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Optimal Thermal Control with Sufficient Nutrition May Reduce the Incidence of Neonatal Jaundice by Preventing Body-Weight Loss Among Non-Low Birth Weight Infants Not Admitted to Neonatal Intensive Care Unit

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Keywords

Neonatal jaundice · Physiology · Body temperature · Body-weight loss · Breastfeeding · Bottle feeding · Prevention

Abstract

Background: Neonatal jaundice is strongly attributable to excess body-weight loss as a result of insufficient calorific intake. ***Objectives:*** To examine the incidence of neonatal jaundice (defined by use of phototherapy) and body-weight loss, as well as their association, among neonates under optimal thermal control with sufficient nutrition, a local protocol for temperature and nutritional regulation. ***Methods:*** We retrospectively identified a cohort of 10,544 neonates (birth weight ≥2,500 g) placed in thermo-controlled incubators for 2 h immediately after birth. Neonates were fed with 5% glucose solution 1 h after birth and breastfed every 3 h (with supplementary formula milk if applicable) according to basal maintenance expenditure. Total serum bilirubin levels at day 4 (peak level) were assessed. Phototherapy was performed on the basis of total serum bilirubin level ≥18 mg/dL. Risk ratio (RR) and 95% CI for the use of phototherapy against maximum body-weight loss were estimated using Poisson regression with robust variance. ***Results:*** Incidence of phototherapy use was low (0.3%) and the mean total serum bilirubin level was 8.5 mg/dL (SD 2.7 mg/dL), with a low mean maximum body-weight loss (1.9%) and low incidence of excess body-weight loss ≥7% (0.4%). Maximum body-weight loss was associated with risk of neonatal jaundice (RR 1.27; 95% CI 1.04–1.54), and became significant at approximately 4% of maximum body-weight loss. ***Conclusion:*** Optimal thermal control and sufficient nutrition may greatly reduce the incidence of neonatal jaundice by preventing neonatal body-weight loss.

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Introduction

The thermal environment neonates are exposed to in the few hours after birth is a key environmental determinant for neonatal health. Optimal thermal environment during that time is an ambient room temperature of ~34 °C (93.2°F), which "allows body temperature to remain normal while oxygen consumption and evaporative water loss are both at a minimum" [1]. In contrast to the ambient room temperature (~24 °C/75.2°F), this optimal thermal environment helps neonatal body temperature to remain normal with circulatory stability [2–4], resulting in improving digestive function such as prevention of vomiting and promotion of meconium excretion [2, 3]. As a result, neonates in this neutral thermal environment are fed sufficiently according to basal maintenance expenditure (~50 kcal/kg) [5], which may help prevent hypoglycemia and hypernatremia associated with severe neurologic damage [3, 6, 7].

Placing neonates in a neutral thermal environment with sufficient nutrition, that is, local thermal and nutritional regulation according to basal 50 kcal/kg maintenance expenditure [3, 5], may also have benefits for neonatal hyperbilirubinemia [3]. Neonatal jaundice is a common physiological condition worldwide (incidence ranges from ~2 to 35%) [8–15], and the toxic effects of unconjugated hyperbilirubinemia are associated with neurological damage [16, 17]. Additionally, the risk of neonatal jaundice associated with excess body-weight loss (as a result of insufficient calorific intake) has been an emerging concern [10, 13, 14], even after adjusting for gene polymorphisms [10]. However, among non-low birth weight neonates not admitted to the neonatal intensive care unit (NICU), studies evaluating the contribution of this combination method (thermal control with sufficient nutrition) on neonatal jaundice, excess body-weight loss, and their mutual association remain sparse.

Using data with the combination method among neonates with normal birth weight that were not admitted to the NICU, we examined the incidence of neonatal jaundice and excess body-weight loss during the first few days of life. We also examined whether body-weight loss was associated with the risk of neonatal jaundice within the treated population.

Materials and Methods

Study Setting and Population

This retrospective, longitudinal study of neonates during the initial 4 days of life used clinical data from a cohort of neonates with normal birth weight (January 1989 to June 2017). Data were collected from the database of Kubota Maternity Clinic in Fukuoka, Japan, a general obstetrics and gynecological hospital that provided general obstetrics care for a general population in Fukuoka, as well as other areas of Japan and closed in 2017. There were not any restrictions (such as referral) to access the hospital. The characteristics of our population (such as gestational age and birth weight) were similar to those reported in previous studies (Table 1) [10–12]. All neonates were treated with the combination method, a local thermal and nutritional regulation protocol based on basal 50 kcal/kg maintenance expenditure [3, 5], and discharged by a physician on day 4 or later, when serum bilirubin level was <15 mg/dL, body weight was recovered from its lowest level, and phototherapy was no longer required [11, 18].

