

PostScript

LETTERS

Hospital admissions for bronchiolitis in preterm infants in the absence of respiratory syncytial virus prophylaxis

Respiratory syncytial virus (RSV) is the causative agent in more than 50% of cases of bronchiolitis, with mycoplasma pneumonia, Para influenza 3, adenovirus, and some other viruses accounting for most of the remaining cases. Mortality from bronchiolitis ranges from 1% to 3%. Although as yet there is no safe and effective vaccine, passive immunity with Palivizumab has been shown to reduce hospital admissions of preterm babies, but no reduction in mortality, intensive care admissions, or ventilation days was observed.¹ Critical appraisal of this study reveals that the number of infants to be treated to prevent one hospital admission is between 17 and 22.

The objectives of our study were to document local admission rates of premature infants from clinical bronchiolitis, assess local mortality and morbidity secondary to bronchiolitis, and examine seasonal and annual variation of bronchiolitis admissions. By examining hospital admission databases in Cork University Hospital, all admissions between 1997 and 2001 for clinical bronchiolitis, including intensive care admissions, were identified. Parents of premature infants (32 weeks) born in the Maternity Services in Cork in 1997–2001 were contacted by telephone and postal questionnaire, with a response rate 82%.

Thirty five of 174 babies (20%) were admitted for bronchiolitis over this five year period. Total hospital inpatient stay was 175 days. Average length of stay was five days per infant. Peak incidence of bronchiolitis in our region was between November and March. Whereas the number of preterm infants < 32 weeks born in our region

increased over the years, the percentage admitted with bronchiolitis decreased (fig 1). None of the preterm infants admitted with bronchiolitis required admission to the intensive care unit. Indeed only five infants, all born at term gestation without underlying conditions, required intensive care admission and ventilation for clinical bronchiolitis during this time. There were no deaths from bronchiolitis in either premature or term infants.

Palivizumab cost €940 and €564 per 100 and 50 mg vial respectively. At a dose of 15 mg per kg, with five doses per season (as recommended by the American Academy of Paediatrics), provision of prophylaxis to all our premature babies (32 weeks) would cost > €400 000 compared with inpatient hospital cost for premature infants with bronchiolitis approximating < €50 000.

Bronchiolitis due to RSV and other viruses is still a major problem in preterm infants. The role of parental education (RSV: Reduce exposure, no Smoking, Very good hand washing) has not been evaluated. We believe that, given the absence of a reduction in mortality and significant morbidity (ventilation, admissions to intensive care), the role of Palivizumab for RSV prophylaxis for premature infants remains questionable, with the potential long term benefit of RSV prophylaxis as yet undetermined.

P Bala, C A Ryan, B P Murphy

Department of Paediatrics and Child Health, University College Cork, Ireland; pronabbala@doctors.org.uk

Competing interests: none declared

doi: 10.1136/adc.2003.036012

Reference

- The Impact Study Group.** Palivizumab, a humanized respiratory syncytial virus monoclonal antibody, reduces hospitalisation from respiratory syncytial virus infection in high infants. *Pediatrics* 1998;102:531–7.

Current use of nasal continuous positive airways pressure in neonates

Neonatal applications of nasal continuous positive airways pressure (NCPAP) include prevention of extubation failure,¹ apnoea of prematurity,² and as an alternative to intubation and ventilation in respiratory distress syndrome,³ in very preterm infants,⁴ and in exacerbations of chronic lung disease. On our neonatal unit we deliver all CPAP using the Infant Flow Driver (IFD) (EME Ltd, Brighton, UK). We were interested in how other units currently use the IFD and wean infants from NCPAP.

Between December 2003 and April 2004 we surveyed all 58 neonatal units with intensive care cots in the Northern Region of England. We posted a questionnaire and stamped addressed envelope to the unit nurse manager. We made a follow up telephone call to all units that did not respond and for incomplete or ambiguous replies. We obtained a 100% response rate. Table 1 summarises the main indications for NCPAP and weaning practices in 54 units that used the IFD.

Other indications cited were: chronic lung disease (five units); thoracic dystrophy (one unit); post-diaphragmatic hernia repair (one unit). Three units gave CPAP only through an endotracheal tube, and one surgical unit did not use CPAP in any form.

