ABSTRACT

Purpose: Extremely-low-birth-weight infants (ELBWIs), especially those ≤24 gestational weeks (GW), presented extremes in IWL and changes of water balance. The purpose of the present study was to retrospectively investigate fluid and electrolyte balance in infants of ≤24-GW during the first postnatal week under high humidification.

Methods: Medical records of extremely-low-birth-weight infants (ELBWIs) who were born and admitted to the Neonatal Intensive Care Unit at Samsung Medical Center during March 2004–September 2010 were reviewed. Fluid intake, urine output, insensible water loss (IWL) and electrolyte balance of 22-GW (n=14), 23-GW (n=40) and 24-GW (n=67) infants nursed in high humidity (95%) were compared with ≥26-GW (n=65) infants nursed in 60% humidity.

Results: Survival rate until discharge was 33%, 82%, 75% and 89.3% in 22-GW, 23-GW, 24-GW and ≥26-GW infants, respectively. Compared to ≥26-GW infants, fluid intake and IWL was higher in 22-GW and 23-GW, but not as different in 24-GW. At postnatal day (P) 3–5, urine output was significantly lower in ≥26-GW infants than in the other age groups. Serum sodium level was significantly higher in 22-, 23- and 24-GW (P1–2) than in ≥26-GW infants. Hypernatremia (>150 mEq/dl sodium) was more frequent in 22-GW (71%), 23-GW (41%) and 24-GW (21%) than in ≥26-GW infants (14%).

Conclusion: High-humidity environments significantly decreased fluid intake and improved electrolyte imbalance in 24-GW, but not in 22- and 23-GW infants. Increased IWL in the latter might be related to more immature skin, implicating the need for additional nurturing conditions.

Key Words: Electrolytes, Extremely-low-birth-weight infant, Humidity, Insensible water loss
INTRODUCTION

Recent advances in neonatal medicine have improved prognosis and survival rate of extremely-low-birth-weight infants (ELBWIs)\(^1\). The limit of viability has been lowered to more immature and smaller infants. Indeed, micropremies as young as 22 gestational weeks (GW) of age have been recently resuscitated in some units. Proper body fluid metabolism and well-balanced electrolytes levels during early postnatal period in ELBWIs is considered to be the most important factor to morbidities such as patent ductus arteriosus, bronchopulmonary dysplasia, and necrotizing enterocolitis\(^2-7\). However, immature epithelial layer, larger surface area, and increased skin vascularity of preterm infants eventuate in markedly high insensible water loss (IWL), which contributes to significant electrolyte imbalance and dehydration with hyperosmolarity\(^8\).

The fetal epidermis at 23 weeks of gestation is composed of 3-5 cell layers lined by a thin stratum corneum; later, during the third trimester, the stratum corneum becomes multilayered\(^9,10\). Transepidermal water loss (TEWL) depends on the degree of epidermal maturation and barrier formation of the infant, and inversely relates to both gestational age at birth and postnatal age\(^11\). To overcome TEWL in preterm infants, various strategies, such as increased intake of fluid volume, semi-occlusive skin barriers, plastic hoods, and high-humidity environments, have been adopted. Several studies reported that highly humidified incubators are most effective in reducing fluid requirement and improving electrolyte balance and weight gain\(^12,13\).

It has been known that the more premature the infants, the more difficult to manage fluid and electrolyte balance due to higher IWL. However, there are few reports about fluid and electrolyte balance in micropremies of ≤24 GW, especially those with significant immature cutaneous cuticle, who are prone to severe transepidermal fluid loss. Moreover, the value of high-humidity environments in ≤24-GW micropremies at the margin of viability still remains obscure. In the present study, we retrospectively investigated fluid and electrolyte balance in ≤24-GW micropremies nursed in a highly humidified environment during the first postnatal week.

MATERIALS AND METHODS

Medical records of 437 ELBWIs admitted to the Neonatal Intensive Care Unit (NICU) at Samsung Medical Center from March 2004 to September 2010 were reviewed retrospectively (Fig. 1). One-hundred twenty infants who were born at another hospital and transferred to our unit, and 23 other infants who succumbed within 7 days of life were excluded due to insufficient information on fluid intake. In addition, 25-GW infants were excluded due to inconstant management of high-humidity conditions. A total of 218 infants were grouped according to their age: 22 GW (n=14), 23 GW (n=40), 24 GW (n=67), and ≥26 GW (n=97).

