Wrap group (N=61)	Control group (N=61)	p-value
Morbidity and treatment			
Hyperthermia, n (%)	1(1.6)	2(3.3)	0.549
Hypoglycemia, n (%)	3(4.9)	10(16.7)	0.037
Metabolic acidosis, n (%)	8(25.0)	12(34.3)	0.407
Skin breakdown, n (%)	2(3.3)	2(3.3)	0.987
Respiratory support, n (%)	36(59.0)	36(59.0)	0.99
O_2 requirement, n (%)	26(42.6)	25(41.0)	0.854
FiO_2 , mean ± SD	0.30± 0.16	0.26± 0.09	0.041
Intraventricular hemorrhage, n (%)	4(12.1)	5(14.3)	0.793
Blood chemistry, mean ± SD			
Serum sodium (meq/l)	142.10± 6.21	143.13± 6.70	0.558
Serum potassium (meq/l)	5.08± 1.04	5.42± 1.37	0.32
Serum HCO_3 (meq/l)	18.7± 4.45	19.41± 3.61	0.575
Blood pH at 0-2 hour	7.299± 0.081	7.289± 0.075	0.064
Blood pH at 2-6 hour	7.317± 0.075	7.322± 0.073	0.302
Base deficit at 0-2 hour (meq/l)	4.03± 4.97	4.77± 3.97	0.319

CHAPTER V

DISCUSSION

Hypothermia is a common problem of premature infants during immediate postnatal period. Current standard recommendation for neonatal care is not always effective in maintaining normal body temperature of small premature infants. Many infants still get hypothermic (core temperature <36.5 °C) on admission to nursery. Moreover, the need to resuscitation and performing treatment procedure lead to inadequate thermal care for these infants. We therefore need an effective intervention to prevent hypothermia during the most vulnerable period. The intervention should prevent heat loss and allow heat from warmer or incubator to reach the infants. At the same time it should not interfere with resuscitation or treatment procedures.

Placing premature infants in plastic bag to prevent heat loss is one of the intervention studied in recent years. This approach has increasingly gained interest from clinicians and nurses. The efficacy of such approach has been assessed in several studies. Several recent reports suggest that clinicians have begun to use this method of thermal protection in very preterm and very low birth weight infants [36, 37, 38, 39, 40, 41, 42, 43]. However, at the time of our literature review there were only 3 studies which were randomized controlled trials [40, 42, 43]. All the studies demonstrated the efficacy of using plastic bag to wrap premature infants for the prevention of heat loss. However, there was variation of plastic material used in these trials. Polyurethane and polyethylene plastics are 2 common materials used in many purposes. Low density polyethylene (LDPE) is used in household and groceries in the form of plastic bags on rolls. It is cheaper and more available in Thailand than polyurethane bags (Zip lock bags). The plastic bags used in this study are commercial bags on roll used for grocery food made from low density polyethylene (LDPE). LPDE is the first grade of polyethylene. The density of LDPE is 0.92 g/cm^3. it is translucent and has excellent flexibility. LPDE bag is soft and very pliable. Its most common use is in plastic bags The bag was prepared and sterilized by ethylene oxide before use [46].

Furthermore, polyethylene bags are softer and more pliable. It may cause less irritation to immature skin. We therefore are interested in the use of polyethylene plastic bags to keep premature infants warm, if it showed statistically and clinically proven efficacy. Among the 3 randomized controlled trials that were reviewed, only one study in which polyethylene plastic bags were used had good research methodology [43]. However, The sample size of that study was small (27 and 26 infant in study and control group). Besides, the primary outcome in that study was rectal temperature on admission. There was no information about the incidence of hypothermia during the first few hours of life, during which premature infants are at risk of developing hypothermia. To confirm the promising result and to determine the effects of plastic wraps on temperature outcomes during stabilization period, more studies are needed before we adopt this intervention as our standard care protocol. As such, we conducted a randomized controlled trial to evaluate the efficacy of occlusive wrapping with polyethylene bag applied immediately after birth for the prevention of hypothermia in premature infants of 34 weeks gestation or less.

Due to the obvious different intervention in the study and the control group, the study cannot be blinded. However, we tried to eliminate as many confounders as possible. We stratified the infants according to gestational age at randomization to ensure that each group had comparable gestational age distribution. The treatment allocation was concealed in opaque envelopes that were open just prior to delivery so that the person who took care of the infant did not know the allocation in advance. The protocols of each step in the study were printed and distributed to all personnel involved. Instruction was put at the bedside and verbal communication was made to all staffs to make sure they followed the instruction in the protocol. Primary outcome measurement was done with a standardized digital thermometer in stead of mercury thermometer to eliminate inter-observer variation in temperature reading. The primary outcomes are expressed in terms of the occurrence of hypothermia and absolute admission temperature to determine the relevance of temperature stabilization in both qualitative and quantitative terms.