We found that briefly intubating, giving surfactant, then starting NCPAP is common in infants with severe respiratory distress syndrome and in very preterm infants. This is despite scant evidence to date that the practice decreases chronic lung disease or need for mechanical ventilation.⁵

The optimal method of weaning infants from NCPAP remains unanswered.⁶ We found that although some units try abrupt discontinuation of NCPAP, most wean on an ad hoc basis by gradually decreasing either time spent on the IFD or the CPAP pressure. Only three units (6%) had a weaning protocol, although most respondents (85%) would welcome formal weaning guidelines.

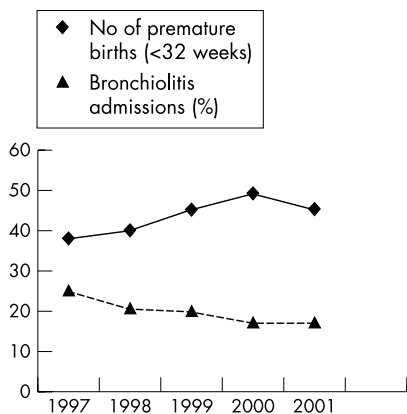


Figure 1 Premature births (< 32 weeks) and bronchiolitis admission rates over five years.

Table 1 Use of Infant Flow Driver nasal continuous positive airways pressure (NCPAP) in the Northern Region of England

Indications	Routinely	Rarely	Never
Initial management of RDS	41 (76)	13 (24)	0 (0)
Severe RDS/very preterm in conjunction with surfactant	25 (46)	21 (39)	8 (15)
Apnoeas	24 (45)	25 (46)	5 (9)
After extubation	50 (93)	3 (5)	1 (2)
NCPAP weaning			
<i>Method</i>		<i>Who decides when to wean?</i>	
Time off	36 (66)	Doctors	10 (18)
Pressure	2 (4)	Nurses	1 (2)
No set method	16 (30)	Joint decision	43 (80)

Values are number (%) of units. RDS, Respiratory distress syndrome.

The wide variation in local practice undoubtedly reflects the lack of published trials. Formal comparisons of weaning regimens are necessary to minimise morbidity resulting from undertreatment and overtreatment with NCPAP.

Acknowledgements

We thank all the neonatal units that contributed to this survey.

L Bowe, P Clarke

Correspondence to: Neonatal Intensive Care Unit, Hope Hospital, Salford M6 8HD, UK; Lynn.Bowe@srrh.nhs.uk

Competing interests: none declared

doi: 10.1136/adc.2004.061085

References

- 1 Davis PG, Henderson-Smart DJ. Nasal continuous positive airways pressure immediately after extubation for preventing morbidity in preterm infants (Cochrane Review). *Cochrane Library*. Issue 2. Oxford: Software Update, 2004.
- 2 Miller MJ, Carlo WA, Martin RJ. Continuous positive airway pressure selectively reduces obstructive apnea in preterm infants. *J Pediatr* 1985;106:91-4.
- 3 Stevens TP, Blennow M, Soll RF. Early surfactant administration with brief ventilation vs selective surfactant and continued mechanical ventilation for preterm infants with or at risk for RDS (Cochrane Review). *Cochrane Library*. Issue 2. Oxford: Software Update, 2004.
- 4 Tooley J, Dyke M. Randomized study of nasal continuous positive airway pressure in the preterm infant with respiratory distress syndrome. *Acta Paediatr* 2003;92:1170-4.
- 5 De Paoli AG, Morley C, Davis PG. Nasal CPAP for neonates: what do we know in 2003? *Arch Dis Child Fetal and Neonatal Ed* 2003;88:F168.

