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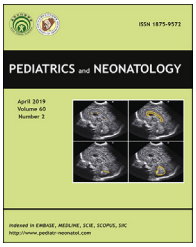

Original Article

The association of early postnatal weight loss with outcome in extremely low birth weight infants

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Key Words
ELBW;
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Abstract *Background:* To compare outcomes of extremely low birth weight (ELBW) infants having different weight losses in the first 3 days of life.
Methods: One hundred and twenty six ELBW infants were evaluated retrospectively for weight loss percentages on the third day of life compared to their birth weight. We examined the weight loss on the third day of life compared to the birth weight for the ELBW infants and tested its association with mortality and morbidities. The mortality was subgrouped as overall mortality and mortality in the first 7 days of life. The morbidities were patent ductus arteriosus (PDA), intraventricular hemorrhage (IVH) and bronchopulmonary dysplasia (BPD). BPD was defined as need for supplemental oxygen at 36 weeks' postconceptional age. We grouped the infants into four quartiles according to weight loss percentage on the third day of life: Group 1 (Quartile 1), infants with weight loss of 0—3% of birth weight; Group 2 (Quartile 2); infants with weight loss of 3.1—7.5%, Group 3 (Quartile 3), infants with weight loss of 7.51—12%; and Group 4 (Quartile 4), infants with weight loss of more than 12%. The mortality and morbidities were analyzed according to these groups and other risk factors.
Results: Overall mortality and mortality in the first 7 days of life were significantly higher in Groups 1 (36% and 27%) and 4 (43% and 24%), compared to Groups 2 (10% and 10%) and 3 (18% and 9%), respectively.
Conclusion: Weight loss less than 3% and more than 12% was significantly associated with an increase in mortality. There was a positive correlation between weight loss on the third day of life and IVH.

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Conclusion: Inappropriate weight loss in ELBW infants is associated with increased mortality and IVH. Appropriate weight loss can improve outcomes in this population.

1. Introduction

Extremely low birth weight infants (birth weight <1000 g, ELBW) are exclusive prematures and they have a higher body and extracellular water content than term infants. During the first few days of life, they undergo a physiologic decrease in extracellular fluid (ECF) accompanied by early postnatal weight loss (EPWL). The physiologic contraction of ECF may not occur in preterm infants if inappropriately high fluid or sodium intake is provided and this is reflected by a lack of EPWL.[1] Physiological weight loss in the first 3 days is important in ELBW.[2,3] Abnormalities in body fluid metabolism and a problem in weight loss during early postnatal life result in significant morbidities in preterm infants.[4] These are associated with BPD, NEC, RDS and PDA.[3–6]

Respiratory problems, particularly respiratory distress syndrome (RDS), hypercarbia, hypernatremia and severe acidosis are risk factors for intraventricular hemorrhage (IVH). The relationship between weight loss percentage and subsequent hyperbillirubinemia was documented.[7] An association of IVH and hypernatremia has been reported[8] but postnatal weight loss as a risk factor for IVH has not been described in the literature. Inappropriate weight loss can lead to acidosis and serum sodium abnormalities. IVH has been shown to be related to adverse neurodevelopment outcomes[9] and it is a factor influencing quality of life of ELBW infants.[10]

The current study was undertaken to evaluate the association between postnatal weight loss and mortality and IVH among ELBW infants.

2. Methods

We retrospectively analyzed 126 ELBW infants admitted to the tertiary neonatal intensive care unit in our hospital over 2 years. We selected infants who survived beyond 72 h of age as our study subjects. All infants' initial and subsequent fluid treatments were the same, following the protocol of our hospital (first day 70 cc/kg, second day 90 cc/kg, third day 110 cc/kg, at fluid regimen of our clinic, kg is based on birth weight until the baby reaches birth weight). All infants were nursed in high humidity (90–95%). The fluid regimen was regulated according to changes in electrolyte values of the infant. The demographic characteristics, birth weight and weight on the third day, percentage of weight loss and the morbidities (Patent ductus arteriosus (PDA), intraventricular hemorrhage (IVH) and bronchopulmonary dysplasia (BPD), severe hyponatremia (<125 mEq/L) and severe hypernatremia (>152 mEq/L) were recorded. We grouped the infants into four quartiles according to weight loss percentage on the third day of life: Group 1 (Quartile 1), infants with weight loss of 0–3% of the birth weight; Group 2 (Quartile 2), infants with weight loss of 3.1–7.5%; Group 3 (Quartile 3), infants with weight loss of 7.51–12%; and Group 4 (Quartile 4), infants with weight loss of more than 12%. Our study was approved by the local ethics committee.