The study results showed that baseline characteristics of the infants in both groups were comparable regarding demographic variables, initial illnesses and level of

treatment. Although mean birth weight of the infants in the control group was lower than that of the wrap group, this is not statistically significant. We demonstrated in logistic regression analysis later that birth weight in this study did not have significant influence on temperature outcome. Regarding the environmental factors that may affect the outcome, the baseline settings were well matched in terms of delivery room temperature and transport incubator temperature. This is because all temperature setting protocols were standardized and this study was done in a single center. The only baseline data that showed statistically significant difference was nursery temperature (26.1°C in wrap group and 26.9 °C in the control group). However, the temperature range in both groups was within standard recommendation for the newborn nursery. Although nursery temperature in the wrap group was lower than that in the control group, the temperature outcome still favored the treatment with plastic bags. Considering the efforts to control potential confounding environmental factors and given the comparable numbers at the time of study, we therefore decided not to include these environmental temperature variables in multivariate analysis.

In the present study, we demonstrated that the use of polyethylene plastic bag to wrap premature infants provided better thermal protection in the delivery room than conventional drying. Wrapped infants were less likely to develop hypothermia during the first 3 hours after birth and they also had higher admission body temperature compared with control infants. In this study, wrapping increased the mean rectal temperature on admission to the nursery by 0.35 °C. [95% CI, 0.13, 0.57] Significant temperature difference was also seen at 1 hour after admission. Moreover, the infants in wrap group maintained their normal core body temperature after admission and throughout the 3 hours study period. The protective effect remained significant after important potential confounding factors were adjusted (birth weight, small for gestational age, umbilical catheter placement, low Apgar score). The adjusted odds ratio of hypothermia during the study period for infants in the control group was 2.58, with 95% CI [1.15, 5.77]. Multiple logistic regression analysis did not demonstrate significant influence of any covariables on temperature outcome on admission.

With subgroup analysis according to gestational age strata, we found that the efficacy of the plastic bag wrap was significant in the subgroup of more premature

infants (gestational age less than 31 weeks). The statistical differences were seen in favor of treatment in terms of admission temperature, incidence of hypothermia on admission and during 3 hours after admission. Placing small premature infants in plastic bags caused a difference in mean admission temperature of infants younger than 31 weeks gestation of 0.62 °C, 95% confidence interval [0.18, 1.05]. The temperature was also maintained higher at all 3 subsequent measurements. On the other hand, the effects were not statistically significant in infants 31-34 weeks' gestation. Older infants might be more able to maintain their rectal temperature with just conventional drying. Our finding was consistent with the result of Vohra's study [40]. In that study, the effectiveness of plastic bag wrap was seen in infants younger than 28 weeks' gestation but not in older infants.

Interestingly, we found that hypothermia still occurred during the next few hours after admission even though the admission temperature was mormal. The incidence of hypothermia within 3 hours was higher than the incidence of hypothermia on admission (44.3 %and 26.2 % in the wrap group and 70.5 % and 50 % in the control group. This may be due to the need resuscitation and procedure that made the interruption of the warming process and accelerated heat loss from the body.

We opted to use an intention-to-treat analysis to test the hypothesis. There was one infant in wrap group with protocol violation and the infant became hypothermic after unwrapped. This infant was still included in the wrap group for analysis. The result favoring wrapping reflects the robustness of the treatment effect.

For secondary outcome analysis, we did not find any statistically significant difference in other outcome except for the occurrence of hypoglycemia and oxygen concentration. Since we aimed to determine temperature status as the primary outcome, the study was not designed to have enough power to detect other different outcome. Even so, we demonstrated the decreased risk of hypoglycemia in wrapped infants. Infants in control group had higher risk of hypoglycemia during the first 3 hours of life. Since hypoglycemia is closely associated with hypothermia or "cold stress", our finding supports the advantage of wrapping premature infants with plastic bags in delivery room. Beside the temperature stabilizing effect, this intervention also helped prevent morbidity/complication associated with hypothermia.