Consensus on neonatal infusion pumps and pressure monitoring

Wilkins and Emmerson¹ highlighted the lack of consensus on the management of extravasation injuries in neonates. Modern neonatal infusion pumps can measure inline intravenous pressure and could theoretically detect early infiltration and subsequent extravasation injuries.² But in clinical practice, extravasation injuries appear to occur even when inline pressures are monitored and cannulae sites are inspected hourly. However, it is a common misconception that occlusion alarms on infusion pumps will signal infiltration. In fact, pumps will alarm only when downstream pressure reaches a specified value, and elevated pressures resulting from infiltration are typically far lower than occlusion alarm triggering levels.³ In infants, monitoring of inline intravenous pressure is not useful for predicting or detecting infiltration of peripheral catheter sites.⁴ Resistance measurements may be useful in detecting infiltration injuries, but are not widely available and at present there are no commercially available infusion pumps that can reliably detect infiltration.^{3,5} We undertook a telephone survey of 14 tertiary neonatal centres to determine whether there was consensus on monitoring infusion pumps and pressures, cannulae sites, and the management of any resulting tissue burns.

Only two units had their own written guidelines on the monitoring of infusion pumps and pressures, cannulae sites, and

the management of any resulting tissue burns. A variety of volumetric (43% Ivac) and syringe (50% Alaris) pumps were used. Monitoring of infusion pressures were by either actual inline pressure readings or a standardised "bar" system depicting pressure readings, or by both methods. Pressure alarms were calibrated for individual babies, set to 10 to 150 "units" above the baseline reading, or preset by the manufacturer to arbitrary settings. Pressure readings were recorded hourly on either the fluid or intensive care charts (78%), and the remainder only observed the pressure readings.

Some units used cannulae for total parenteral nutrition (four), 15% dextrose or higher (six), and inotropes (one). A selection of cannulae were used, although none of the units had written guidelines on the removal of presumed tissue cannulae. All units used clinical judgment for deciding on the removal of presumed tissue cannulae regardless of the pressure reading. A variety of procedures were undertaken including flushing the cannula and checking the cannulae site more frequently. Cannulae removal was recorded on either fluid charts or intensive charts, nursing or medical notes, or care plans.

This study has highlighted the lack of consensus on how tertiary neonatal centres monitor and manage infusion pumps and pressure readings and cannulae and the lack of written guidelines. The lack of consensus on the use of neonatal infusion pumps and their pressure readings probably stems from the lack of evidence that at present monitoring infusion pump pressures reduces the incidence of extravasation injuries. Nevertheless, this study has further consolidated the need for standardisation in the overall management of extravasation injuries, and calls for further research in this neglected field of neonatology.

M G Gnanalingham, V Irving, N J Shaw
Neonatal Intensive Care Unit, Liverpool Women's Hospital, Liverpool, UK, L8 7SS; ben.shaw@lwh-tr.nwest.nhs.uk

Competing interests: none declared

doi: 10.1136/adc.2004.057224

References

- 1 Wilkins CE, Emmerson AJB. Extravasation injuries on regional neonatal units. *Arch Dis Child Fetal Neonatal Ed* 2004;89:F274-5.
- 2 Guy B, Pons de Vincent JF. Value of approach monitoring of infusion pressure in neonatology. *Pediatrics* 1992;47:487-92.
- 3 Infiltration during infusion therapy. <http://www.mdsr.ecri.org/TOC/index.asp>.
- 4 Phelps SJ, Tolley EA, Cochran EB. Inability of inline pressure monitoring to predict or detect infiltration of peripheral intravenous catheters in infants. *Clin Pharm* 1990;9:286-92.
- 5 Scott DA, Fox JA, Cnaan A, et al. Resistance to fluid flow in veins. *J Clin Monit* 1996;12:331-7.

Cytokine polymorphisms and chronic lung disease in small preterm infants

There is increasing evidence that pulmonary inflammation contributes to the pathogenesis of chronic lung disease (CLD).¹ Cytokines are key factors in the inflammatory response. The response of various cytokines to stressful stimuli have been shown to be partly due to interindividual variation at a genetic level.² The possibility that genetic factors play a role

in susceptibility to CLD has been reported.^{3,4} We decided to investigate whether gene polymorphisms for tumour necrosis factor α (TNF α -308 G/A) and interleukin 1 (IL1) influence the risk of developing CLD in small preterm (<30 weeks gestation) infants. A total of 224 ventilated small preterm infants were enrolled into a case-control study to investigate the association between TNF α -308 G/A and IL1 polymorphisms in ventilated, small preterm infants with CLD. CLD was defined as dependence on active respiratory support or oxygen supplementation at 36 weeks postconceptional age. Typing of the genotype polymorphisms was performed by polymerase chain reaction and restriction analysis. Genotype distribution and allelic frequencies were compared between infants with CLD and those without CLD. According to the definition of CLD, 112 infants developed CLD, and 112 infants did not. The following clinical risk factors for CLD did not differ between the groups: prenatal steroid use, premature rupture of the membranes, presence of amnionitis, Apgar score, sex, gestational age, birth weight, surfactant therapy, patent ductus arteriosus, and sepsis.

