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I can achieve intrauterine growth rete if you give me enough nutrition: preterm infant born at ≤ 29 weeks gestation

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Abstract

Introduction: In general, everyone believes that the smallest preterm infants should achieve normal intrauterine growth rates, but many thinks that this is not possible with current nutrition guidelines. There is resistance to giving enough nutrition for fear of "toxicity". The difference in weight Z-score between birth and a corrected gestational age (CGA) at discharge is assess in postnatal growth in our unit.

Material and methods: An observational study was done between January 2018 and December 2020 where all cases that had ≤ 29 weeks of GA at birth and survived to 36 weeks corrected GA or that were discharged home. An aggressive nutrition protocol including parenteral as well as enteral nutrition was followed. Patients and their weight trajectory was plotted on the Fenton 2013 growth curve. The patients who had had a smaller WZP difference were also plotted.

Results: A total of 32 cases were found. The median change in Z-score between birth and discharge of the whole group was -0.52 (IQR 0.53). Six of 32 (19%) had a more than one WZP, all of whom had severe pathologies. The median decline in Z score for this group with poor growth was 1.24 (IQR 0.22). There were 26 cases with a < 1 WZP (81%) and a median Z score fall of 0.39 (IQR 0.55). No important complications secondary to the ingested volumes or parenteral nutrition were reported.

Conclusion: The group of cases with a > 1 WZP drop had severe pathologies. All the other cases had adequate growth parallel to normal weight growth charts and a few cases had some catch-up growth. The study showed that it is possible for many preterm infants to achieve normal intrauterine growth rates if they are given enough nutrition, but bigger multicenter studies are needed to confirm these findings.

Key words: Very preterm infants, Z-score on weight, neonatal nutrition, appropriate intrauterine neonatal growth

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Introduction

There is a wide variety of nutrition concepts followed in newborn units around the world. In general, most believe the smallest preterm infants should achieve normal intrauterine growth rates(1) but some also think that this is not possible with current nutrition guidelines(2). There is resistance to giving enough nutrition for fear of "toxicity," especially with parenteral nutrition(3-5), mainly of proteins and lipids. Another limitation is the fear of volume overload after the second week of life because bronchopulmonary dysplasia may occur although this has not been proven to result from the feeding volume(6). Furthermore, there is also a fear that overfeeding preterm infants may cause an "excess adiposity"(7) or metabolic diseases in adulthood. In regard to adiposity, Dr. Lingwood et al. have shown that adiposity is related to poor nutrition intake during the first two weeks of life, including lipids, and not to excessive nutrition(8).

It would take a few pages to discuss all the arguments for and against these assertions because they have a basis in reality though it is one that is often distorted and out of context. However, no one has shown that it is harmful to give the baby enough nutrition to achieve normal intrauterine growth rates before 36 weeks corrected gestational age (CGA). On the other hand, there is sufficient evidence that poor nutrition and poor growth have serious adverse consequences(1, 9-12).

For many years, volumes that many would consider too high have been used in our units. Nevertheless, more and more people are now accepting them (13-15). This higher volume was based on observations starting many years ago when we cared for preterm babies until they reached a weight of more than 2,500 grams and could be put up for adoption. When they were fed on demand, these preterm babies ingested between 200 and 300 mL/kg/day and occasionally more. After weighing benefits versus risks, our conclusion was that at least 200 mL/Kg/day should be provided after the initial stage when growth began, and the basic problems of the first few weeks had already been dealt with. Also, our concept of parenteral nutrition has changed, it is now started earlier and with higher quantities of macronutrients in a more concentrated nutrition to limit the initial volume. In recent years, the EpicLatino (16), a Latin American database, has shown that our unit has much better nutrition results than almost all the other units. The objective of this work is to describe these nutritional results in small preterm infants starting from 2018 when a minimal handling protocol to prevent intraventricular hemorrhage was set up.

Material and methods

In late 2017, a minimal handling protocol was set up to prevent intraventricular hemorrhage in preterm babies born at ≤30 weeks gestation. The protocol included high parameters of parenteral nutrition and initiation of enteral nutrition on the first day of life and is still being continued.

In summary, for our nutrition protocol:

1. Parenteral fluids are started by central catheter with a mixture of 3% amino acids and 10% dextrose and continue until it is possible to prepare a personalized parenteral nutrition (within the next 12-36 hours) at an infusion of 70 mL/Kg/day. Humidity is kept at 80% and handling is minimal. This amount is not increased if diuresis remains appropriate (> 1mL/K/hour).
2. Personalized parenteral nutrition is calculated using the following parameters:

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2.1. Protein at 4 gr/Kg/day
2.2. Lipids at 3 gr/Kg/day
2.3. Glucose 4 mg/Kg/minute
2.4. Vitamins, calcium, phosphorus, magnesium (after the 3rd day) and trace elements.
These parameters are not changed for 3 days and parenteral nutrition is concentrated to about 80 mL/kg/day.