Based on the Samsung Medical Center NICU protocol, all infants younger than 24 GW were nursed in a highly humidified (95%) hybrid humidified incubator (Giraffe Omnibed, GE Healthcare, Maryland, USA) immediately after admission. In addition, minimal handling care was provided, including minimizing direct touch and stressful investigations such as blood tests, and limiting the number of incubator door openings to less than 8 times per day, with meticulous and continuous observation.

From postnatal day (P) 3, 95% humidity was gradually decreased to 60% with improving IWL during the first week. The rate and degree of weaning humidity was individually adjusted according to the IWL, electrolytes, and changes in body weight. In the case of 25-GW infants, high-humidity (95%) management was determined on the basis of skin immaturity and extent of IWL, in which case some infants received 60% rather than 95% humidity. Infants older than 26 GW was cared in the incubator with 60% humidified ambient air. Total intake fluid was initiated at a rate of 60-80 mL/kg/day on day 1 and increased up to 120-140 mL/kg/day on day 7. The fluid infusion rate of each infant was adjusted twice per day or more according to changes in serum sodium levels, body weight, urine output, and IWL. Sodium and potassium supplementation to the total parenteral nutrition was started at day 2-4 of life according to...
the infant’s electrolyte and urine output status. After stabilizing body temperature, an umbilical central line was inserted to infants nursed in high-humidity incubators who required strict minimal handling to prevent skin breakdown from frequent blood sampling or repetitive insertion of peripheral catheter. However, ≥26-GW infants without severe distress conditions were placed a simple peripheral intravenous line, and blood samples were withdrawn by heel stick puncture once or twice per day using conventional procedures. The blood gas and electrolytes levels were measured with a point-of-care blood gas and metabolite analyzer (i-STAT® System; Abbott Laboratories, Abbott Park, IL, USA).

We analyzed the following variables during the first 7 days of life: total intake amount, IWL, urine output, weight loss percentage, and electrolyte imbalance including serum sodium and potassium. Gestational age was determined by maternal last menstrual period and modified Ballard test. IWL was estimated daily as [total fluid intake (one day before) − urine output (one day before) + weight loss]/body weight on the day.

Statistical analysis was performed with the SPSS software (version 17; SPSS, Chicago, IL, USA). For continuous variables such as total intake fluid intake, urine output, IWL, and electrolytes with a normal distribution, analysis of variance (ANOVA) test was performed. For comparing nominal variables, including incidence of electrolytes imbalance, chi-square test was performed. Data are expressed as mean±standard error of the mean (SEM), and \( P<0.05 \) was considered significant.

RESULTS

1. Survival rates

Survival rate until discharge was 24%, 71%, 72%, and 81% in 22-GW, 23-GW, 24-GW, and ≥26-W, respectively. Survival rate until 7th day of life was 82%, 87%, 94%, and 91% in 22-GW, 23-GW, 24-GW, and ≥26-W, respectively (Fig. 2).

