Early Human Development (2007) **83**, 527–534

available at www.sciencedirect.com

ScienceDirect

www.elsevier.com/locate/earlhumdev

The effect of perinatal risk factors on growth in very preterm infants at 2 years of age: The Leiden Follow-Up Project on Prematurity

Monique Rijken [a,*], Jan M. Wit [a], Saskia Le Cessie [b], Sylvia Veen [a] on behalf of The Leiden Follow-Up Project on Prematurity

[a] *Department of Paediatrics, Leiden University Medical Center, Leiden, the Netherlands*
[b] *Department of Medical Statistics, Leiden University Medical Center, Leiden, the Netherlands*

Accepted 12 October 2006

KEYWORDS
Very premature infants;
Very low birth weight;
Small for gestational age;
Growth and development;
Dexamethasone

Abstract

Objective: To describe growth in infants <32 weeks GA. To assess the relationship between growth and perinatal factors (like intrauterine growth retardation and the postnatal use of dexamethasone) and neurodevelopmental outcome.
Design: Regional, prospective study in two health regions in the Netherlands. Part of the Leiden Follow-Up Project on Prematurity (LFUPP).
Patients: 196 live born infants with GA <32 weeks.
Methods: At two years corrected age length, weight and head circumference of 160 of 196 surviving infants (82%) were evaluated. Standard Deviation Scores were calculated and means were compared to Dutch growth references. Mean SDS for length was corrected for the mean SDS for target height. Birth weight (BW)-SDS for gestational age (GA) was calculated according to Swedish references.
Results: Length, weight and weight-for-length were equally impaired in both sexes at two years in premature infants compared to Dutch growth charts. Catch-up in length and weight occurred mostly in the first year of life. Intrauterine growth retardation was associated with impairment of all growth parameters. The use of postnatal dexamethasone was associated with shorter length, lower weight, lower weight for length and smaller head circumference; this effect remained after correction for GA, BW and BW-SDS. Growth retardation (length and weight) was associated with an abnormal neurologic examination; smaller head circumference also with mental and psychomotor delay.
Conclusion: Growth at two years corrected age in children born <32 weeks is impaired. Postnatal dexamethasone is associated with impairment of all growth parameters including head circumference, which may be a significant contributing factor for abnormal neurodevelopmental outcome.

Abbreviations: BMI, body mass index; BPD, bronchopulmonary dysplasia; BW, birth weight; GA, gestational age; HC, head circumference; *L*, length; Lcorr, length corrected for target height; MDI, mental developmental index; PDI, psychomotor developmental index; PVL, periventricular leucomalacia; SDS, standard deviation score(s); SES, socio-economic status; SGA, small for gestational age; TH, target height; *W*, weight; *W*/*L*, weight-for-length.

* Corresponding author. Department of Paediatrics, J6-S Leiden University Medical Center, Albinusdreef 2, 2333 ZA Leiden, The Netherlands. Tel.: +31 71 5262909; fax: +31 71 5248199.
E-mail address: M.Rijken@lumc.nl (M. Rijken).

0378-3782/$ - see front matter © 2006 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.earlhumdev.2006.10.002

1. Introduction

In the last decades an increase in survival of very premature infants is described, but concern remains about their neurodevelopmental outcome and catch-up growth. Most studies describe growth (length and weight) to lag behind in very low birth weight infants, although different percentages of catch-up growth are reported [3,4,6,7,16]. Authors usually agree that most catch-up growth occurs in the first year of life and that later catch-up is disappointing. Because postnatal growth seems to be related to neurodevelopmental outcome [6,21], paediatricians usually aim for rapid catch-up growth in the first years in these preterm infants.

Different causes for poor growth are reported, like intrauterine growth retardation [14,16] and the presence of risk factors like chronic lung disease [18,24]. Data about the use of postnatal dexamethasone and growth are conflicting. Romagnoli reported no differences at the corrected age of 3 years in premature infants with or without dexamethasone [28,29]; Yeh et al. [34] found impaired growth (length and head circumference) at two and eight years of age after the use of dexamethasone.

The purpose of this prospective study was to describe length, weight, weight-for-length and head circumference of premature infants at the corrected age of two years, compared to the Dutch growth references [9]. Furthermore we assessed the relationship between growth and perinatal parameters like body size at birth, bronchopulmonary dysplasia and use of postnatal dexamethasone. The possible relationship between growth and the neurologic examination and the mental and psychomotor development at two years was also analysed.