3. Enteral nutrition is started in the first 24 hours with a preterm formula (we do not have bank milk) with 1-3 mL/K every 3 hours (approx. 10-20 mL/K/day) until we have the mother's milk; this is continued for 3 days.
4. After the 3rd day the enteral nutrition is increased, and parenteral nutrition decreased to maintain approximately 4 g/Kg/day of protein in total. This assumes a fecal loss of around 15-20% and considers the fact that the digestible and usable protein of breast milk that is used for growth is only 1-1.5 gr/K/day before fortifying, especially after the second week (17-19). As soon as the mother is able to produce enough breast milk, it is fortified with bovine fortifiers since no other type is available to us. The amount is increased 20-40 mg/Kg/day based on tolerance until it reaches 200 mL/Kg/day. Each patient is graphed on Fenton curves and, occasionally, their nutrition needs to be increased due to poor growth.
5. If the patient has grown adequately at around 35-36 weeks corrected gestational age, fortification or preterm formula is discontinued. They are often discharged at this time.

The Z score, a measure that represents the distance from the 50th percentile of a growth curve, with "0" being the 50th percentile, negative numbers if they are below and positive if they are above, is used to monitor growth. The Z score allows mathematical calculations while the percentiles do not. The difference in Z-score between birth and a specific gestational age was chosen because birth weight is the non-modifiable reality for each patient, and it is necessary to know what growth occurred afterwards. The measurement of g/Kg/day often used in units every day was nor used since for investigation purpose the growth rate changes according to gestational age. Using growth in g/kg/day from the 50th percentile Fenton curve at week 25-26, normal growth is: 18.2 g/kg/day. On the other hand, if it is calculated at 35-37 weeks, it is 15.9 g/kg/day.

As of January 1, 2018, all cases with ≤ 29 weeks of GA at birth that survived to 36 weeks CGA, or that were discharged home if this occurred earlier were reviewed for this report. The weight Z score was calculated at birth using the 2013 Fenton curves and at discharge to see the difference, and it was also calculated at 36 weeks in preterm infants who had not gone home at the CGA.

Patients who had lost more than one Z-score point are described separately to show the weight trajectory plotted on the Fenton 2013 growth curve and review their clinical characteristics. All the other patients who had had a smaller Z-score difference were also graphed to see their trajectory on the Fenton curves. The number of cases, medians, and interquartile ranges for all groups are described. An exception was obtained from the ethics committee.

Results

The total number of cases born at ≤ 29 weeks of GA between January 2018 and December 2020 that survived 36 weeks or were discharged home was 32. The median change in weight Z-score between birth and discharge of the entire group was -0.52 (IQR 0.53). Six patients had a change in Z score between birth and discharge of more than 1 point (19%) including 1 case that had a

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difference of 2.2; all cases had severe pathologies (Figure 1). The median decline in the weight Z score of this group with poor growth was 1.24 (IQR 0.22). All preterm infants at discharge who had more than 1 point difference in the Z-score already had this difference at 36 weeks CGA. Median weight gain in g/kg/day using weekly weight after regaining birthweight was 21,3 g/kg/day for the hole group and 21,5 for the patients in figure 2.