Regarding the oxygen concentration at the end of the study, Infants in the wrap group received higher FiO_2 than infants in the control group (0.30 vs 0.26, p=0.041). Although the difference reached statistical significance, the magnitude is small and not to be of clinical significance. It also may be interpreted that the infant in the wrap group were sicker and required more support during the first few hours of life. Even so, they maintained normal body temperature better than the control infants.

For the concern of skin damage, we did not find significant difference in the incidence of skin damage after treatment between the 2 groups. All skin damages found in this study were minor bruises. There was no blister or major skin breakdown found in our study.

We followed the infants after completion of study for only 72 hours. The follow up duration is too short to see other intermediate and long term morbidity. Regarding immediate and long term outcomes, more studies with appropriate follow up are needed to determine the effects of plastic wraps.

Considering the safety of treatment, the risk of adverse effects such as overheating and damage to infant's skin also was our concern. The incidence of adverse events in the current study was low and these were no statistically significant differences in the occurrence of adverse events between two groups. Regarding the risk of hyperthermia, we did not find any case of hyperthermia after nursery admission. All infant with hyperthermia had high body temperature at the time of admission due to maternal fever. Subsequent temperature record showed temperature decreased below 37.8 °C in all cases with initial hyperthermia. All infants seemed to tolerate the occlusive plastic wrap well.

With the appropriate sample size of this study, the result of the study has confirmed that occlusive skin wrapping with polyethylene plastic bags applied immediately after birth is efficacious in the prevention of postnatal hypothermia in premature infants of 34 weeks gestation or less. Compared with other studies [40,42,43], the study results are consistent with the results of previous studies regarding the beneficial effect of plastic wrap on thermal stability and the decreased risk of hypothermia at the time of nursery admission. Moreover, we further demonstrated that placing premature infants in plastic bags helps prevent hypothermia during the

subsequent 3 hours after admission [OR = 0.387 , 95% CI [0.173, 0.865]. Unlike the studies of Knobel [42] and Vohra [43], the effects of temperature stability was sustained beyond 1 hour in our study. Thus, our study added new significant finding to the existing evidence.

On subsequent logistic regression analysis, we did not find significant influence of the following cofactors: birth weight, small for gestational age, umbilical catheter placement, low Apgar score. Birth weight was a significant cofactor in univariate analysis but when taken into logistic regression the influence was not statistical significant. This was different from the found that birth weight is an important determinant of the incidence of hypothermia on admission. This finding was different from that in Vohra's study [43] that the smallest infants are most in need of special thermal protection at birth. The difference in this regard may be due to inadequate sample size for logistic regression. Also birth weight of the infants in our study varies within a wide range (535-2525 g). The effects of birth weight may not be obvious.

Since the literature review was done 3 years ago, recently we also performed the literature search again to see if there were more publications on the use of plastic bags to prevent hypothermia in premature infants, using the same search strategy. There are 2 more studies added to PubMed database [47, 48]. The plastic material used in the 2 studies was polyethylene film for use in food packaging (Cling Wrap). However, the wrap was done after nursery admission, not in delivery room. The primary outcome of both studies was skin temperature. The use of skin temperature however, may be not as accurate as rectal temperature because it does not represent core temperature. As in our study, we also measured skin temperature but we did not use skin temperature for analysis because there were frequent discrepancies between the 2 measurement methods. The results of both studies also showed the beneficial effects of plastic wrap. In Duman's study [47], the study subjects included infants weighing <1500 g randomized to either wrap or control group. The study result showed that infants in the wrap group reached a normal axillary temperature faster then non-wrap infants and required lower incubator temperatures. The infants' temperature on admission was very low in both treatment and control groups since the wrap was not applied immediately

after birth. This approach therefore cannot prevent hypothermia in delivery room, which can occur very rapidly.

In another study by Kaushal et al [48], premature infants with birth weight between 750 and 1500 g were randomized into wrap or no wrap group. The plastic film was placed over the bassinette instead of wrapping around the body. The primary outcomes were the incidence of hypothermia (axillary temperature < or = 36 degrees C) during the first 7 days and cumulative weight loss at 48 hours of age. The results showed that the babies in the wrap group maintained normal axillary temperature during in the first 7 days but 36% in the no wrap group ($p = 0.001$) developed hypothermia. Babies in the wrap group who took less time to reach normal temperature and had less weight loss in the first 48 ($p = 0.06$). Although both studies demonstrated the protective effects of plastic wrap, a significant portion of infants in the wrap group still developed hypothermia on admission. The ideal approach for thermoregulation should be how to prevent hypothermia as early as possible and help the infants maintain their normal temperature throughout the first few hours of life during which hypothermia can easily developed. As such, the application of plastic bag should be started as soon as possible, that is, immediately after birth.

