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Early postnatal growth in preterm infants

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Changes in weight of 50 preterm infants (gestational age 32.7 ± 0.3 weeks, birthweight 1772 ± 49 g) were studied during the period of the 0—4 postnatal weeks. Intrauterine weight gain of fetuses with equivalent gestational age, weight percentile position and sex was calculated and used as a control. Study infants achieved significantly less weight by age of 4 weeks (116.2 ± 1.2%) than it could have been expected theoretically (144.7 ± ± 1.0%). Growth performance did not correlate significantly with calorie intake, but was closely related with gestational age.

The outlook for survival of low birthweight and/or preterm infants with major pathology has been improving remarkably due to recent progress in intensive perinatal care. The successful treatment of severe acute disorders of neonatal adaptation, however, results in new challenges to the clinician. Among these the clarification of the criteria of optimum postnatal growth and nutrition of preterm infants [4] seems to have a special importance from the point of view of long term prognosis [2].

Our study was undertaken to investigate the growth performance of preterm newborn infants during the highly critical period of the first four postnatal weeks, on the one hand. On the other hand, an attempt was made to look for factors which determine or influence early postnatal growth in preterm infants.

Patients and Methods

During the period from 1/1/1983 to 31/12/1983 all preterm (gestational age ≤ 36 weeks) babies admitted to our Neonatal Intensive Care Unit within 24 h of birth were enrolled in the study, provided that full or partially oral feeding could be established within 7 days postnatally and hospital care was necessary for 4 weeks at least. Those with congenital malformations were excluded but not the ones with any other kind of pathology. After all, the data of 50 preterm babies (33 males and 17 females) with gestational age and birthweight (mean±SEM, range in parentheses) of 32.7 ± 0.3 (28—36) weeks and 1772 ± 49 (1050—2500) g, respectively, could be used for further analysis. Of the 50 study subjects 14 were considered to be small for dates both by physical characteristics and their weight for gestational age (≤ 10 percentile).

In 15/15(30%) cases the pregnancy was complicated with pathology; 6/50(12%) newborn infants suffered from severe prepartal or sub partu asphyxia and needed resuscitation. 35/50(70%) babies developed

hyaline membrane disease or asphyxia-related cardiorespiratory disorders; all of them needed oxygen or ventilation therapy. Antibiotics were administered to 21/50(42%) patients because of proved or suspected infections of various origin. In 4 of the newborn infants the postnatal course was completely uneventful.

For feeding, banked human milk was used primarily. 8 infants received only 5—10% glucose in water drip infusion throughout the first 3.1 ± 0.5 days of life. In 41 babies human milk feeding had to be completed with 5—10% glucose in water infusion for 4.6 ± 0.4 days, before full oral feeding could be established. From day 13.7 ± 1.2 onwards, 28 infants received a humanized formula milk (Robebi-A EGYT) supplementation. All babies were fed either by bottle or gavage. They were weighed daily to an accuracy of 10.0 g. Total calorie intake was calculated every day in each infant, considering the daily volume and quality of food and/or infusion fluid administered. The energy content of the banked human milk and the formula milk was determined by using reference data as to their nutrient composition.

For statistical analysis standard mathematical methods were used. Changes in weight were expressed both in g/kg and per cent of birthweight, considering the weight at birth as being 100%, in the latter case. In an attempt to qualify the postnatal growth it was assumed that it should closely correspond to the growth rate of fetuses of the same gestational age and sex. Therefore, for comparison the 4 weeks time growth rate of fetuses matched by gestational age, sex and weight percentile position, was calculated by using our local intrauterine growth charts.

Results

Table I shows the weekly changes in calorie intake, body weight and the incremental changes in weight of the 50 preterm babies studied. It can be seen that most of the infants regained their birthweight by the age of 2 weeks, from which time onwards a steady rise in weight could be observed (Fig. 1). In fact, however, by the end of the 4th postnatal week the study infants gained significantly less weight than their theoretical in utero controls (116.2 ± 1.2% vs 144.7 ± ± 1.0%, $p < 0.001$; birthweight considered to be 100%). On correlation analysis no significant relationship was found between mean total energy intake (120.8 ± 2.2 kcal/kg/day) and percentual rise in body weight throughout the 4 weeks study period, and no significant correlation existed between the weekly incremental changes in weight and weekly mean calorie intake either.

