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LETTERS

Influence of duration of parenteral nutrition on retinopathy of prematurity

Prospects for premature infants have improved dramatically over the past 30 years. During this time, nutritional support has assumed increasing importance, not least because early interventions are now known to have long-term effects.^{1 2}

Although the mortality rate has diminished, the proportion of surviving infants with severe sequelae has not.¹ Retinopathy of prematurity (ROP) is the main cause of visual impairment in premature infants. It was associated with excessive oxygen use shortly after the initial description. However, even with careful oxygen control we see a second epidemic of ROP, only partially explained by low gestational age (GA) and low birth weight (BW).³ Most studies of these risk factors are inconclusive.

In a search for new indicators which might be used to isolate subgroups at increased risk and find new preventive strategies to reduce morbidity, we compared the characteristics of infants who developed ROP with those who did not. Therefore we performed a retrospective chart review in all very low birth weight (≤ 1500 g) infants admitted to the neonatal intensive care unit at the University Hospitals of Leuven from January 2000 through February 2005 (n = 412).

We found that BW, GA, use of dopamine and postnatal steroids, length of mechanical ventilation/nasal continuous positive airway pressure/oxygen, sepsis, intraventricular haemorrhage and patent ductus arteriosus were associated with an increased risk of

ROP (table 1), confirming previous findings.³ Another interesting finding was that the duration of parenteral nutrition (PN) is also an indicator for the development of ROP ($p < 0.001$). After multiple logistic regression analysis, GA, BW, length of oxygen use, but also duration of PN were found to be significant predictors of ROP ($p < 0.002$, $p < 0.001$, $p = 0.019$, $p = 0.001$).

From published reports, we know that earlier establishment of full enteral feeding might be associated with reduced incidence of sepsis and bronchopulmonary dysplasia, without exacerbation of necrotising enterocolitis.⁴ As the duration of PN is implicated in these two major morbidity factors, we found that this also has an impact on ROP. For future strategies, duration of PN might be an available indicator of a high-risk category of infants who will develop ROP. Identifying these infants on time, might provide a brief opportunity for preventive strategies.

Large prospective randomised controlled trials should be performed to investigate the influence on, and the mechanism behind, duration of PN on the occurrence of ROP.

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All contributors to this study are members of the neonatal intensive care unit. SV: study coordinator, practising neonatologist; CV: practising neonatologist; FdZ: practising endocrinologist; KA: practising neonatologist.

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Table 1 Descriptive data, morbidity, treatments and mortality in the group with retinopathy of prematurity (ROP) and the control group

Data	ROP (n = 109)	No ROP (n = 303)	p Value
BW (g)*	800	1235	<0.001
GA (weeks)*	26	29	<0.001
Small for gestation ($\leq P10$) (%)	58	47	0.15
Multiple gestation (%)	37	38	0.93
Mortality (%)	0	1	0.9
Prenatal corticosteroids (%)	68	69	0.85
Dopamine* (%)	72	29	<0.001
Postnatal steroids* (%)	69	28	<0.001
Sepsis* (%)	73	38	<0.001
NEC (%)	23	9	0.21
PDA* (%)	43	19	<0.001
IVH* (%)	21	8	0.04
Mechanical ventilation (days)*	20	4	<0.001
nCPAP (days)*	39	13	<0.001
Oxygen (days)*	59	16	<0.001
Parenteral nutrition (days)*	52	27	<0.001

Values are median or percentage. Mann-Whitney U test was used for statistical analysis.

*Variables included in multivariate analysis.

BW, birth weight; GA, gestational age; IVH, intraventricular haemorrhage; nCPAP, nasal continuous positive airway pressure treatment; NEC, necrotising enterocolitis; PDA, patent ductus arteriosus

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Bubble CPAP must be used with care to avoid harm

In models of neonatal care for countries with limited resources, bubble continuous positive airway pressure (CPAP) may be the first type of ventilatory support that is recommended. It is low cost and safe when administered by nurses, which make it ideal for this purpose.¹

We would like to report the case of a newborn baby who sustained a pneumothorax secondary to inaccurate use of a bubble CPAP delivery system in a developing country.

A 2820 g female infant was born at 37 weeks' gestation to a healthy mother by caesarean section at a level III perinatal centre. She was transferred to our neonatal intensive care unit for grunting and tachypnoea. Chest x-ray films taken on admission disclosed bilateral alveolar filling with retained pulmonary fluid. The infant was placed on a bubble nasal CPAP (Bubble CPAP System, Fisher and Paykel Healthcare, USA) at 6 cm H₂O and 0.50 fractional inspired oxygen (FiO₂) because of transient tachypnoea of the newborn. The following day the patient was weaned to CPAP at 5 cm H₂O and 0.30 FiO₂. On the third day of life, the infant appeared to have increased respiratory distress. Chest x ray films showed a right-side pneumothorax, and a chest tube was placed. At this time, team noticed a technical problem: the bubble CPAP delivery system pressure level was at 10 cm H₂O.