Given the proven efficacy of the plastic bags in thermal protection for premature infants and the simplicity and convenience of this approach, we are convinced that the use of polyethylene plastic bags to wrap the infants immediately after birth is a practical and effective method in preventing hypothermia and its associated complication. Further clinical study on cost effectiveness and cost benefit of using such technique should be done to address the economical standpoints.

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CHAPTER VI

CONCLUSION

The use of polyethylene plastic bag to wrap premature infants of 34 weeks' gestation or less immediately after birth resulted in a lower rate of hypothermia and significantly higher admission body temperature when compared with current standard thermal care. The advantage was observed to be sustained for one hour after admission to nursery. Infants who were wrapped also had lower risk of hypoglycemia. There was no statistically significant difference in the occurrence of other adverse events. The statistically significant benefit was found among the infants of less than 31 weeks gestation. Occlusive skin wrapping with polyethylene plastic bag applied immediately after birth is efficacious in the prevention of postnatal hypothermia in premature infants of 34 weeks' gestation or less. Its use therefore should be recommended during stabilization of premature infants in delivery room and nursery to improve the outcome of this high risk population, especially in infants of less than 31 weeks gestation.

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APPENDICES

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APPENDIX A

ใบยินยอมเข้าร่วมการวิจัย

ชื่อโครงการวิจัย : การศึกษาประสิทธิผลของการใช้ถุงพลาสติกห่อตัวทารกเพื่อป้องกันภาวะอุณหภูมิกายต่ำในทารกคลอดก่อนกำหนด

ก่อนที่จะลงนามในใบยินยอมให้บุตรของข้าพเจ้าเข้าร่วมในการวิจัยนี้ ข้าพเจ้าได้รับการอธิบายถึงวัตถุประสงค์ของการวิจัย วิธีการวิจัย อันตราย หรืออาการที่อาจเกิดขึ้นจากการวิจัย รวมทั้งประโยชน์ที่จะเกิดจากการวิจัยอย่างละเอียด และมีความเข้าใจดีแล้ว

ผู้วิจัยรับรองว่าจะตอบคำถามต่างๆ ที่ข้าพเจ้าสงสัยด้วยความเต็มใจไม่ปิดบังซ่อนเร้นจนข้าพเจ้าพอใจ

การให้คำยินยอมให้บุตรของข้าพเจ้าเข้าร่วมการศึกษานี้ เป็นไปโดยสมัครใจ ข้าพเจ้ามีสิทธิที่จะบอกเลิกการเข้าร่วมในการวิจัยนี้ของบุตรข้าพเจ้าเมื่อใดก็ได้ และการบอกเลิกการเข้าร่วมในการวิจัยนี้จะไม่กระทบต่อการดูแลรักษาที่บุตร ของข้าพเจ้าพึงจะได้รับจากแพทย์

ผู้วิจัยรับรองว่าจะเก็บข้อมูลเฉพาะเกี่ยวกับบุตรของข้าพเจ้าเป็นความลับ และจะเปิดเผยได้เฉพาะในรูปที่เป็นสรุปผลการวิจัย การเปิดเผยข้อมูลเกี่ยวกับบุตรของข้าพเจ้าต่อหน่วยงานต่างๆที่เกี่ยวข้องกระทำได้เฉพาะกรณีจำเป็น ด้วยเหตุผลทางวิชาการเท่านั้น

ผู้วิจัยรับรองว่าหากเกิดอันตรายใดๆแก่บุตรข้าพเจ้า จากการวิจัยดังกล่าว บุตรของข้าพเจ้าจะได้รับการรักษาพยาบาลโดยไม่คิดมูลค่า

ข้าพเจ้าได้อ่านข้อความข้างต้นแล้ว มีความเข้าใจดีทุกประการ และได้ลงนามในใบยินยอมนี้ด้วยความเต็มใจ

ลงนาม .....

(.....)

ผู้ปกครอง/ผู้อุปการะโดยชอบด้วยกฎหมาย

วันให้คำยินยอม วันที่.....เดือน.....พ.ศ.....

ลงนาม..... พยาน

(.....)