Table 1. Demographic and clinical characteristics of 10,544 neonates who received optimal thermal control with sufficient nutrition and their mothers

Characteristics	*n* (%) or mean ± SD
Total, *n*	10,544
Female	5,066 (48.0)
Gestational age, weeks	39.0±1.1
Birth weight, g	3,043±300
Apgar score at 1 min	9.6±0.6
Cesarean delivery	810 (7.7)
Maternal age, years	30.9±4.0
Maternal body mass index	20.1±2.0
Multipara	4,982 (47.2)
Body-weight loss, %	1.9±1.5
Excess body-weight loss ≥7%	39 (0.4)
Bilirubin level at day 4, mg/dL	8.5±2.7
Bilirubin level at day 4 ≥15.0 mg/dL	142 (1.3)
Phototherapy	30 (0.3)

Since 1989, the hospital collected clinical information on all neonates and their mothers (including gestational age, body weight, serum bilirubin levels, phototherapy, and maternal age), except those who had neonatal asphyxia, congenital heart failure or malformation, or were transferred to a tertiary hospital (such as a university hospital) for neonatal intensive care. We obtained an anonymized dataset through a research agreement with the hospital; the research ethics committees of Hakata Clinic approved the study. The research protocol was registered at UMIN-CTR (UMIN000030011).

All eligible 10,747 term and preterm neonates treated with the combination method (1) with a birth weight ≥2,500 g, (2) Apgar score ≥7, and (3) who were not admitted to the NICU were included. We excluded neonates with incomplete data (1.9%), yielding a final study population of 10,544 neonates.

Neutral Thermal Environment with Sufficient Nutrition

Body temperature of neonates was optimally regulated with their neutral thermal environment [2–4]. Following delivery in a delivery room maintained at ~25 °C (77°F), neonates were immediately wiped with cotton towels, given intraoral suction on a warm bed (~40 °C [104°F]), hugged by their mothers (skin-to-skin contact), and then placed in a transparent thermo-controlled incubator (N-ideal H-2000, Nakamura Medical Industry, Tokyo, Japan) within 2 min of birth [2, 3]. Transparent thermo-controlled incubators were placed next to delivery beds in the delivery room: that is, neonates were not placed in an NICU. Neonates remained visible and were continuously observed not only by physicians and nurses (e.g., Apgar score), but also by mothers.

Neonates remained in incubators for 2 h. For the first hour, incubators were set at 34 °C (93.2°F) [2, 3]. Bed linen and clothing were also warmed at 34 °C (93.2°F), and neonates were dressed after their respiration stabilized. For the second hour, the temperature was turned down to 30 °C (86°F) to help neonates adapt to normal room temperature. Finally, neonates were transferred to a bed in a normal monitoring room set at ~24–26 °C (75.2–78.8°F) [2, 3].

For sufficient nutrition treatment, 1 h after birth, neonates were orally fed 5% glucose solution (10 mL/kg) with 1 mL of vitamin K syrup (containing 2 mg menatetrenone) [3]. Orally fed 5% glucose solution has been shown to be a convenient and efficient method to prevent hypoglycemia and neonatal jaundice, while allowing continuous breastfeeding [3, 6]. Neonates were then breastfed every 3 h. To maintain 50 kcal/kg basal maintenance expenditure [5], neonates were additionally bottle-fed with formula milk until they were sated (if breast milk production was insufficient) [3]. Additional bottle-feeding with formula milk was based on findings suggesting that production of breast milk was insufficient after a few days of birth and/or estimated calories provided by breast milk were below the basal maintenance expenditure among the study population [3]. For example, (1) breastfed neonates born to primipara mothers additionally consumed 55 kcal/kg of formula milk at day 1, 70 kcal/kg at day 2, and 90 kcal/kg at day 3, which were identical to those in formula-fed neonates, (2) breastfed neonates born to multipara mothers showed the same pattern for the first 2 days, and continued to consume additional formula milk (70 kcal/kg) from day 2 to 4, and (3) as the additional formula milk intake substantially decreased after day 6 in neonates born to primipara mothers and day 5 in those born to multipara mothers, the sufficient nutrition strategy did not affect breastmilk production after a few days of birth. High-calorie formula milk (16 kcal/20 mL) was given for the first 48 h; then normal-calorie formula milk (13 kcal/20 mL) was given after 48 h. The hospital purchased formula milk from Megmilk Snow Brand (Hokkaido, Japan) and Icreo (Tokyo, Japan).