2.1. Statistical analyses

SPSS 16 for Windows® was used for statistics in the study. Statistical analyses were carried out using Student's t-test and chi-square test. Kaplan Meier test was used for survival analysis and the data were expressed as mean ± SD. Cox regression analysis was performed for the multivariate analysis to detect factors that had an effect on survival. A p-value of <0.05 was considered statistically significant.

3. Results

We included 126 ELBW infants in our study. Mean weight loss percentage compared to birth weight was 0.84 ± 1.04% in Group 1, 5.41 ± 1.26% in Group 2, 7.53 ± 1.16% in Group 3 and 15.88 ± 4.47% in Group 4. Infants having less than 3% (Group 1) or more than 12% (Group 4) weight loss were analyzed as an inappropriate weight loss group. Infants having 3–12% (Groups 2 and 3) weight loss were analyzed as an appropriate weight loss group. Demographic characteristics of patients were not different between the groups. Severe hyponatremia or hypernatremia were not found. Demographic patterns of the groups are shown in Table 1.

In 126 preterm infants the mean postnatal weight loss on the third day of life was 7.84 ± 6.07% of birth weight. Birth weight was regained at a mean postnatal age of 12 ± 5 days, but significantly earlier (10 ± 5 days) in Group 1 and later (14 ± 4 days) in Group 4, as expected.

Overall mortality and mortality in the first 7 days of life were significantly higher in Groups 1 (36% and 27%) and 4 (43% and 24%), compared to Groups 2 (10% and 10%) and 3 (18% and 9%). Weight loss less than 3% and more than 12% were significantly associated with an increase in mortality (Fig. 1).

Birth weight quartiles, gestational week quartile, and weight loss quartile significantly affected mortality in univariate survival analysis (Table 2).

Birth weight (<750 g vs. 751–1000 g), gestational week (<25 vs. 26–30 vs. 31–33 weeks), and weight loss in third day quartiles were included in the Cox regression analysis. Analysis showed that birth weight (<750 g) and inappropriate postnatal weight loss (Quartile 1 and Quartile 4) independently increased the risk of death, HR: 2.890

Table 1 Demographic characteristics of patients.

	Groups 1 and 4 n = 64	Groups 2 and 3 n = 62	p
Gestational age (weeks) (mean ± SD)	26.6 ± 2.2	26.9 ± 2.3	0.44
Birth weight (gr) (mean ± SD)	819 ± 184	839 ± 119	0.24
Gender (M/F)	33/31	35/27	0.59
Low APGAR			
Yes	29 (45.2%)	32 (51.8%)	0.58
No	35 (54.8%)	30 (48.2%)	
Preeclampsia			
Yes	17 (26.6%)	17 (27.4%)	1.00
No	47 (73.4%)	45 (72.6%)	
Oligohydramnios			
Yes	11 (17.2%)	9 (14.5%)	0.80
No	53 (82.8%)	53 (85.5%)	
Polyhydramnios			
Yes	3 (4.7%)	2 (3.2%)	1.00
No	61 (95.3%)	60 (96.8%)	
PPROM			
Yes	9 (14.1%)	8 (12.9%)	1.00
No	55 (85.9%)	54 (87.9%)	
SGA			
Yes	15 (23.4%)	9 (14.5%)	0.25
No	49 (76.6%)	53 (85.5%)	
Diabetes Mellitus			
Yes	1 (1.6%)	3 (4.9%)	0.35
No	63 (98.4%)	58 (95.1)	

(95% CI: 1.406−5.944 p = 0.004) and HR: 2.462, (95% CI: 1.135−5.340, p = 0.023), respectively.

When mortality was compared between Group 1 and the appropriate weight loss group (Groups 2 and 3), the overall mortality and mortality in the first seven days of life were significantly higher for Group 1 (p = 0.015, p = 0.026, respectively). When Group 4 and the appropriate weight loss group (Group 2 and 3) were compared, the overall mortality and mortality in the first seven days of life were significantly higher in Group 4 (p = 0.003, p = 0.007, respectively).