ลงนาม..... ผู้ทำวิจัย

(น.พ.สันติ ปุณณะหิตานนท์)

สถาบันวิทยบริการ
จุฬาลงกรณ์มหาวิทยาลัย

APPENDIX B

ข้อมูลสำหรับผู้ป่วยและบิดามารดาผู้ป่วย

การศึกษาทางคลินิก การวิจัยเรื่อง การศึกษาประสิทธิผลของการใช้ถุงพลาสติกห่อตัวทารกเพื่อป้องกันภาวะอุณหภูมิกายต่ำในทารกคลอดก่อนกำหนด

เรียน ท่านบิดามารดา

เนื่องจากบุตรของท่านซึ่งเป็นทารกคลอดก่อนกำหนด มีความจำเป็นต้องได้รับการรักษาในหน่วยทารกแรกเกิด โรงพยาบาลจุฬาลงกรณ์ ซึ่งเป็นสถาบันทางการแพทย์ที่ให้การรักษาพยาบาลทารกแรกเกิด และเป็นสถาบันฝึกอบรมแพทย์ที่มีการเรียนการสอนตลอดจนการวิจัยทางการแพทย์ ขณะนี้หน่วยทารกแรกเกิด กำลังพัฒนาคุณภาพการบริการให้ดียิ่งขึ้น โดยมีความพยายามรักษาและป้องกันการเจ็บป่วยที่เกิดขึ้นย่อยในทารกคลอดก่อนกำหนดมีโอกาสเกิดภาวะอุณหภูมิกายต่ำได้ง่ายและบ่อย โดยเฉพาะทารกน้ำหนักตัวน้อย ถึงแม้ว่าทารกเหล่านี้จะได้รับการดูแลตามมาตรฐานแล้วก็ตาม เนื่องจากข้อจำกัดที่ตัวทารกเอง ทำให้มีการสูญเสียความร้อนจากร่างกายอย่างรวดเร็วภายหลังคลอด ภาวะอุณหภูมิกายต่ำจะทำให้ทารกมีอาการผิดปกติและทำให้เกิดการเจ็บป่วยที่รุนแรงตามมา จนอาจทำให้ทารกเหล่านี้มีอาการหนักหรือเสียชีวิตได้ การรักษาอุณหภูมิกายในทารก จึงถือเป็นสิ่งสำคัญอย่างยิ่งในการดูแลทารกคลอดก่อนกำหนด

คณะผู้วิจัยขอเรียนให้ท่านทราบว่า ขณะนี้มีโครงการวิจัยเกี่ยวกับการดูแลรักษาอุณหภูมิทารก ที่หน่วยทารกแรกเกิด โรงพยาบาลจุฬาลงกรณ์ โดยมีจุดมุ่งหมายเพื่อลดอัตราการเกิดภาวะอุณหภูมิกายต่ำในทารกคลอดก่อนกำหนด โครงการวิจัยนี้จะทำการประเมินประสิทธิผลของการใช้ถุงพลาสติกห่อหุ้มทารกทันทีหลังคลอด เพื่อป้องกันภาวะอุณหภูมิกายต่ำ โดยเปรียบเทียบกับวิธีรักษาอุณหภูมิกายแบบเดิมที่ปฏิบัติในปัจจุบัน ผู้วิจัยหวังว่าการใช้ถุงพลาสติกห่อหุ้มทารก จะช่วยป้องกันไม่ให้ทารกก่อนกำหนดมีอุณหภูมิลดลง จนอาจเกิดอันตรายต่อสุขภาพได้ เนื่องจากบุตรของท่าน เป็นทารกคลอดก่อนกำหนด มีโอกาสเกิดภาวะตัวเย็น หรืออุณหภูมิกายต่ำได้มากกว่าเด็กปกติ บุตรของท่านจึงจัดอยู่ในกลุ่มประชากรเป้าหมาย ที่ผู้วิจัยต้องการให้เข้าร่วมในการศึกษาวิจัยครั้งนี้ คณะผู้วิจัยจึงขอเชิญให้ท่านยินยอมให้บุตรของท่าน เข้าเป็นส่วนหนึ่งของโครงการการวิจัยดังกล่าว แต่ก่อนที่ท่านจะตัดสินใจอนุญาต ผู้วิจัยขอเรียนชี้แจงให้ท่านทราบเกี่ยวกับโครงการวิจัยดังต่อไปนี้

การศึกษานี้ ผู้วิจัยจะทำการเปรียบเทียบการรักษา 2 แบบ คือ การใช้ถุงพลาสติกห่อหุ้มทารกทันทีหลังคลอด กับการให้ความอบอุ่นแก่ทารกแบบเดิมโดยไม่ใช้ถุงพลาสติก ทารกจะถูกแบ่งเป็น 2 กลุ่ม ในกลุ่มทารกที่ถูกห่อด้วยถุงพลาสติก ผู้วิจัยจะใช้ถุงที่สะอาดปลอดเชื้อ ห่อหุ้ม