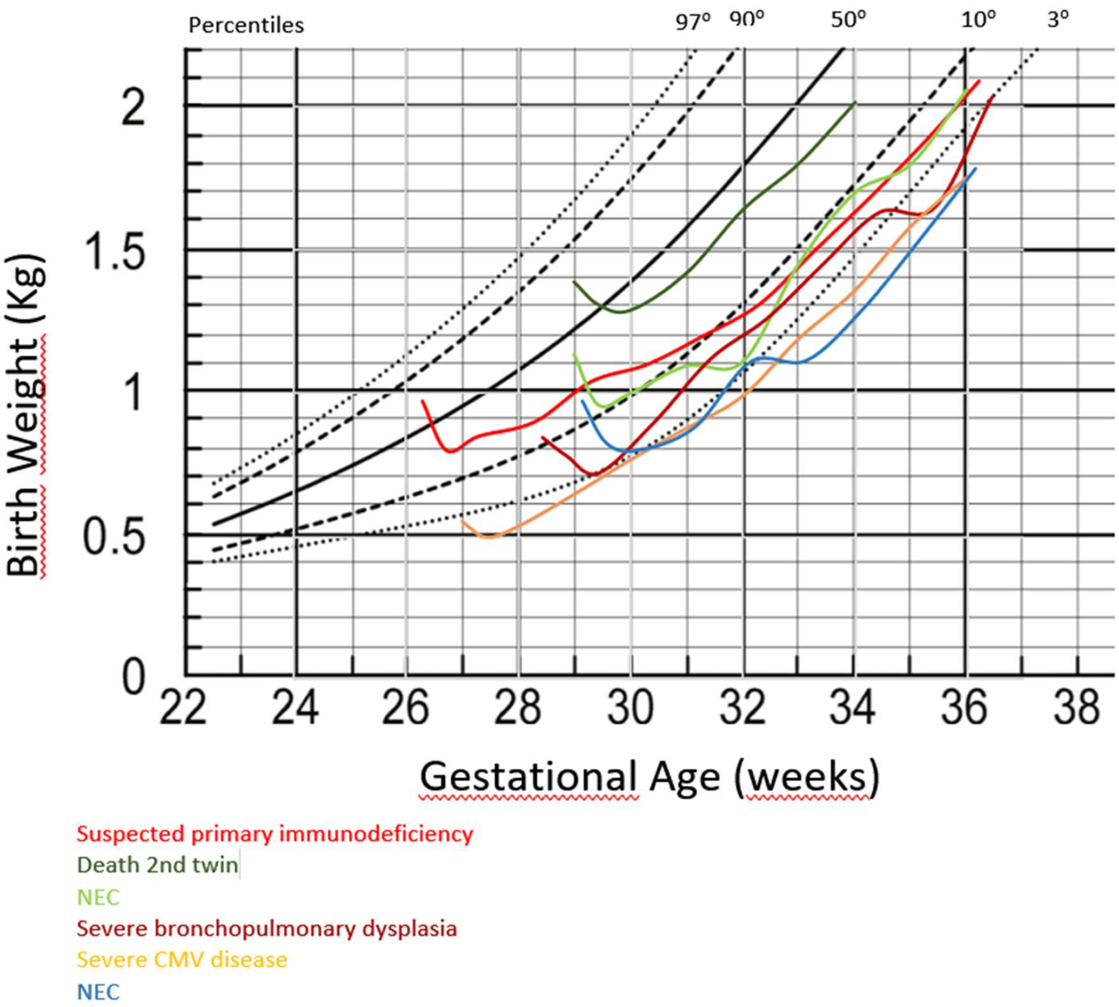

Figure 1: Growth curves Graph of six preterm infants (19%) whose weight Z-scores between birth and discharge fell more than 1 point and their underlying pathologies plotted on the 2013 Fenton curves up to 36 weeks of corrected age or discharge. NEC: necrotising enterocolitis, CMV: cytomegalovirus.