2. Patients and methods

The data of all live born infants with a gestational age of <32 weeks, born in 1996/1997, in the regions The Hague and Leiden were studied. At the corrected age of two years, 196 of the 225 infants (87%) were alive. Data were taken from the The Leiden Follow-Up Project on Prematurity, a Dutch regional prospective study, which included live born infants of <32 weeks of gestation, born in 1996/1997 in the health regions The Hague, Leiden and Delft (n=266) [31]. The infants from the health region of Delft were excluded because of the high percentage of missing growth data (59%).

Antenatal and perinatal data were collected including health status and diseases of the mother, socio-economic status, diseases and medication during pregnancy, gestational age, birth weight and data about perinatal morbidity and medication. Twenty-three infants were considered small for gestational age (SGA) with birth weight $<P_{10}$ (−1.3 standard deviation (SD) according to the charts of Niklasson [26]); for infants born between 24–28.5 weeks the reference-data were extrapolated.

Twenty-nine infants received dexamethasone. In 1996/1997 dexamethasone was given in an initial dose of 0.5 mg/kg, tapered over 42 days to 0.1 mg/kg. It was started at a mean postnatal age of 17.5 days (range 5–42 days) and given for an average of 38 days (range 5–60 days with one infant receiving dexamethasone for 143 days). The cumulative dose ranged between 2.0 and 14.3 mg/kg. It was not possible to distinguish the influence of prenatal or postnatal steroids: 25 of the 115 infants who received antenatal steroids were also treated with dexamethasone postnatally; only 4 infants received dexamethasone without antenatal steroids.

The Medical Ethics Committee of the LUMC approved the study and informed consent of the parents was obtained.

2.1. Follow-up

At term age and at the corrected age of one and two years a neonatologist experienced in developmental examination assessed the infants. A complete physical examination was performed and data about length, weight and head circumference were collected. Length was measured in supine position with straight back and knee on a standardized infantometer. Infants were weighed undressed on a calibrated infant balance scale. Head circumference was measured with a standard measuring tape taking the largest measurement across the occipito-frontal line. Length (L), Weight (W) and head circumference (HC) were expressed as standard deviation scores (SDS) according to the Dutch growth charts [9] at the ages of one and two years. To correct for genetic growth potential, at the age of two years another outcome measure for length was used: SDS_{Lcorr}. In SDS_{Lcorr}, length is corrected for the target height (TH). The formula used was TH boys = (height father + height mother + 13) / 2 + 4.5 cm.; TH girls = (height father + height mother − 13) / 2 + 4.5 cm. Parental heights were obtained by self-report. SDS for the TH were calculated: based on the mean ± SD adult height for males (184 ± 7.1 cm) and females (170.6 ± 6.5 cm). Infants born from non-Caucasian parents were also plotted on the Dutch growth charts because at the age of two years the influence of ethnic origin is negligible [10,11].

At term age special growth curves were developed because the growth charts according to Niklasson [26] can be used until the postmenstrual age of 40 weeks and the growth charts according to Fredriks [9] from 42 weeks onwards. So for the children examined between 40–42 weeks postmenstrual age the two reference-curves were interpolated.

None of the included infants had a post-hemorrhagic hydrocephalus for which a ventriculoperitoneal shunt was needed. In 3 patients a single lumbar puncture was performed with good result; the head circumference of all these infants was within the normal range at two years.

At the corrected age of two years infants were neurologically examined according to Hempel [17] focused on major as well as minor neurologic dysfunctions. The children were considered definitely abnormal (DA) when muscle tone and reflexes were both abnormal (which meant the presence of a cerebral palsy), mildly abnormal (MA) when mild deviations in muscle tone regulation, reflexes, fine or gross motor performance were present, or normal (N).

Mental and psychomotor development was assessed by a developmental psychologist using the Dutch version of the Bayley-Scales of Infant Development I (BSID I) [1,23]. During the study period the BSID II were not validated yet for the Dutch population. The BSID I have a mean value of 100 and a standard deviation of 16. A Mental Developmental Index (MDI) or Psychomotor Developmental Index (PDI) ≥84 (≥−1 SDS) was considered normal (N), MDI or PDI between 68 and