There was no significant association between the genotype or the allelic frequency of the TNF α or IL1 β exon5 or IL1 receptor antagonist (IL1RA) polymorphism with CLD and the duration of intermittent mandatory ventilation supplement. The most common genotypes for TNF α -308 polymorphism for CLD and their healthy control infants were the G homozygote. The proportions of A homozygote/G heterozygote for the TNF α -308 polymorphism for CLD and their healthy controls were 5.4/21.4/73.2% and 5.4/32.1/62.5% respectively. The most common genotypes for IL1RA for CLD and their healthy controls were the I/I homozygote. The proportions of I homozygote/II heterozygote for IL1RA for CLD and their healthy controls were 87.5/12.5% and 85.7/14.3% respectively. The most common genotypes for IL1 β exon 5 for CLD and their healthy controls were the E1 homozygote. The proportions of E1 homozygote/E2 heterozygote for IL1 β exon 5 for CLD and their healthy controls were 92.9/7.1% and 94.6/5.4% respectively. We conclude that TNF α -308, IL1RA, and IL1 β exon 5 polymorphisms are not useful markers for predicting the susceptibility of the Chinese population in Taiwan to CLD.

H C Lin, F-J Tsai, C H Tsai

Department of Pediatrics, China Medical University Hospital, Taichung, Taiwan

Y-Y Hsieh

Department of OBS GYN, China Medical University Hospital

C M Hsu, F-J Tsai

Department of Medical Genetics, China Medical University Hospital

C H Tsai

Taichung Healthcare and Management University, Taichung

Correspondence to: Professor Fuu-Jen Tsai, Department of Medical Genetics and Pediatrics, China Medical University Hospital, No 2 Yu-Der Road, Taichung, 404, Taiwan; d0704@www.cmuh.org.tw

Competing interests: none declared

doi: 10.1136/adc.2004.061713

References

- 1 **Speer CP.** Inflammation and bronchopulmonary dysplasia. *Semin Neonatal* 2003;**8**:29–38.
- 2 **Fishman D, Faulds G, Jeffery R.** The effect of novel polymorphisms in the interleukin-6 (IL-6) gene on IL-6 transcription and plasma IL-6 levels, and an association with systemic-onset juvenile chronic arthritis. *J Clin Invest* 1998;**102**:1369–76.
- 3 **Manar MH, Brown MR, Gauthier TW, et al.** Association of glutathione-S-transferase-P1 (GST-p1) polymorphisms with bronchopulmonary dysplasia. *J Perinatol* 2004;**24**:30–5.
- 4 **Clark DA, Pincus LG, Oliphant M.** HLA-A2 and chronic lung disease in neonates. *JAMA* 1982;**248**:1868–9.

Lower placental weight is associated with raised cord serum insulin concentrations at birth

A growing body of evidence suggests that the malnourished fetus may develop peripheral insulin resistance¹ and that low birth weight is a risk factor for metabolic and cardiovascular disease in adulthood.^{2,3} As intrauterine nutrition and fetal growth depends on the placenta, we hypothesise that low weight placenta may be linked to the increase in serum insulin concentration in small for gestational age (SGA) term newborn infants.

We compared 20 SGA babies with 40 of appropriate size for gestational age (AGA) in a cross sectional study matched by mother's age, weight before pregnancy, weight increase throughout pregnancy, and duration of gestation. Risk factors related to retardation of fetal growth and conditions that affect glucose metabolism during labour were exclusion criteria. Gestational age ≥ 38 and < 41 weeks, birth weight < 10 th centile, serum insulin concentration ≥ 30 pmol/l, and weight of placenta < 400 g defined term babies, SGA, high serum insulin concentration, and low weight placenta.