ทารกตั้งแต่ลำคอลงไปโดยจะทำในห้องคลอดทันทีที่ทารกคลอด ทารกจะถูกห่ออยู่ในถุงพลาสติกนานประมาณ 2 ชั่วโมง ในระหว่างนี้ทารกจะได้รับการดูแลรักษาตามมาตรฐานการรักษาของโรงพยาบาล ส่วนทารกที่ได้รับการดูแลแบบมาตรฐาน จะได้รับการควบคุมอุณหภูมิกายโดยใช้เครื่องมือให้ความอบอุ่นที่ใช้อยู่ในปัจจุบัน ผู้วิจัยจะวัดอุณหภูมิกายทารกทุกคนเป็นระยะทุกชั่วโมงในช่วงเวลา 3 ชั่วโมงแรก เพื่อประเมินว่า ทารกมีอุณหภูมิกายปกติหรือไม่อย่างไร หลังจากนั้นจะทำการเปรียบเทียบอุณหภูมิกายของทารกทั้งสองกลุ่ม แล้วดูว่าทารกในกลุ่มใดเกิดปัญหาเรื่องอุณหภูมิต่ำมากกว่ากัน

ในการแบ่งทารกเป็น 2 กลุ่ม จะทำโดยวิธีการสุ่ม ผู้วิจัยและบุคลากรที่เกี่ยวข้องจะไม่ทราบล่วงหน้าว่าทารกแต่ละคนจะได้รับการรักษาแบบใด ในระหว่างการศึกษา ทารกทั้งสองกลุ่มจะได้รับการรักษาในด้านอื่นๆ อย่างเท่าเทียมกันตามมาตรฐานการรักษาทารกแรกเกิด หากในระหว่างการศึกษา ทารกคนใดมีอาการแทรกซ้อนที่อาจเป็นอันตรายแพทย์จะหยุดการศึกษาและให้การดูแลรักษาทารกดังกล่าวตามข้อบ่งชี้

สิ่งที่ท่านควรทราบ หากท่านยินยอมให้บุตรของท่านเข้าร่วมโครงการวิจัยนี้ได้แก่

1. ท่านไม่ต้องเสียค่าใช้จ่ายเพิ่มเติมแต่อย่างใด
2. การวิจัยนี้ไม่มีการเจาะเลือดหรือการตรวจพิเศษที่เพิ่มเติมจากการรักษาพยาบาลที่บุตรของท่านจำเป็นได้รับ จึงไม่ก่อให้เกิดความเจ็บปวดทรมานแก่บุตรของท่านแต่อย่างใด
3. การวิจัยนี้ไม่ก่อให้เกิดความเสี่ยงเพิ่มขึ้นกับบุตรของท่าน ไม่ว่าบุตรของท่านจะได้รับการรักษาในกลุ่มใด เนื่องจากการดูแลอุณหภูมิทารกแรกเกิดที่ทารกทุกคนได้รับ เป็นการรักษามาตรฐานที่ปฏิบัติอยู่แล้วในโรงพยาบาล สำหรับทารกในกลุ่มศึกษาจะได้รับการดูแลเพิ่มเติมจากการรักษาปกติด้วยการใช้ถุงพลาสติกห่อตัวทันทีภายหลังคลอด วิธีนี้มีผู้ทำการศึกษาแล้วว่าปลอดภัย ไม่ก่อให้เกิดอันตรายต่อทารก และไม่มีรายงานว่าการใช้ถุงพลาสติกห่อตัวทารกมีผลข้างเคียงที่ไม่พึงประสงค์แต่อย่างใด ท่านจึงมั่นใจได้ว่า บุตรของท่านจะไม่ได้รับอันตรายเพิ่มขึ้นจากการศึกษา อย่างไรก็ตาม แพทย์ผู้ดูแลจะเฝ้าระวังอาการผิดปกติที่เกิดขึ้นตลอดระยะเวลาการศึกษาวิจัย หากพบว่า ทารกคนใดมีอาการผิดปกติที่เกิดจากการศึกษา แพทย์จะให้การดูแลรักษาทันที โดยที่ท่านไม่ต้องเสียค่าใช้จ่ายใดๆทั้งสิ้น
4. การวิจัยนี้ไม่ทำให้บุตรของท่านเสียเวลาอยู่ในโรงพยาบาลนานขึ้น เนื่องจากใช้เวลาเพียง 3 ชั่วโมงหลังคลอด และในระหว่างนี้ บุตรของท่านจะได้รับการดูแลอย่างใกล้ชิดอยู่แล้
5. ผลการวิจัยที่ได้จะเป็นประโยชน์อย่างยิ่งในการปรับปรุงคุณภาพการดูแลรักษาทารกคลอดก่อนกำหนด ซึ่งมักมีปัญหาในการควบคุมอุณหภูมิร่างกายให้ปกติ การที่ท่าน