In a bubble CPAP delivery system, the distal end of the expiratory tubing is immersed under sterile water to a specific depth to provide the desired level of CPAP.² Kahn *et al* described the implementation of bubble CPAP in a developing country and investigated the feasibility of nurses implementing bubble CPAP. Their study showed that tubing submersion depth was a highly inaccurate measure for setting the level of bubble CPAP, and operators should instead rely on intra-prong pressure measurement.³

In our case the bubble CPAP tubing was immersed to a depth greater than the desired CPAP level. The patient-care team believe that use of an inaccurate CPAP level provided more positive end expiratory pressure and caused a pneumothorax. It is

known that nursing is critical to the handling of CPAP. We have observed that the distal end of the expiratory tubing system may easily be immersed too far below the water surface during cleaning, for example, without this being noticed. There is a common belief that medical errors and subsequent adverse events are a serious challenge to the healthcare system. We would like to emphasise that the design of the bubble CPAP generator should be developed and that training of the teams operating the equipment should be done well to improve patient safety.

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Thyroid volumes in newborns of different gestational ages: normative data

Reference ranges for thyroid volumes in newborns of different gestational ages have not been previously determined. We assessed thyroid volume within the first week of life in a sufficient number of neonates of different gestational ages to establish normal

ranges for babies born in Turkey. In addition, we evaluated interobserver and intraobserver variations in sonographic measurement of thyroid volume.

- The inclusion criteria for our study were¹:
- ▶ gestation between 25 and 42 weeks;
 - ▶ birth weight between the 10th and 90th percentiles of mean gestational age related birth weight;
 - ▶ blood thyroglobulin concentration 2–54 ng/ml.

We included neonates whose mothers did not have a history of thyroid disease were included in the study, but babies who had any thyroid disease were excluded. The neonates were divided into four groups (100 per group) according to gestational age: group I (25–28 weeks), group II (29–32 weeks), group III (33–37 weeks) and group IV (38–42 weeks). Two experienced sonographers performed the ultrasound studies with the same ultrasound scanner, a 1200× PLUS high-resolution grey-scale sonography system (Shimadzu, Kyoto, Japan). Thyroid volume was calculated using Klingmuller and colleagues' formula²: length × breadth × depth × 0.479. The thyroid volumes calculated were first averaged separately for each sonographer and then the average of the volumes calculated by both sonographers was used to calculate true mean thyroid volume. Means and standard deviations (SD) of the errors were calculated, and 95% confidence intervals for each variation were computed by adding 2×SD to the mean.

Table 1 shows the characteristics of the neonates included in the study. Intraobserver variation as calculated to be 3.4% (8.9%) (95% CI 15.7%). Interobserver variation was calculated to be 4.2% (10.3%) (95% CI 18.7%). The mean thyroid volume for infants in groups I, II, III and IV was 0.40 (0.05) ml, 0.50 (0.04) ml, 0.60 (0.07) ml and 0.72 (0.09) ml, respectively; differences between the groups were significant ($p < 0.001$).

Our study provides reference thyroid values that can be used for comparisons in the evaluation of infants with suspected thyroid disease. To our knowledge, this is the largest report of its kind. The mean

thyroid volume of 0.72 ml in term neonates in our study is lower than the values reported from Germany (1.1 ml), Belgium (0.84 ml) and the UK (1.62 ml).^{2–4} We could not find any study reporting thyroid measurements in preterm neonates in the literature. Thyroid volume can be expected to vary from country to country in relation to iodine intake. As blood thyroglobulin level greater than 54 ng/ml has been defined as a biochemical criterion of excessive thyroid stimulation in newborns, newborns with the raised thyroglobulin levels were not included in the present study. Our aim was to establish reference ranges for thyroid volume in Turkish newborns with normal iodine status.

As regional factors influence thyroid volume, we suggest that interested centres collect their own normative data for use in the assessment of the newborn.

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Table 1 Characteristics of the neonates

Characteristics	Group I 25–28 weeks (n = 100)	Group II 29–32 weeks (n = 100)	Group III 33–37 weeks (n = 100)	Group IV 38–42 weeks (n = 100)
Number of boys (%)*	48 (48)	52 (52)	51 (51)	47 (47)
Gestational age (weeks)	27.3 (0.9)‡	31.2 (0.9)¶	35.9 (1.5)§	39.2 (1.3)††
Birth weight (g)	976.2 (121.9)‡	1419.6 (117.6)¶	2195.6 (344.3)§	3460.2 (149.2)††
Length (cm)	35.4 (1.2)‡	40.3 (3.3)¶	44.8 (3.4)§	49.9 (3.9)††
Head circumference (cm)	25.8 (0.9)‡	28.4 (0.6)¶	32.0 (1.0)§	35.0 (0.5)††
Maternal age (years)	26.5 (4.0)	27.2 (4.2)	27.0 (3.6)	27.4 (4.1)
Parity (n)†	3 (2–5)	3 (2–5)	3 (1–5)	3 (1–5)
Mode of delivery (caesarean section) (n (%))*	79 (79)	75 (75)	65 (65)**	12 (12)††

Values are mean (SD) except *percentage (%), †median (range). p Value <0.05 was considered significant.

Difference significant with respect to: ‡groups II, III and IV; ¶groups I, III and IV; §groups I, II and IV; **groups I and IV; ††groups I, II and III.

Rationalising the use of “growing bloods” in stable preterm infants

Current neonatal practice involves weekly blood sampling of growing stable preterm infants to assess liver, bone and haematological variables and identify signs of osteopenia and anaemia of prematurity. There are few data, however, to support this practice, with much evidence of increased transfusion requirements in this vulnerable population