Measurement of Serum Bilirubin Levels and Body Weight

Blood samples were collected by heel prick [3, 10]. Although transcutaneous bilirubin levels were not measured, total serum bilirubin levels (mg/dL) at day 4, corresponding peak levels among Japanese neonates [11, 12], were routinely measured among 10,541 out of 10,544 neonates using a modified method based on previous studies involving direct spectrophotometry of centrifuged blood samples in micro-hematocrit tubes (BL-200, Toitu, Tokyo, Japan) [3, 10, 11]. On the basis of bilirubin levels ≥18 mg/dL in combination with other clinical findings, phototherapy was performed [3, 10, 18]. However, some neonates (3 out of 10,544) presented clinical symptoms of jaundice, such as yellow skin color, earlier than day 4; thus, these neonates underwent phototherapy before day 4. Definitions of neonatal jaundice included (1) use of phototherapy and (2) total serum bilirubin ≥15 mg/dL.

Using body weight measured at birth and every day for the first 4 days (SW-5200, Toitu, Tokyo, Japan), we determined maximum body-weight loss ([[birth weight – minimum weight]/birth weight] ×100%). Excess body-weight loss was defined as maximum body-weight loss ≥7% [18].

Statistical Analysis

We assessed the cumulative incidence of neonatal jaundice and excess body-weight loss by day 4 after birth. For total serum bilirubin levels, we estimated the coefficient (β) and 95% CI of maximum body-weight loss using linear regression. For risk of neonatal jaundice, we estimated risk ratios (RRs) and 95% CIs for use of phototherapy and total serum bilirubin ≥15 mg/dL against maximum body-weight loss using Poisson regression with robust variance [19]. We also drew cubic spline curves (knotted at 5, 27.5, 50, 72.5, and 95th percentile points), using data up to the 99th percentile of maximum body-weight loss. Covariates were sex, gestational age, birth weight, Apgar score, cesarean delivery, maternal age, maternal body mass index, and parity.

For supplementary analysis, the incidence of neonatal jaundice, serum bilirubin levels, and maximum body-weight loss were ecologically compared with published data from previous studies [8–10, 12–15].

Alpha was set at 0.05, and all *p* values were 2-sided. Data were analyzed using STATA/MP 13.1 (Stata-Corp, College Station, TX, USA).

Results

Overall, the cumulative incidence of neonatal jaundice was low: 0.3% met the criteria for phototherapy and 1.3% had total serum bilirubin levels ≥15 mg/dL (Table 1). The mean total serum bilirubin level at day 4 was 8.5 mg/dL (SD 2.7 mg/dL; Fig. 1), while the mean maximum body-weight loss was 1.9% (SD 1.5%), and incidence of excess body-weight loss ≥7% was 0.4% (Table 1). We did not observe any neonatal morbidity or mortality events through the study period.

A weak association between maximum body-weight loss and bilirubin levels was observed (adjusted β 0.14; 95% CI 0.11–0.17); however, the association remained clinically insignificant. Although the absolute cumulative incidence of neonatal jaundice and excess body-weight loss was low, maximum body-weight loss was associated with an increased risk of use of phototherapy (adjusted RR 1.27; 95% CI 1.04–1.54) and total serum bilirubin levels ≥15 mg/dL (Table 2). Indeed, the risk of the use of phototherapy and total serum bilirubin levels ≥15 mg/dL became statistically significant at ~4% of maximum body-weight loss (Fig. 2, 3).