ยินยอมให้บุตรของท่านเข้าร่วมการศึกษา และยอมให้ผู้วิจัยใช้ข้อมูลจากบุตรของท่านในการวิเคราะห์ผลเท่ากับท่านได้ช่วย เหลือวงการวิชาการแพทย์ทำให้เกิดความรู้ใหม่และวิธีการรักษาทารกที่สามารถนำไปช่วยเหลือทารกที่เจ็บป่วยอีกจำนวนมาก นับเป็นกุศลอันยิ่งใหญ่ที่ท่านและบุตรสามารถทำร่วมกันได้ในคราวเดียว โดยไม่ต้องลงทุนแต่อย่างใด

6. การให้คำยินยอมให้บุตรของท่านเข้าร่วมการศึกษานี้ เป็นไปโดยสมัครใจ ท่านอาจปฏิเสธที่จะให้บุตรของท่านเข้าร่วม หรือขอถอนตัวจากการศึกษานี้ได้ทุกเมื่อ โดยไม่กระทบต่อการดูแลรักษาที่บุตรของท่านจะได้รับจากแพทย์
7. ผู้วิจัยยินดีตอบคำถามต่างๆ ที่ท่านสงสัยโดยละเอียด ตลอดเวลาของการวิจัย
8. ผลการศึกษานี้จะใช้สำหรับวัตถุประสงค์ทางวิชาการเท่านั้น การเปิดเผยทำได้เฉพาะในรูปที่เป็นสรุปผลการวิจัย ข้อมูลต่างๆของผู้ป่วยจะถูกเก็บเป็นความลับ ไม่มีการเปิดเผยต่อสาธารณชน ขอรับรองว่าจะไม่มีการเปิดเผยชื่อของท่าน หรือบุตรของท่านโดยเด็ดขาด

หากท่านมีปัญหา หรือข้อสงสัยประการใด กรุณาติดต่อ ผศ.นพ. สันติ ปุณณะหิตานนท์ หน่วยทารกแรกเกิด ตึกนวมินทราชินี ชั้น 4 โรงพยาบาลจุฬาลงกรณ์ โทร 02-256-4804-5 หรือ 09-1666-882

ผู้วิจัยขอขอบคุณในความร่วมมือของท่านมา ณ ที่นี้

สถาบันวิทยบริการ
จุฬาลงกรณ์มหาวิทยาลัย

APPENDIX C

CASE RECORD FORM

Efficacy of polyethylene plastic wrap for the prevention of hypothermia during immediate postnatal period in preterm infants:

A randomized controlled trial

CASE RECORD FORM

Principle investigator:

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สถาบันวิทยบริการ
จุฬาลงกรณ์มหาวิทยาลัย

Eligibility criteria checklist

Inclusion criteria	Yes	No
■ Gestational age ≤ 34 complete weeks (according to best obstetric estimate at the time of delivery)	[ ]	[ ]
Exclusion criteria		
■ Major congenital malformations with open lesions	[ ]	[ ]
■ Pre-viable infant (Gestational age ≤ 24 complete weeks)	[ ]	[ ]
■ Infants born 5 minutes or more before the pediatric team arrive	[ ]	[ ]
■ Informed consent denied	[ ]	[ ]
Conclusion		
■ Patient fulfils inclusion criteria and none of the exclusion criteria	[ ]	[ ]

สถาบันวิทยบริการ
จุฬาลงกรณ์มหาวิทยาลัย

Patient's description

Treatment allocation ☐ wrap ☐ control

Sex ☐ male ☐ female

Date of birth (dd/mm/yy) __ __/ __ __/ 25__ __

Gestational age __ __ Weeks by ☐ date ☐ score

Birth weight __ __ __ __ grams ☐ AGA ☐SGA ☐ LGA

Mode of delivery ☐ spontaneous vaginal ☐ C/S

Apgar score 1 min..... 5 min..... 10 min .....