A total of 123 infants had IVH. The classification system for intraventricular hemorrhage was initially described by Papille and colleagues.[11] Their grading system is based on the presence of subependymal and intraventricular hemorrhage, ventriculomegaly, and parenchymal abnormalities. Grade 1 is subependymal hemorrhage only; grade 2 is subependymal and intraventricular hemorrhage; grade 3 is subependymal and intraventricular hemorrhage and ventriculomegaly; and grade 4 is subependymal and intraventricular hemorrhage, ventriculomegaly, and intraparenchymal abnormalities. Twenty -three infants had Grade 1 IVH (18.6%), 71 infants had Grade 2 IVH (57%), 10 infants had Grade 3 IVH (8%), and 19 infants had Grade 4 IVH (15.4%). There was a positive correlation between weight loss and IVH (r = 0.263, p = 0.006). This means that as weight loss percentage increased, risk for IVH was increased.

PDA was detected in 26 (40%) infants in the inappropriate weight loss group and 27 (43%) infants in the appropriate weight loss group. There was no significant difference between the groups for having PDA (p = 0.97). There was also no significant difference between Groups 1 and 4 (p = 0.96).

BPD was detected in 9 (14%) infants in the inappropriate weight loss group and 14 (22%) infants in the appropriate weight loss group. There was no significant difference between the groups for having BPD (p = 0.43). There was no a significant difference between Groups 1 and 4 (p = 0.6).

Twenty-four infants were small for gestational age (SGA). Weight loss in ELBW infants in the first 3 days was less in SGA infants as compared with appropriate for gestational age (AGA) infants (4.6% vs. 8.6%, p = 0.003).

4. Discussion

There is no precise guideline for fluid therapy in ELBW infants, and there is no specifically defined weight loss limit for ELBW infants. Our study showed that postnatal inappropriate weight loss of less than 3% or more than 12% on the third day increases mortality.

During the first few days of life, appropriate fluid and electrolyte balance is reflected by an approximate weight loss of 15% in premature infants with very low birthweight.[5,12] It was suggested that fluid restrictions could reduce the mortality and morbidity of low-birth-weight infants.[6] With restricted water intake, there are trends toward increased risk of dehydration and reduced risks of BPD, intracranial hemorrhage, and death, but these trends are not statistically significant.[13] The impact of postnatal weight loss was not described clearly in these studies. There is a lack of scientific evidence about the utility of body weight in making decisions to prevent morbidities regarding fluid therapy in this period.