The incidence of neonatal jaundice and averages of total serum bilirubin levels and maximum body-weight loss

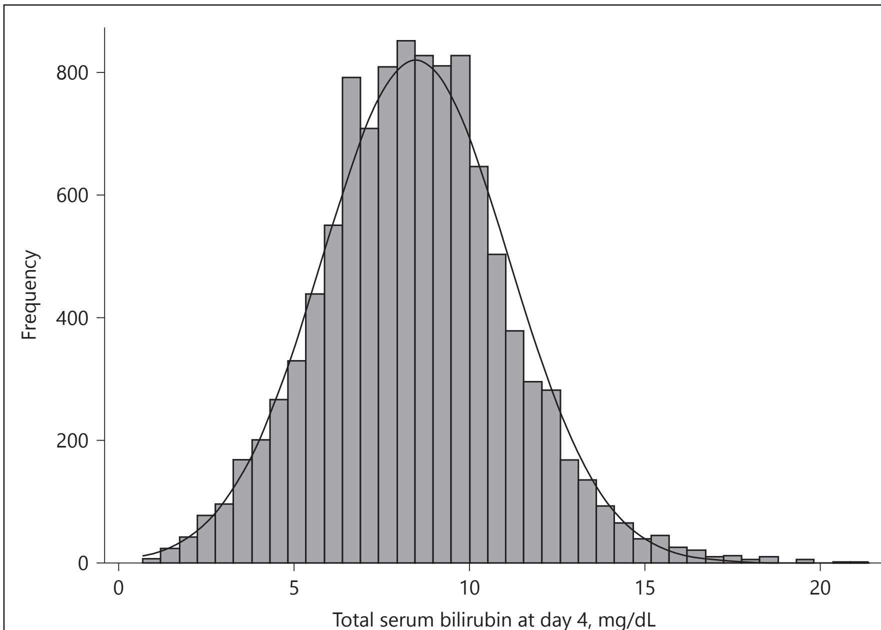

Fig. 1. Distribution of total serum bilirubin level at day 4 in 10,544 neonates who received optimal thermal control and sufficient nutrition.

Table 2. Risk of neonatal jaundice associated with maximum body-weight loss in 10,544 neonates, estimated using multivariable Poisson regression with robust variance

Characteristics	Use of phototherapy		Total serum bilirubin ≥15 mg/dL	
	RR (95% CI)	*p* value	RR (95% CI)	*p* value
Maximum body-weight loss, %	1.27 (1.05–1.54)	0.02	1.21 (1.09–1.34)	<0.001
Female	0.42 (0.19–0.93)	0.03	0.69 (0.49–0.97)	0.03
Gestational week	0.60 (0.45–0.80)	0.001	0.78 (0.67–0.91)	0.001
Birth weight per 100 g	1.05 (0.94–1.17)	0.40	1.04 (0.98–1.12)	0.14
Apgar score	0.75 (0.41–1.36)	0.34	0.57 (0.45–0.72)	<0.001
Maternal age	1.02 (0.92–1.13)	0.69	1.04 (0.99–1.08)	0.13
Maternal body mass index	1.12 (0.94–1.34)	0.19	1.02 (0.94–1.12)	0.61
Multipara	0.39 (0.17–0.86)	0.02	0.56 (0.40–0.79)	0.001

RR, risk ratio.

appeared to be lower than values projected in previous studies (Table 3). Changes of the type of formula milk over time did not affect this association (data not shown).

Discussion

Under a local thermal and nutrition regulation protocol based on basal maintenance expenditure, we have presented a low incidence of neonatal jaundice and excess body-weight loss. In this population, mean peak bilirubin levels were shifted toward a lower level (population approach) [20], and cumulative incidence of neonatal jaundice was at most 1%; as far as we are aware, this is the lowest reported incidence (previous reports indicate range from ~2 to 35%) [8–10, 12–15]. Although neonatal jaundice was nearly eliminated by the lowest reported incidence of excess body-weight loss (0.4%) [8, 10, 12–15], a residual risk of body-weight loss remained associated with neonatal jaundice.

While the impact of the combination method against exclusive breastfeeding was not directly assessed with a

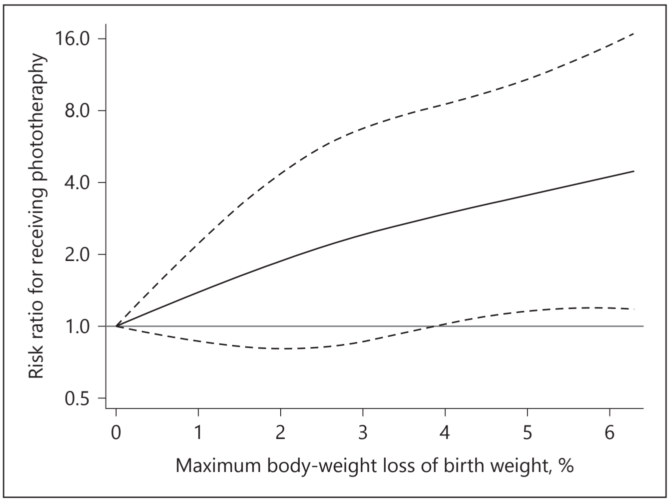

Fig. 2. Cubic spline curves showing the risk for receiving phototherapy against percentage of maximum body-weight loss of birth weight. Risk ratios (solid line) and 95% CIs (dashed lines) were estimated by Poisson regression with robust variance, adjusted for sex, gestational age, birth weight, Apgar score, maternal age, maternal body mass index, and parity.