2. IWL and water balance

Fluid intake was the highest in 22-GW, followed by 23-GW, as compared to ≥26-GW infants. However, there was no difference between 24-GW and ≥26-GW infants (Fig. 3A). IWL of 22-GW infants was the highest on P1, P2, P5, and P6, and that of 23-GW infants was higher than in ≥26-GW infants on P2-3. No differences in IWL were found between 24-GW and ≥26-GW infants during the first week of life. Urine output was not different among the 3 age groups, 22-GW, 23-GW, and 24-GW. However, that of ≥26-GW infants was significantly lower than those in the other age groups on P3-5 (Fig. 3C). The percentage of weight loss at 7th day of life was highest in 22-GW, followed by 23-GW and 24-GW. However, that of ≥26-GW infants was significantly lower than those in the other age groups on P3-5 (Fig. 3C). The percentage of weight loss at 7th day of life was highest in 22-GW, followed by 23-GW and 24-GW. However, that of ≥26-GW infants was significantly lower than those in the other age groups on P3-5 (Fig. 3C). The percentage of weight loss at 7th day of life was highest in 22-GW, followed by 23-GW and 24-GW. However, that of ≥26-GW infants was significantly lower than those in the other age groups on P3-5 (Fig. 3C). The percentage of weight loss at 7th day of life was highest in 22-GW, followed by 23-GW and 24-GW. However, that of ≥26-GW infants was significantly lower than those in the other age groups on P3-5 (Fig. 3C). The percentage of weight loss at 7th day of life was highest in 22-GW, followed by 23-GW and 24-GW. However, that of ≥26-GW infants was significantly lower than those in the other age groups on P3-5 (Fig. 3C). The percentage of weight loss at 7th day of life was highest in 22-GW, followed by 23-GW and 24-GW. However, that of ≥26-GW infants was significantly lower than those in the other age groups on P3-5 (Fig. 3C). The percentage of weight loss at 7th day of life was highest in 22-GW, followed by 23-GW and 24-GW. However, that of ≥26-GW infants was significantly lower than those in the other age groups on P3-5 (Fig. 3C). The percentage of weight loss at 7th day of life was highest in 22-GW, followed by 23-GW and 24-GW. However, that of ≥26-GW infants was significantly lower than those in the other age groups on P3-5 (Fig. 3C). The percentage of weight loss at 7th day of life was highest in 22-GW, followed by 23-GW and 24-GW. However, that of ≥26-GW infants was significantly lower than those in the other age groups on P3-5 (Fig. 3C). The percentage of weight loss at 7th day of life was highest in 22-GW, followed by 23-GW and 24-GW. However, that of ≥26-GW infants was significantly lower than those in the other age groups on P3-5 (Fig. 3C).

3. Electrolyte imbalance during the first postnatal week

During the first 7 days of life, serum sodium level was the highest in 22-GW infants, followed by 23-GW infants. There were no differences between 24-GW and ≥26-GW infants except on the 2 first days of life (Fig. 4A). The incidence of hypernatremia (>150 mEq/dl) was significantly higher in 22-GW (71.4%) and 23-GW (41.2%) than in the other age groups (Fig. 4B). In contrast, no differences were found between 24-GW (21.1%) and ≥26-GW infants (9%).

Discussion

IWL is defined as evaporative losses through the skin (60–70%) and respiratory tract (30–40%)\(^{14}\). Almost two-thirds of water loss occurs through the skin. Indeed, the skin barrier is a key factor for fluid balance and thermoregulation in the premature neonate. TEWL reaches almost 90 g/m\(^2\)/h in infants of 25 GW of age. Not-
ably, this value is 15 times greater than that of term infants. As the fetus grows and the gestational period is prolonged, the TEWL is decreased, reaching 50 g/m²/h at 26 GW. Increased TEWL in preterm infants results from greater water permeability through a yet immature epithelial layer of skin, a higher surface area to body weight ratio, and increased skin vascularity.

Previously, several reports have shown that ambient air humidity is effective in decreasing TEWL. An ambient vapor pressure
induced by high humidification diminishes evaporative water loss through the skin\textsuperscript{10,19}. One study reported that high humidity decreases fluid intake and improves water and electrolyte balance, ultimately resulting in enhanced weight gain and decrease of bronchopulmonary dysplasia (BPD) incidence\textsuperscript{10}. In this study, subject who nursed in high humidified ambient was whole ELBWIs regardless of gestational age and starting highest humidity was 80% and sustained for 7 days.

In the present study, IWL, water balance, and electrolytes were analyzed as function of the gestational age of the infants. 22-GW and 23-GW infants showed significantly higher IWL and need for fluid intake than the others. However, 24-GW infants exhibited similar IWL and fluid intake as ≥26-GW infants during the first postnatal week. This may partly indicate that high humidity significantly decreased fluid intake and improved electrolyte imbalance in 24-GW, but was insufficient in 22-GW and 23-GW infants. Especially in 22-GW infants, the severity of IWL and electrolyte imbalance was notably prominent despite of 95% humidity environment. This might implicate that these extremely immature infants need additional considerable efforts, including cautious minimal handling, strict limitation of intervention, and alert and gentle management of temperature. The interpretation of the comparison of IWL between 22-24-GW infants and ≥26-GW infants must be careful because the IWL is not only associated with humidity but also the epidermal barrier function and the maturation of the kidney function which was simply not taken into consideration in this study.