Resuscitation at birth ☐ none ☐ PPV ☐ intubation ☐ chest compression

Maternal condition and treatment

PPROM ☐No ☐ Yes

Chorioamnionitis ☐ No ☐ Yes

Antibiotic treatment ☐ No ☐ Yes

Maternal fever ☐ No ☐ Yes

Last Maternal temperature __ __ . __ °C

Antibiotics Rx ☐ No ☐ Yes, duration... h

Infant's illness and treatment

RDS ☐ No ☐ Yes

Presumed sepsis ☐ No ☐ Yes

Shock ☐ No ☐ Yes

Inotropic treatment ☐ No ☐ Yes

Initial Ventilation support ☐ No ☐ NCPAP ☐IMV

Umbilical vein catheter ☐ No ☐ Yes

Umbilical artery catheter ☐ No ☐ Yes

Pneumothorax ☐ No ☐ Yes

Skin breakdown/ bruises ☐ No ☐ breakdown ☐ bruises

สถาบันวิทยบริการ
จุฬาลงกรณ์มหาวิทยาลัย

TIME OF EVENTS

Event/Activity	Date	Time
1. Birth	__/__/ 254_	__ : __
2. Admission to nursery	__/__/ 254_	__ : __
3. BT_0	__/__/ 254_	__ : __
4. BT_1	__/__/ 254_	__ : __
5. BT_2	__/__/ 254_	__ : __
6. BT_3	__/__/ 254_	__ : __
7. Transfer into incubator	__/__/ 254_	__ : __
8. (For infant in wrap group only) **plastic bag removed**	__/__/ 254_	__ : __

Duration of stabilization in delivery room __ min.

Duration of stabilization under radiant warmer __ min.

Wrap time __ min. ☐ not wrapped

Environmental temperature

Delivery/ operating room temperature* ___.__ °C

Transport incubator temperature# ___.__ °C

Nursery temperature¶ ___.__ °C

* Measurement within 1 hour of delivery

temperature recorded at the time of transport

¶ temperature recorded within 1 hour of admission

OUTCOMES

Primary outcome

1. **Hypothermia during 3 hours of stabilization**

   ☐ No ☐ Yes , Duration of hypothermia _ _ hr. _ _ min.

2. **Body temperature measurements**

	Time	Rectal temperature (°C)	Skin temperature (°C)	Warmer/ incubator temperature(°C)
Admission	_ _ : _ _	_ _ . _	_ _ . _	_ _ . _
1 hour	_ _ : _ _	_ _ . _	_ _ . _	_ _ . _
2 hour	_ _ : _ _	_ _ . _	_ _ . _	_ _ . _
3 hour	_ _ : _ _	_ _ . _	_ _ . _	_ _ . _
4 hour *	_ _ : _ _	_ _ . _	_ _ . _	_ _ . _
5 hour *	_ _ : _ _	_ _ . _	_ _ . _	_ _ . _
6 hour *	_ _ : _ _	_ _ . _	_ _ . _	_ _ . _

* Record if infant is still hypothermic at 3 hr.

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Secondary outcomes

1. **Infant's respiratory status/ support at the end of the study period :**

   ☐ Room air

   ☐ Oxygen hood FiO_2.....

   ☐ NCPAP settings : FiO_2..... PEEP.....cmH_2O

   ☐ CMV settings: FiO_2..... PEEP.....cmH_2O

   PIP.....cmH_2O rate...../min

2. **Hyperthermia** (BT> 37.5 ° C) ☐ No ☐ Yes
3. **Skin breakdown after birth** ☐ No ☐ Yes
4. **Hypoglycemia** ☐ No ☐ Yes
5. **Blood gas at 0-2 hr :**

   pH _ . _ _ **HCO_3** _ _ _ meq/L **BE** _ _ _ meq/L ☐ Not done

6. **Blood pH at 2-6 hr :**

   pH _ . _ _ **HCO_3** _ _ _ meq/L **BE** _ _ _ meq/L ☐ Not done

7. **Electrolyte at 24-48 hr**:

   Na _ _ _ . _ meq/L **K** _ . _ _ meq/L **CO_2** _ _ . _ meq/L ☐ Not done

8. **IVH screening at 72-120 hr** ☐ No ☐ Yes ☐ Not done
9. **Death within 72 hours** ☐ No ☐ Yes
10. **Other adverse events** ☐ No ☐ Yes, describe .....

VITAE

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