Fig. 3. Cubic spline curves showing the risk for total serum bilirubin levels ≥15 mg/dL against body-weight loss. Risk ratios (solid line) and 95% CIs (dashed lines) were estimated by Poisson regression with robust variance, adjusted for sex, gestational age, birth weight, Apgar score, maternal age, maternal body mass index, and parity.

multivariable analysis, given that the magnitude of RR ranged from 0.02 to 0.12 in Table 3, we speculate that the combination method is a clue for emerging concern about body-weight loss leading to neonatal jaundice, as well as hypoglycemia and hypernatremia dehydration, among exclusively breastfed neonates [3, 6–15, 17]. Neonates exclusively breastfed without thermal control may not have the advantage of improved digestive function [3]. For example, (1) gastric emptying time was better in breastfed neonates with thermal control (<1 h) than breastfed neonates without thermal control (>1 h), (2) compared with average serum glucose levels during the first 8 h of birth in breastfed neonates without thermal control (~40 mg/dL) and breastfed neonates with thermal control only (~50 mg/dL), neonates with the combination method had higher levels (ranging from ~50 to 70 mg/dL), and (3) regarding the time required for serum level of free fatty acids to start decreasing, compared with breastfed neonates without thermal control (8 h of birth) and breastfed neonates with thermal control only (8 h of birth), neonates with the combination method appeared to start earlier (4 h of birth). In addition, exclusive breastfeeding may not always provide sufficient calorific intake to neonates according to basal maintenance expenditure [3]. This problem is illustrated by our observation of a lower incidence of jaundice in neonates born to multipara mothers compared with those born to primipara mothers (RR ranged from 0.39 to 0.56), who are likely to have lower levels of breast milk [3].

However, in the present study, the risk of neonatal jaundice was already significant at ~4% of body weight loss. Even with our intensive treatment regimen, significant weight loss occurred in a limited number of neonates, predisposing them to jaundice. Therefore, this group might require further preventive intervention and phototherapy without delay [16], and their body-weight loss should not be diagnosed with physiological body-weight loss.

Some limitations should be considered. First, our study did not have a control group; thus, we could not perform a direct comparison with multivariable analytic models. However, our supplementary analysis suggests a potential impact of the combination method. Second, we could not fully assess factors before treatment (such as history of previous neonates who received phototherapy or hemolytic disease) [15]; however, body-weight loss, neonatal sex, and gestational age may be the most relevant risk factors [8, 10, 13–15], which coincides with our results. Additionally, although we could not assess other bilirubin-related outcomes, such as direct/indirect bilirubin and transcutaneous bilirubin levels, or control for other possible factors such as genetic variation, genetic factors may not affect the

Table 3. Ecological comparison of neonatal jaundice, serum bilirubin level, and body-weight loss with previous studies

Neonatal jaundice	Setting	Nutrition	Total, *n*	*n* (%)	RR	*p* value
Phototherapy[a]						
Flaherman et al. [8], 2017	USA	Breast (62.9%), mixed (33.1%), formula (4.6%)	143,889	3,453 (2.4)	0.12	<0.001
Mantagou et al. [9], 2012	Greece	Unspecified	7,302	450 (6.2)	0.05	<0.001
Han et al. [15], 2015	China	Breast (36.3%), mixed (25.7%), formula (38.0%)	8,215	876 (10.6)	0.03	<0.001
Sato et al. [10], 2013	Japan	Breast-fed	401	56 (14.0)	0.02	<0.001
Total serum bilirubin ≥15 mg/dL[b]						
Chen et al. [13], 2012	Taiwan	Breast	323	114 (35.3)	0.04	<0.001
Serum bilirubin level	**Setting**	**Nutrition**	**Total, *n***	**Mean (SD), mg/dL**		***p* value[c]**
Chen et al. [14], 2011	Taiwan	Formula	30	9.8 (3.2)		0.02
Chen et al. [14], 2011	Taiwan	Mixed	24	10.8 (2.4)		<0.001
Sato et al. [10], 2013	Japan	Breast	401	12.0 (2.6)		<0.001
Chen et al. [13], 2012	Taiwan	Breast	323	13.2 (2.7)		<0.001
Chen et al. [14], 2011	Taiwan	Breast	30	13.2 (3.0)		<0.001
Percentage of body-weight loss	**Setting**	**Nutrition**	**Total, *n***	**Mean (SD), %**		***p* value[d]**
Itoh et al. [12], 2001	Japan	Formula	494	4.0 (1.7)		<0.001
Itoh et al. [12], 2001	Japan	Breast	177	6.6 (1.6)		<0.001
Sato et al. [10], 2013	Japan	Breast	401	8.4 (2.6)		<0.001