Table I

Weekly calorie intake, percentual changes in weight and incremental changes of body weight in 50, 0—4 weeks old preterm babies (mean ± SEM). Birthweight considered to be 100%

	Calorie intake kcal/kg/day	Body weight in per cent of birthweight	Weekly incremental changes in weight, g
1st week	83.5±3.1	96±0.6	— 66.2±13.3
2nd week	131.2±3.1	99±0.8	+ 69.8±10.0
3rd week	133.9±2.7	106±0.9	+ 125.0± 8.5
4th week	133.8±3.1	116±1.2	+ 172.2±10.8

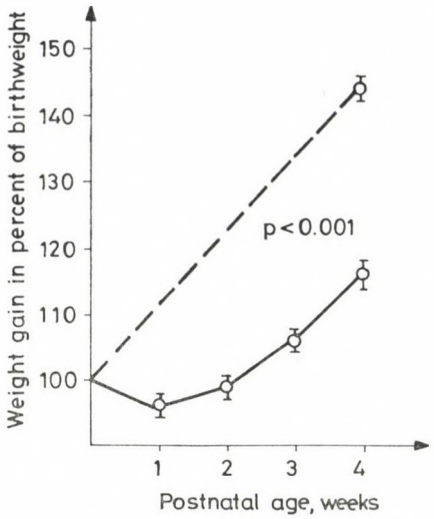

FIG. 1. Postnatal weight gain (mean ± SEM) in 50 preterm infants (——) expressed in percentage of birthweight (= 100%), compared with calculated weight gain of fetuses with equivalent gestational age, weight percentile and sex (— —), during a period of 4 weeks

In studying the relationship of gestational age and birthweight to postnatal growth performance, a significant positive correlation was found between the maturity of the infants and the percentage increase in weight, attained by 4 weeks age ($r = 0.43$, $p < 0.01$). Correspondingly, a strong negative correlation ($r = -0.66$, $p < 0.001$) existed between gestational age and the difference between the optimum (control) and the *de facto* growth performance produced by the end of the study period (Δ OPG). Birthweight was not related with early changes in weight.

In order to eliminate the effect of the initial weight loss and stagnation, the weight gain of each infant between his or her minimum and peak value has also been calculated and expressed as a function of birthweight kg. Figure 2 shows that minimum-maximum weight increase/kg birthweight correlated significantly ($r = 0.53$, $p < 0.001$) with gestational age, but again, not with calorie intake. Furthermore, no close relationship was found between calorie intake and gestational age either.

Early postnatal growth of newborn infants may well be influenced by the duration of weight stagnation and/or the extent of the initial weight loss as well. Therefore, we examined whether or not the gestational age correlated with the extent of maximum weight loss and the postnatal age of babies when they began to thrive steadily, after having regained their birthweight. No significant correlation could however be detected between these parameter-pairs.

Table II shows some growth characteristics of the 14 small for dates preterm infants when they were con-

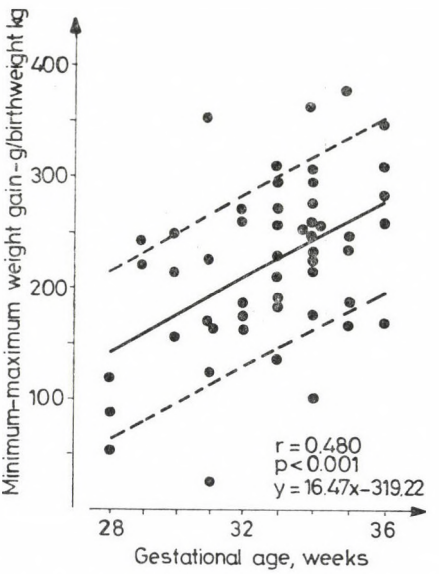

FIG. 2. Minimum-maximum weight gain (g/birthweight kg) by the age of 4 weeks against gestational age in 50 preterm newborn infants

sidered separatedly from normally grown babies. Despite of a closely similar mean calorie intake over the 4 weeks long study period, small for dates infants had significantly less initial weight loss (2.7 $\pm$ 0.6 vs 8.0 $\pm$ 0.7% of birthweight, $p < 0.001$) and began to thrive much sooner (11.6 $\pm$ 0.8 vs 16.5 $\pm$ 0.8 postnatal days, $p < 0.01$) than the normal for dates babies. This may well explain that by the age of 4 weeks, growth retarded infants had gained significantly more weight, expressing it as a percentage of birthweight (24.9 $\pm$ $\pm$ 2.4 vs 12.3 $\pm$ 1.0%, $p < 0.001$) or

TABLE II

Characteristics of early postnatal growth in 4 weeks old small for dates and normal for dates preterm infants (mean $\pm$ SEM)

	SFD (14)	NFD (36)	p
Birthweight (g)	1668$\pm$73	1813$\pm$62	ns
Gestational age (week)	34.3$\pm$0.4	32.1$\pm$0.3	**
Calorie intake (kcal/kg/day)	121$\pm$4.8	119$\pm$5.3	ns
Maximum weight loss (per cent)	2.7$\pm$0.6	8.0$\pm$0.7	***
Thriving begins (day)	11.6$\pm$0.8	16.5$\pm$0.8	**
Weight gain (per cent of birthweight)	24.9$\pm$2.4	12.3$\pm$1.0	***
Minimum-maximum weight gain (g/kg birthweight)	282$\pm$19	196$\pm$10	***
ΔOPG (per cent)	17.5$\pm$3.1	32.8$\pm$1.5	***