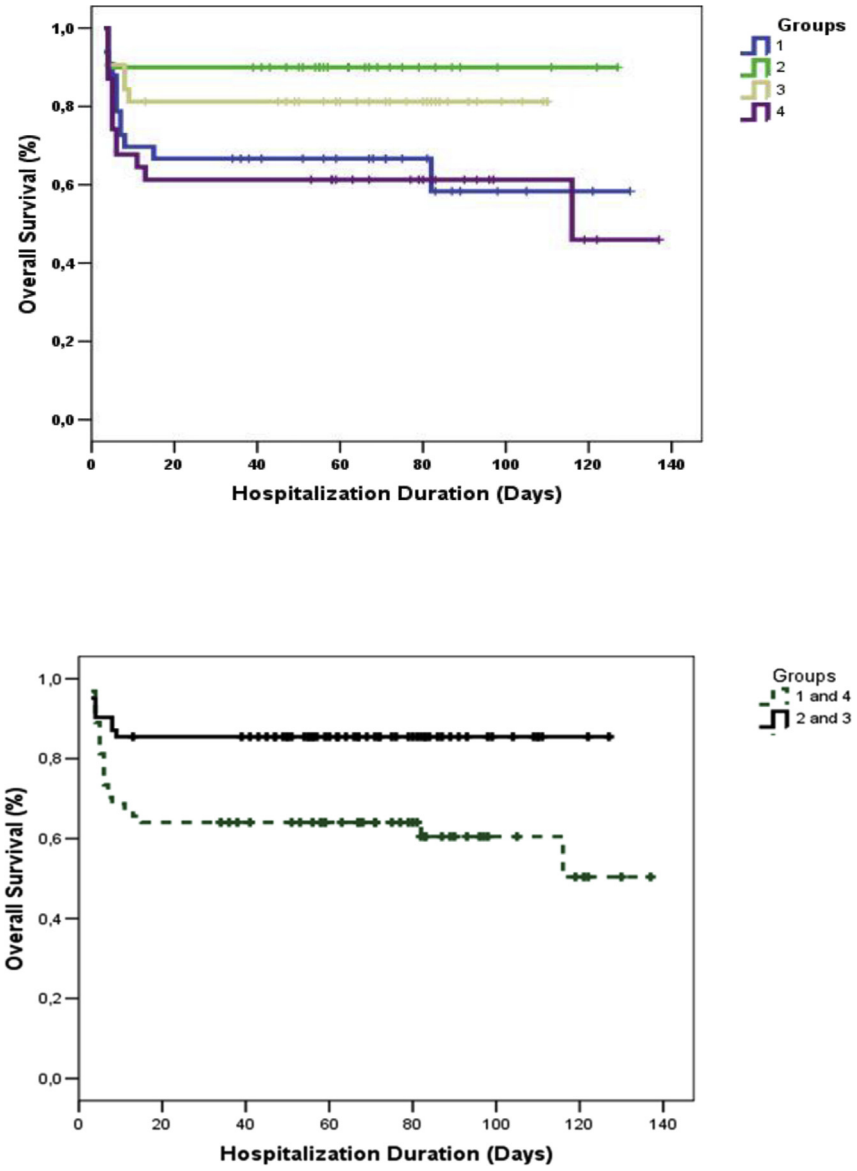

Figure 1 Overall mortality of groups according to weight loss on the third day of life.

Table 2 Factors that affect the survival in univariate analysis.

	Survival rate (%)	p
Birth weight		
<750 g	43.8%	<0.001
751—1000 g	82.8%	
Gestational week		
<25 week	57.5%	0.011
26—30 week	77.9%	
31—33 week	100.0%	
Weight loss in third day		
Quartile 1	63.6%	0.032
Quartile 2	90.0%	
Quartile 3	81.3%	
Quartile 4	58.1%	

Inadequate weight loss may lead to pulmonary edema, lower lung compliance, and cardiac impairment. Less weight loss during the first 10 days of life was associated with an increased risk of BPD.[4] In our study, BPD did not differ between the groups, but we evaluated only the third day weight loss. It is early to evaluate the process to diagnose BPD in the postnatal 36th gestational week. However, the weight losses could have changed on the 10th day or later.

Excessive weight loss may lead to dehydration, hypotension, hypernatremia and renal impairment. Hypernatremia has been shown to cause brain shrinkage and resultant vascular rupture with cerebral bleeding and IVH. In response to brain shrinkage induced by hypernatremia, the human brain initiates an adaptive response to form idiogenic osmoles that increase intracellular sodium concentrations and restore lost water.[14] Lim et al. showed that fluctuations of sodium seemed to be related to early severe IVH among preterm infants.[8] In our study, severe hyponatremia or hypernatremia was not detected, but fluctuations in sodium

were not detailed. However, in the inappropriate weight loss group, fluctuations of sodium were expected. In our group, as the weight loss percentage increased, risk for IVH increased, thereby providing a reasonable explanation for the findings of Lim et al.[8]

It has been proven that restricted water intake significantly increases postnatal weight loss and significantly reduces the risk of PDA.[13] In different studies, a high volume of fluid intake is associated with PDA.[15,16] In our study, there was no difference between the groups regarding to PDA. This can be a result of a high PDA rate in the groups because the study design involved only ELBW infants. We did not compare the water intake between the groups because the protocol used in our center was standard at the beginning and then modified according to weight loss, electrolyte balance and clinical findings.

Weight loss in ELBW infants in the first 3 days was less in SGA infants as compared with AGA infants and this is consistent with the literature.[1,17] Infants who are SGA usually have a significantly smaller postnatal weight loss because they are maturationally capable of achieving an adequate caloric intake earlier than premature neonates. However, less EPWL is not clearly determined in SGA infants. It could be because of compensatory mechanisms formed by on-going response to intrauterine stresses.

Our study has some limitations. The sodium levels were recorded as existence of severe hypernatremia or hyponatremia. The levels of the sodium were not recorded if there was not hyponatremia or hypernatremia. There was no severe hypernatremia or hyponatremia so we did not record them, this is a limitation.

In conclusion, inappropriate weight loss in ELBW infants, is associated with increased mortality. In ELBW infants, as weight loss percentage increases, so does the risk for IVH. Decisions while treating ELBW infants must be made by targeting an appropriate weight loss of more than 3% and less than 12% for the first three days of life. Appropriate weight loss strategies can improve outcomes in this population.

Conflict of interest

The authors have no conflicts of interest releavant to this article.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.pedneo.2018.06.003.