BETTER GROWTH IS PROTECTIVE AGAINST THE DEVELOPMENT OF RETINOPATHY OF PREMATURITY IN EXTREMELY PRETERM INFANTS

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AIM

To investigate the relationship between postnatal growth during hospital stay and development of retinopathy of prematurity (ROP).

BACKGROUND

The risk for a preterm infant to develop ROP is, among other factors, related to:

- Low gestational age and low birth weight z-score
- Postnatal weight gain
- Low total energy intake in the early postnatal period

STUDY DESIGN

Daily nutritional- and breast milk intakes during the first 28 postnatal days, in addition to growth measurements (weight, length and head circumference) and development of neonatal morbidities was prospectively collected from birth until discharge in a Swedish cohort of 90 extremely preterm infants.

RESULTS

Neonatal characteristics are presented in Table 1. Infants without ROP received a higher mean enteral energy (kcal/kg/d) intake during postnatal days 2-28 than infants with ROP ($p=0.026$).

CONCLUSION

Higher early intake of enteral nutrition and improved postnatal growth is associated with normalized retinal angiogenesis, i.e. less retinopathy of prematurity, in extremely preterm infants.

Growth data is presented in Table 2 and Figure 1. Infants not developing ROP had higher postnatal growth z-scores throughout hospitalization compared to their ROP affected peers. Statistically significant differences between the two groups were primarily seen for z-score growth at actual time points, as opposed to delta growth, at postnatal age (PNA) 28 days, postmenstrual age (PMA) 32 and 36 weeks. After adjustment for gestational age and birth weight z-score in logistic regression models significance remained for z-score weight ($OR=0.175$, $p=0.030$) and length ($OR=0.276$, $p=0.012$) at PMA 32 weeks, and z-score length ($OR=0.412$, $p=0.043$) at PMA 36 weeks.

Figure 1. Difference in weight z-score at postnatal age 28 days and postmenstrual age 32 and 36 weeks, where infants with no ROP ($n=17$) had a better weight development than infants with any ROP ($n=61$). $\star p<0.05$.

Table 1. Neonatal characteristics, mean nutritional intakes postnatal days 2 to 28 and presence of ROP. Data is presented as either median (min-max) or n (%).

	Any ROP ($n=61$)	No ROP ($n=17$)	P value
Sex (female)	31 (50.8 %)	4 (23.5 %)	0.045
Gestational age (weeks)	25.3 (22.9-27.9)	27.0 (22.7-27.9)	<0.001
Birth weight (g)	725 (415-1250)	1020 (635-1260)	<0.001
Birth weight z-score	-0.69 (-5.24-0.43)	-0.08 (-2.23-1.28)	0.003
SGA	10 (16.4 %)	1 (5.9 %)	ns
EUGR	14 (24.1 %) ^a	2 (14.3 %) ^b	ns
Total energy intake (kcal/kg/d)	111 (93-149)	123 (92-140)	ns
Enteral energy intake (kcal/kg/d)	83 (4-136)	109 (26-134)	0.026
Total protein intake (g/kg/day)	3.6 (2.7-5.0)	3.8 (2.9-4.4)	ns
Enteral protein intake (g/kg/day)	2.5 (0.1-4.5)	3.4 (0.7-4.3)	ns (0.052)
First day full enteral nutrition (days)	15 (8-63) ^c	11 (8-31) ^d	0.042

Abbreviations and definitions: ROP = retinopathy of prematurity; SGA = small for gestational age, defined as birth weight z-score below -2; EUGR = extrauterine growth restriction, defined as weight z-score below -2 at 36 weeks postmenstrual age; ns = not significant. First day of full enteral nutrition was defined as the first day the infant reached an enteral intake ≥ 150 ml/kg/d.

^a = $n=58$; ^b = $n=14$; ^c = $n=59$; ^d = $n=16$

Note: p-values are statistically significant at the 95 % level.

Table 2. Postnatal growth and presence of ROP. Data is presented as median (min-max). Group any ROP included $n=61$ infants and group no ROP included $n=17$ infants.

	POSTNATAL AGE 28 DAYS			POSTMENSTRUAL AGE 32 WEEKS			POSTMENSTRUAL AGE 36 WEEKS		
	Any ROP	No ROP	P value	Any ROP	No ROP	P value	Any ROP	No ROP	P value
z-score weight	-2.05 (-5.20--0.50) ^a	-1.19 (-2.64-0.53) ^b	0.001	-1.68 (-4.90--0.08) ^a	-0.96 (-2.35-0.98)	0.002	-1.28 (-5.86-0.88) ^c	-0.42 (-2.99-1.95) ^d	0.034
z-score length	-3.14 (-6.16--0.47) ^e	-2.48 (-3.44-0.35) ^f	0.021	-3.62 (-6.30--0.95) ^g	-1.62 (-2.96-0.38)	<0.001	-2.59 (-8.09--0.53) ^h	-0.78 (-2.67-1.53) ^d	<0.001
z-score HC	-1.98 (-3.71--0.33) ⁱ	-1.60 (-2.13--0.50) ^j	0.049	-1.88 (-3.57--0.07) ^g	-0.95 (-2.13-0.78)	<0.001	-1.45 (-5.15-0.86) ^k	-0.61 (-1.29-1.64) ^d	0.001
z-score Δ weight	-1.20 (-2.41-0.56) ^a	-1.15 (-1.91--0.05) ^b	ns	-0.75 (-2.71-0.82) ^a	-0.68 (-1.62-0.40)	ns	-0.05 (-4.59-1.44) ^c	-0.61 (-2.26-1.53) ^d	ns
z-score Δ length	-2.06 (-4.09-0.40) ⁱ	-2.04 (-2.97--0.24) ^f	ns	-1.97 (-5.05-0.78) ^m	-1.33 (-2.70-0.45)	0.010	-1.46 (-5.01-1.30) ⁿ	-0.99 (-1.64-1.36) ^d	ns
z-score Δ HC	-1.18 (-2.79--0.08) ^o	-1.54 (-2.49--0.23) ^j	ns	-1.29 (-2.73-0.55) ^k	-1.09 (-2.16-0.56)	ns	-0.75 (-4.11-2.47) ^m	-0.38 (-1.41-1.75) ^d	ns

Abbreviations and definitions: ROP = retinopathy of prematurity; Δ = delta, delta growth was defined as z-score at actual time point subtracted by z-score at birth; ns = not significant.

^a = $n=60$; ^b = $n=16$; ^c = $n=58$; ^d = $n=14$; ^e = $n=30$; ^f = $n=7$; ^g = $n=59$; ^h = $n=56$; ⁱ = $n=34$; ^j = $n=8$; ^k = $n=57$; ^l = $n=27$; ^m = $n=55$; ⁿ = $n=52$; ^o = $n=33$

Note: p-values are statistically significant at the 95 % level.