[a] Chi-squared test compared with the summary statistics of the current study: the number of phototherapy, 30 out of 10,544 neonates (0.3%).
[b] Chi-squared test compared with the summary statistics of the current study: the number of total serum bilirubin ≥15 mg/dL at day 4, 142 out of 10,544 neonates (1.3%).
[c] *t* test compared with the summary statistics of the current study: total serum bilirubin level at day 4, mean 8.5 (SD 2.7) mg/dL.
[d] *t* test compared with the summary statistics of the current study: percentage of maximum body-weight loss, mean 1.9 (SD 1.5).
RR, risk ratio.

risk of neonatal jaundice when body-weight loss is <5%, and we observed an average body-weight loss of 1.9% [10].

Despite these limitations, our local protocol of thermal control with sufficient nutrition could be a potential neonatal treatment. In the era of early neonatal hospital discharge, the use of thermal control (without using NICU care) may also reduce medical expenditures associated with readmission for phototherapy with costly care in the NICU [8, 16, 17]. At least, the management of ambient room temperature at ~34 °C (93.2°F) using air conditioners and wiping neonates immediately after birth could be a potential alternative method without using incubators, particularly for (but not limited to) low and middle-income countries [21]. Additionally, the initial 2 h spent in the incubator could help to avoid the substantially longer incubation required for phototherapy and could also reduce the time before discharge, thereby potentially increasing opportunities for physical contact between mothers and their babies in the neonatal period [6, 16].

Last, while potential drawbacks of reducing total bilirubin levels (such as antioxidant effects) and use of supplemental feeding (such as the risk of breastfeeding failure, excessive weight gain, and diabetes) are controversial [16, 22, 23], supplemental feeding may not affect breastfeeding [3, 6]. Optimal thermal control may upregulate bilirubin conjugation by reducing free fatty acid via fat oxidation and non-shivering thermogenesis [3]. For the effect of preventing body-weight loss to potentially reduce neonatal jaundice, an association between body weight and heme catabolism may also play a role [24]. Therefore, neonates who are at risk of insufficient calorific intake should undergo clinical treatment with supplements according to basal maintenance expenditure [3, 5, 7].

In conclusion, our results demonstrate a potential population approach involving a simple combination of optimal thermal control and sufficient nutrition to reduce the incidence of neonatal jaundice. The potential of our neonatal regimen should be further assessed in future studies, including randomized controlled trials, in order to challenge the norm of neonatal jaundice.

Disclosure Statement

The authors have no conflicts of interest relevant to this article to disclose.