Agren et al.\textsuperscript{20} reported that higher humidity levels resulted in delayed skin barrier formation as compared with lower humidity, emphasizing the role of the skin barrier in resisting microbial invasion and protecting against environmental toxins. Some studies pointed out increased incidence of Gram-negative and fungal infections in humidified incubators\textsuperscript{12,21}. In our study, very high humidity (95%) was applied to infants of ≤24 GW until P3, and thereafter gradually decreased and adjusted individually on the basis of daily estimated IWL. Kim et al.\textsuperscript{10} reported the effectiveness of hybrid high humidification incubators in decreasing IWL in ELBWIs. In this study, the average gestational age of infants nursed in highly humidified incubators was 26.9 GW, and the mean IWL was 72.3 cc/kg/day. However, at Samsung Medical Center NICU, the indication of high humidification management is restricted to ELBWIs younger than 25 GW. The average GW and the mean IWL of ≥26-GW infants nursed in other humidity conditions were 26.4 GW and 57.3 cc/kg/day (51.3-70.4 cc/kg/day), respectively. Infants of ≥26-GW cared at 60% ambient air humidity did not exhibit higher IWL than those nursed at 80% humidity for 7 days. This result might suggest that the guidelines herein established could be helpful in preventing the overuse of high humidification, which can promote and aggravate infection.

It has been known that higher fluid intake in the early postnatal period is associated with increased risk of BPD\textsuperscript{4,5,7,22}. One study pointed out poor tolerance to fluids in low-birth-weight infants with RDS and documented that fluid restriction could reduce mortality and morbidity\textsuperscript{23}. Because of the limitations of our retrospective study, it was hard to compare IWL and outcomes of identical gestational weeks infants according to the high humidification treatment. Some of 25-GW infants receive high humidification treatment due to the more immature skin, which is more susceptible to the water loss, compared to the infants cared under 60% ambient air humidity. Thus, although the gestational age was same, the immaturity of 25-GW infants may be different according to the humidification level, and compared outcomes between high humidity group and 60% humidity group in 25-GW infants would be a reflection of different degree of immaturity rather than high humidification effect.

In summary, 24-GW infants under high-humidity environment did not show significant difference in IWL and electrolyte imbalance, compared to ≥26-GW infants. However, 22-GW and 23-GW infants demonstrated significantly higher IWL, fluid intake and electrolyte imbalance than 24-GW or ≥26-GW infants. These findings may suggest that high humidity in 24-GW was effective in reducing the IWL and fluid needs and 22/23-GW infants require more sensitive management in addition to high-humidity conditions in order to reduce TEWL and mortality.

REFERENCES


고습환경하 재태 주수 25주 미만 초미숙아의 불감수분손실분석

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목적: 초미숙아에 있어 불감수분손실은 수분평형에 있어 매우 중요한 인자이다. 본 연구의 목적은 고습환경하의 재태 24주 이하의 초미숙아의 수액 및 전해질평형에 대해 분석하고자 함이다.

방법: 2004년 3월부터 2010년 9월까지 삼성서울병원 신생아 집중치료실에 입원하였던 초극소 저체중아의 의무기록을 후향적으로 분석하였다. 고습(95%) 환경 하의 재태 22주(n=14), 23주(n=40) 및 24주(n=67)의 미숙아들이 26주(n=65)와 비교하여 수액투입량, 소변량, 불감수분손실 및 전해질평형에 있어 어떠한 차이가 있는지를 비교하였다.

결과: 재태 22주, 23주, 24주 및 26주 이상 미숙아의 생존율은 각각 33%, 82%, 75% 및 89.3%이었다. 수액투입량 및 불감수분손실량은 재태 26주와 비교하였을 때 22주 및 23주 미숙아에서 더 높았으나 24주에서는 차이가 없었다. 생후 3-5일의 소변량은 재태 26주 미숙아에서도 22-24주 미숙아의 소변량보다 의미있게 적었다. 혈청 나트륨 수치는 26주에 비해 22주, 23주, 24주에서 의미있게 높았다. 고나트륨혈증(＞150 mEq/dL)은 26주에 비해 22주(71%), 23주(41%), 24주(21%)에서 더 혼하게 관찰되었다.

결론: 고습 환경은 재태 24주 영아에게서 수액투입량을 감소시키고 전해질 불균형을 개선시키는 효과가 있었다. 하지만 이러한 효과는 재태 22-23주 영아에 있어서는 나타나지 않아 더욱 개선된 초미숙아 환경관리가 요구된다.