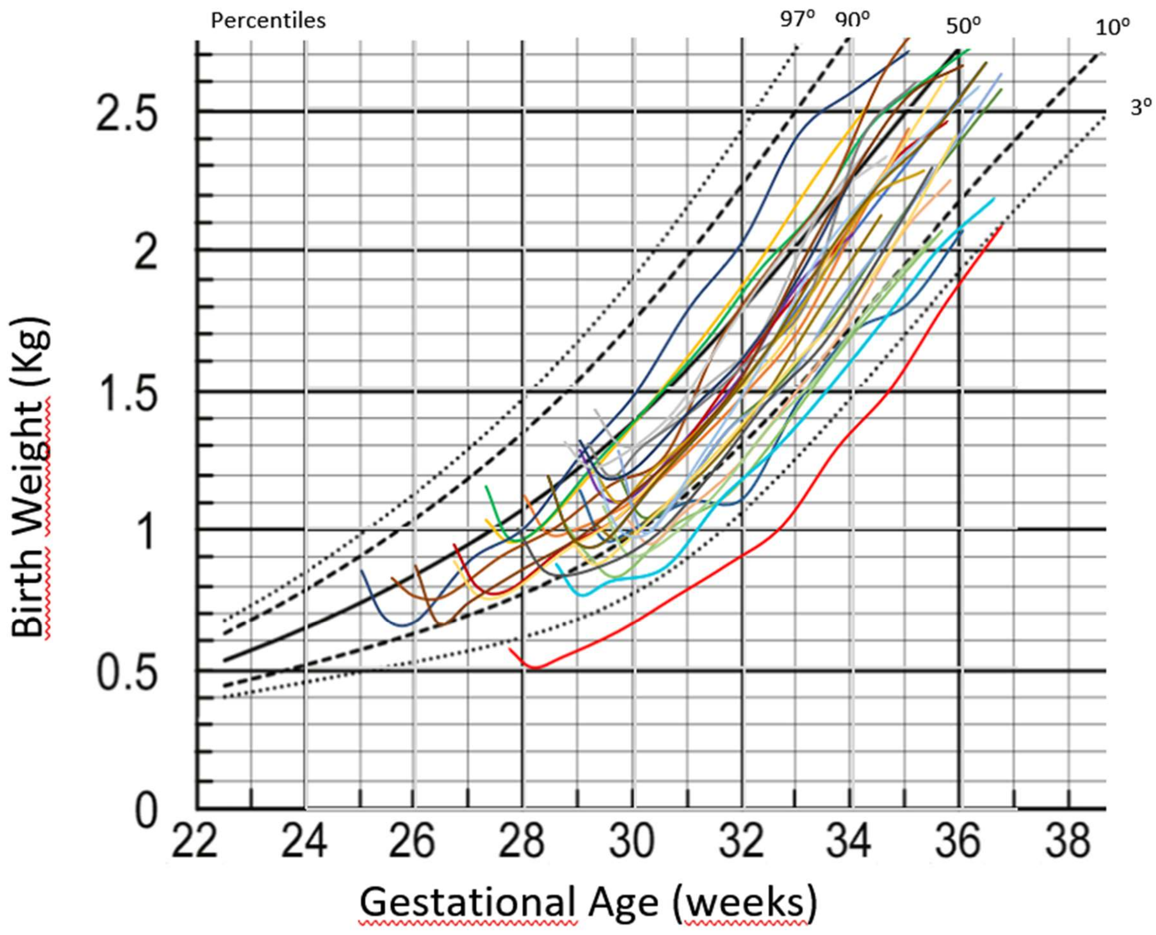

Figure 2: The patients with a fall of less than one Z score point between birth and 36 weeks PCA (81%) graphed according to their growth curve (Fenton 2013). Note the initial drop in volume contraction with the subsequent increase parallel to the growth curves. Some reach 36 weeks near the birth percentile.

There were 26 cases with a <1 point drop in Z score (81%). The median weight Z score drop was 0.39 (IQR 0.55) (figure 2).

All cases had the expected initial fall in weight within the first 2 weeks. All patients reached the 200 mL/Kg/day. No complications secondary to the ingested volumes were reported. Diuretics were not used in any of these cases, and parenteral nutrition was adequately tolerated except for occasional hyperglycemia that was corrected by reducing the glucose intake.

Discussion

Most of infants achieved normal intrauterine growth rates. The exceptions were those described who had severe pathologies, but no reported adverse events due to nutrition. The initial drop in weight due to volume contraction that occurs in all patients and is clearly considered physiological and desirable in the literature on fluids (20) was observed in all cases. However, the contraction should only be one of volume. There should be no malnutrition caused by poor intake, a result very frequently seen in units due to the “fear” of toxicity, especially of parenteral nutrition. Intrauterine growth should be measured from nadir, or when birthweight is regained, but since nutrition is often unknown in the first weeks, it is measured from birth and a slight drop is accepted as normal. The change from birth to discharge/36w in Z score was small in 81% of all cases but was greater in the group of patients (19%) described who had serious illnesses.

It would have been interesting to also document HC and length, but every week measurements in the unit are not accurate. Limitations include inadequate measurements, the shape of the head (dolichocephaly for example), operator-dependent variability, the slow growth resulting in failure to record small changes, and several other factors that influence brain growth that could be playing a role. Only prospective measurements would be reliable.

The cases of hyperglycemia were mild. The glucose was decreased if the plasma level was over 130 mg/dL. None were diagnosed as hyperglycemic.

It is interesting to note that some acute pathologies during the hospital stay such as necrotizing enterocolitis, caused growth to decelerate for a period. It accelerated again but never managed to compensate for the initial drop as seen in Figure 1. Other pathologies (although this was a single case) such as bronchopulmonary dysplasia have a later growth deceleration, probably when the effort is made to give the patient enough nutrients to go home or possibly due to the use of corticosteroids. On the other hand, the pathologies that cause slow, even growth in the infant seem to have an intrauterine origin.

Most cases (81%) show adequate growth rate that approaches the birth percentile but does not often reach it. However, the growth after around the weight nadir is parallel to the growth curves which for us is equivalent to normal intrauterine growth rate.

Growth by g/Kg/days was 21.3 to 21.5 from the regained birthweight but this is not an accurate measurement as described in the section material and methods.

There are no universally accepted postnatal nutrition standards for the smallest preterm infants during their stay in the unit, but there is a universal consensus that these infants should achieve normal intrauterine growth rates as discussed in the introduction. Fear of toxicity has limited the amount of nutrients used in many units. This study is an effort to show that normal intrauterine growth is possible for many preterm babies if they are given enough nutrition. The strength of the study is that aggressive nutrition has been administered without complications for several years, but as a limitation, it is a small, retrospective, observational study that does not control the variables that could affect the results and has no power to rule out complications.

Conclusions

This study shows that it is possible for many preterm babies to experience normal intrauterine growth if they are given enough nutrition, but larger, multicenter studies are needed to confirm these findings.

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