Babies born SGA with low weight placenta (346 (19) g) had the lowest birth weight (2056 (269) g) and the highest serum insulin concentration (51.9 (10.8) pmol/l), whereas babies born SGA with placental weight > 400 g (466 (65) g) had the lowest serum insulin concentration (15.9 (3.3) pmol/l) (values are mean (SD)). On the other hand, babies born AGA exhibited the highest birth weight (3362 (234) g) and placental weight (549 (82) g), with mean serum insulin concentration of 30.9 (8.6) pmol/l. Glucose

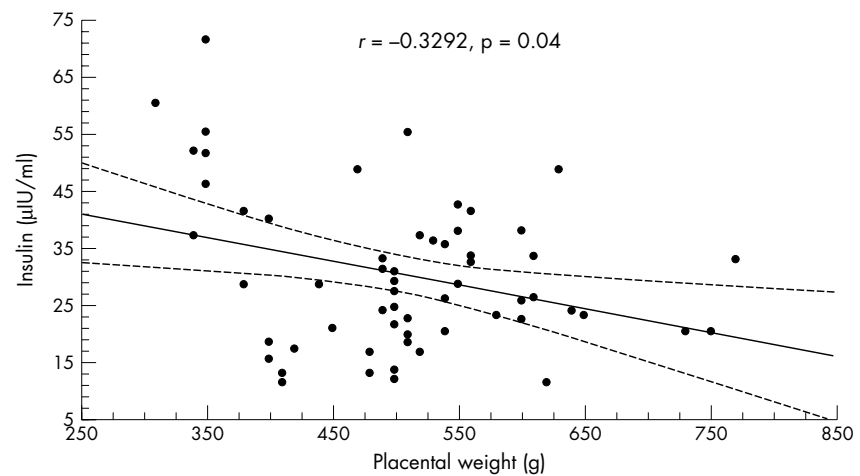


Figure 1 Pearson's correlation (95% confidence interval) between weight of placenta and serum insulin levels in newborns at term (n = 60).

concentrations were similar between the groups, and there were no hypoglycaemic events. Placental weight and serum insulin concentration showed a significant inverse correlation (fig 1).

Multivariate regression analysis of the relation between low weight placenta and high serum insulin concentration found an odds ratio of 2.1, 95% confidence interval 1.3 to 14.3, $p = 0.01$.

Although serum insulin concentrations are lower in lower birth weight babies,⁴ in this study SGA infants with low weight placenta had the lowest birth weight but the highest serum insulin concentration, which suggests that these babies may have developed insulin resistance in utero, a phenomenon that seems to be linked to the low weight placenta. Whether the low weight placenta causes immaturity of the placenta and/or placental dysfunction and this affects the somatotrophic axis in SGA children remains to be established.

Acknowledgements

This work was supported by grants from the National Science and Technology Council of Mexico (SIVILLA 20020402012) and the Research Promotion Fund of the Mexican Social Security Institute (FP 2002/369).

M Rodríguez-Morán, F Guerrero-Romero

Medical Research Unit in Clinical Epidemiology of the Mexican Social Security Institute and Research Group on Diabetes and Chronic Illnesses, Durango, México; rodriguez_moran@hotmail.com

M Levario-Carrillo

Medical Research Unit in Clinical Epidemiology of the Mexican Social Security Institute, Chihuahua, México

Competing interests: none declared

doi: 10.1136/adc.2004.064089

References

- 1 **Karlberg J, Albertsson-Wikland K.** Growth in full-term small-for-gestational-age infants: from birth to final height. *Pediatr Res* 1995;**38**:733–9.
- 2 **Léger J, Jaquet D, Lévy-Marchal C, et al.** Syndrome X: a consequence of intra-uterine malnutrition? *J Pediatr Endocrinol Metab* 2000;**13**(suppl 5):1257–9.
- 3 **Woods KA, van Helvoirt M, Ong KK, et al.** The somatotrophic axis in short children born small for gestational age: relation to insulin resistance. *Pediatr Res* 2002;**51**:76–80.
- 4 **Godfrey KM, Hales CN, Osmond C, et al.** Relation of cord plasma concentrations of proinsulin, 32–33 split proinsulin, insulin and C-peptide to placental weight and the baby's size and proportions at birth. *Early Hum Dev* 1996;**46**:129–40.