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References

1 Hey EN, Katz G: The optimum thermal environment for naked babies. Arch Dis Child 1970;45:328–334.
2 Kubota S, Koyanagi T, Hori E, Hara K, Shimokawa H, Nakano H: Homeothermal adjustment in the immediate postdelivered infant monitored by continuous and simultaneous measurement of core and peripheral body temperatures. Biol Neonate 1988;54: 79–85.
3 Kubota S: The effects of environmental temperature on the mechanism of thermoregulation in infants. Clinical Thermometry and Thermomedicine 2005;23:20–34.
4 Yoshimura T, Tsukimori K, Wake N, Nakano H: The influence of thermal environment on pulmonary hemodynamic acclimation to extrauterine life in normal full-term neonates. J Perinat Med 2007;35:236–240.
5 Gross SJ, David RJ, Bauman L, Tomarelli RM: Nutritional composition of milk produced by mothers delivering preterm. J Pediatr 1980; 96:641–644.
6 Aoshima N, Fujie Y, Itoh T, Tukey RH, Fujiwara R: Glucose induces intestinal human UDP-glucuronosyltransferase (UGT) 1A1 to prevent neonatal hyperbilirubinemia. Sci Rep 2014;4:6343.
7 Seske LM, Merhar SL, Haberman BE: Late-onset hypoglycemia in term newborns with poor breastfeeding. Hosp Pediatr 2015;5:501–504.
8 Flaherman V, Schaefer EW, Kuzniewicz MW, Li SX, Walsh EM, Paul IM: Health care utilization in the first month after birth and its relationship to newborn weight loss and method of feeding. Acad Pediatr 2017.pii S1876–S2859.
9 Mantagou L, Fouzas S, Skylogianni E, Giannakopoulos I, Karatza A, Varvarigou A: Trends of transcutaneous bilirubin in neonates who develop significant hyperbilirubinemia. Pediatrics 2012;130:e898–e904.
10 Sato H, Uchida T, Toyota K, Kanno M, Hashimoto T, Watanabe M, Nakamura T, Tamiya G, Aoki K, Hayasaka K: Association of breast-fed neonatal hyperbilirubinemia with UGT1A1 polymorphisms: 211G>A (G71R) mutation becomes a risk factor under inadequate feeding. J Hum Genet 2013;58:7–10.
11 Kuboi T, Kusaka T, Kawada K, Koyano K, Nakamura S, Okubo K, Yasuda S, Isobe K, Itoh S: Hour-specific nomogram for transcutaneous bilirubin in Japanese neonates. Pediatr Int 2013;55:608–611.
12 Itoh S, Kondo M, Kusaka T, Isobe K, Onishi S: Differences in transcutaneous bilirubin readings in Japanese term infants according to feeding method. Pediatr Int 2001;43:12–15.
13 Chen YJ, Chen WC, Chen CM: Risk factors for hyperbilirubinemia in breastfed term neonates. Eur J Pediatr 2012;171:167–171.
14 Chen CF, Hsu MC, Shen CH, Wang CL, Chang SC, Wu KG, Wu SC, Chen SJ: Influence of breast-feeding on weight loss, jaundice, and waste elimination in neonates. Pediatr Neonatol 2011;52:85–92.
15 Han S, Yu Z, Liu L, Wang J, Wei Q, Jiang C, Guo J, Li M, Yang J, Shah PS, Chen C; Chinese Multicenter Study Coordination Group for Neonatal Hyperbilirubinemia: A model for predicting significant hyperbilirubinemia in neonates from China. Pediatrics 2015;136: e896–e905.
16 Maisels MJ, McDonagh AF: Phototherapy for neonatal jaundice. N Engl J Med 2008;358: 920–928.
17 Suresh GK, Clark RE: Cost-effectiveness of strategies that are intended to prevent kernicterus in newborn infants. Pediatrics 2004;114: 917–924.
18 American Academy of Pediatrics Subcommittee on Hyperbilirubinemia: Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. Pediatrics 2004;114:297–316.
19 Barros AJ, Hirakata VN: Alternatives for logistic regression in cross-sectional studies: an empirical comparison of models that directly estimate the prevalence ratio. BMC Med Res Methodol 2003;3:21.
20 McLaren L, McIntyre L, Kirkpatrick S: Rose's population strategy of prevention need not increase social inequalities in health. Int J Epidemiol 2010;39:372–377.
21 Olusanya BO, Osibanjo FB, Slusher TM: Risk factors for severe neonatal hyperbilirubinemia in low and middle-income countries: a systematic review and meta-analysis. PLoS One 2015;10:e0117229.
22 Sedlak TW, Snyder SH: Bilirubin benefits: cellular protection by a biliverdin reductase antioxidant cycle. Pediatrics 2004;113:1776–1782.
23 Victora CG, Bahl R, Barros AJ, Franca GV, Horton S, Krasevec J, Murch S, Sankar MJ, Walker N, Rollins NC; Lancet Breastfeeding Series Group: Breastfeeding in the 21st century: epidemiology, mechanisms, and lifelong effect. Lancet 2016;387:475–490.
24 Bakken AF, Thaler MM, Schmid R: Metabolic regulation of heme catabolism and bilirubin production. I. hormonal control of hepatic heme oxygenase activity. J Clin Invest 1972; 51:530–536.