Student's *t* test ** $p < 0.01$; *** $p < 0.001$;

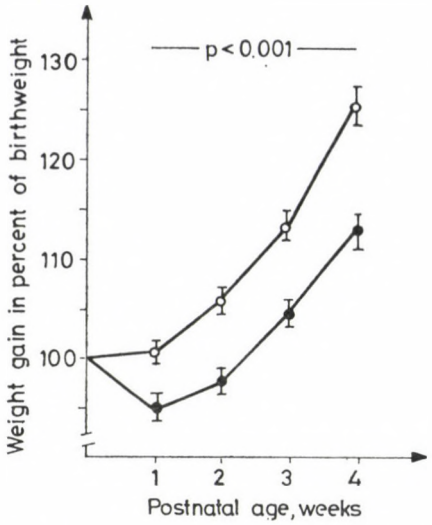

FIG. 3. Early postnatal changes in weight in 36 preterm normal for dates (●—●) and 14 small for dates (○—○) infants (mean ± SEM). Birthweight considered to be 100%

as a weight gain/birthweight kg ratio (282 ± 19 vs 196 ± 10 g, $p < 0.001$). When postnatal growth curves of normal and small for dates infants were compared to each other (Fig. 3) from the age of 2 weeks onwards they seemed to run remarkably parallel. Thus the conclusion was drawn that the growth delay in normally grown preterm infants is probably due to some factor(s) interfering temporalily with food digestion, absorption or utilization. Both maturity per se or gestational age-related perinatal pathology could have a role in this phenomenon, but the present observations provided ground only for speculations.

DISCUSSION

Being borne before term is obviously nonphysiologic, therefore the question arises whether it is possible at all to delineate the normal early postnatal growth of such babies. In spite of well grounded considerations against it, the principle has widely been adopted that the postnatal weight gain of preterm babies should be measured against growth curves of fetuses with equivalent gestational age, percentile position and sex [1, 9].

When comparing the postnatal percentage increase in weight of 50 preterm infants to the percentage rise in weight of 50 fetuses matched for parameters indicated above, a significant delay in growth was observed at the postnatal age of 4 weeks. In contrast with the expected gain in weight of 144.7 ± 1.0% their postnatal weight accumulation was only 116.2 ± 1.2%, on the average. Postnatal slow-down of growth in preterm infants may be caused by a reduced nutrient supply or transient and

partial insufficiency in the utilization mechanisms, or both. As for the first possibility, in accordance with others [3, 7] we could find no relationship between total calorie intake and weight gain of infants, considering the whole study period. From the beginning of the second postnatal week onwards, a calorie intake of around 130 kcal/kg/day was provided to the babies, but the weekly incremental changes in body weight seemed not to be related to the infants' energy supply, neither in the period of weight stagnation (1st— 2nd week), nor in the period when weight gain has already begun (3rd—4th week).

On further search for growth regulating factors we found a very strong positive relationship between gestational age and early postnatal growth. The more mature the infant at birth a higher increase in weight was achieved by the postnatal age for 4 weeks, independently of whether the weight gain was expressed in percentage of birthweight or calculated as a minimum-maximum weight increase per birthweight kg. At the same time, calorie intake, the extent of initial weight loss and the duration of postnatal weight stagnation were not related with the gestational age of the babies.

Gestational age-related early growth delay may be due to perinatal pathology more frequently occurring to more premature babies and interfering in a way with utilization and metabolism of nutrients. A more plausible explanation is, however, that the growth promoting effect of the food supplied in our present clinical practice decreases nearly parallel with the diminishing gestational age of the infants. Consequently, in support of previous reports [3, 5, 6, 7, 8] it may be concluded that calorie intake by itself does not have a primary role in determining early postnatal growth performance. Certainly, much depends on the nutrient composition of the food and also the gestational age-related functional maturity of the newborn infant.

Comparison of the growth parameters of normal and small for dates newborn infants revealed a significantly faster weight gain in retarded than in normally grown babies, in spite of a closely similar mean calorie intake over the whole study period. The explanation for the difference most likely is that small for dates infants being more mature functionally had more efficient food utilization and less severe weight loss, after which they began to thrive much sooner than the normal for dates babies. The notably parallel postnatal weight gain curves of normal and small for dates infants from the time onwards when they had begun to thrive, reflect, however, a similar growth rate capacity in the two groups of infants, if once the period of initial weight stagnation is over. But it is to be emphasized that interpretation of this finding needs caution since the links between fetal nutritional status and postnatal growth are fairly complex, and to investigate it was not the primary aim of the pres-

ent studies. For the reason that small for dates infants had more advanced gestational age than the normally grown babies, the question remains unanswered, whether the difference in growth performance was due to the different maturity or to the different body composition of infants in the two groups.

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