

LETTERS TO THE EDITOR

Neonatal hypoglycaemia after diabetic pregnancy

EDITOR.—The study by Stenninger and colleagues showed that a blood glucose concentration of less than 1.5 mmol/l is associated with long term neurological dysfunction.¹ I am interested to know why the authors chose to define hypoglycaemia thus. They cited our 1988 study,² saying "that many neonatal units diagnose neonatal hypoglycaemia at concentrations exceeding (my italics) 1.5 mmol/l." Shouldn't the word have been less than rather than exceeding?

The authors may not be aware of our 1996 study,³ showing a significant change in the definition of hypoglycaemia among paediatricians and in neonatal textbooks published between 1986 and 1992, compared with that used between 1965 and 1986. In 1992 among the 420 neonatologists in the UK who would maintain blood glucose concentrations of >2 mmol/l, 78% said they would do so for term babies and 87% for preterm babies, compared with 34% and 22%, respectively, cited in our 1988 study.² Furthermore, in 1992 the percentage of paediatricians who preferred to maintain blood glucose concentrations of 2.6 mmol/l or more was three times as high as that cited in 1986.

In view of the epidemiological⁴ and neurophysiological data⁵ showing adverse effects associated with a blood glucose concentration of less than 2.6 mmol/l, it would have been useful to know what results would have been obtained had the authors compared the babies with blood glucose at this level with those babies with a blood glucose of \geq 2.6 mmol/l, and whether any of the babies had recurrent hypoglycaemia.

Would the authors care to recommend what they would consider a safe blood glucose concentration for neonates born to diabetic mothers?

T H H G KOH
Department of Neonatology
Kirwan Hospital
Townsville
Queensland 4817 Australia

- 1 Stenninger E, Fink R, Eriksson B, Sahlén C. Neonatal hypoglycaemia after diabetic pregnancy. *Arch Dis Child* 1998;79:F174-9.
- 2 Koh THHG, Eyre JA, Aynsley-Green A. Neonatal hypoglycaemia—the controversy regarding definition. *Arch Dis Child* 1988;63:1386-8.
- 3 Koh THHG, Vong SK. Definition of hypoglycaemia: is there a change? *J Paed Child Health* 1961;32:302-5.
- 4 Lucas A, Morley R, Cole TJ. Adverse neurodevelopmental outcome of moderate neonatal hypoglycaemia. *BMJ* 1988;297:304-8.
- 5 Koh THHG, Aynsley-Green A, Tarbit M, Eyre JA. Neural dysfunction during hypoglycaemia. *Arch Dis Child* 1988;63:1353-8.

Hypoglycaemia in neonates

EDITOR.—The study by Stenninger and colleagues is another unacceptable contribution to the already confused scientific literature on hypoglycaemia in neonates.¹

Leaving aside the obvious problems of selecting a matched socioeconomic control population for a group of babies known to have complex developmental problems, and

who were exposed to insulin in utero, the authors do not provide us with adequate data on their patients.

They refer us to their original study,² but neither there nor in the current study do they give us any idea of the severity or duration of the hypoglycaemia to which these babies were exposed, nor is it acceptable, nowadays, to discuss the likely effects of hypoglycaemia without providing data on plasma concentrations of other alternative brain fuels. It is perfectly possible, from the data supplied, that some of their hypoglycaemic babies had a blood glucose concentration no lower than 1.2 mmol/l for less than an hour. Surely not even the most fervent apologist for the deleterious effects of neonatal hypoglycaemia believes that this is likely to cause neurological sequelae, no matter how soft and uncontrolled the data?

The implication of the last paragraph of their paper is that transient asymptomatic postnatal hypoglycaemia of infants born to gestationally diabetic mothers should be treated with intravenous glucose. That must be wrong. The iatrogenic damage caused by this, rebound hypoglycaemia, and mother-child separation are likely to be considerably greater than the trivial, non-specific abnormalities they report. I believe, therefore, that this study is not only unsound, but potentially dangerous.

N R C ROBERTON
Sea Cottage
Lower Harvpool
Broadford
Isle of Skye
IV49 9AQ

- 1 Stenninger E, Flink R, Eriksson B, Sahlén C. Long term neurological dysfunction and neonatal hypoglycaemia after diabetic pregnancy. *Arch Dis Child* 1998;79:174-9.
- 2 Stenninger E, Schollin J, Aman J. Neonatal macrosomia and hypoglycaemia in children of mothers with insulin-treated gestational diabetes mellitus. *Acta Paediatrica Scand* 1991;80:1014-18.

Dr Stenninger responds:

We used the definition of neonatal hypoglycaemia as a blood glucose concentration of < 1.5 mmol/l according to criteria from the Swedish Paediatric Association (1978). This definition was in use when we started our 1988 study for neonatal hypoglycaemia in full term babies. We agree with Dr Koh that it would have been interesting to have set the level of hypoglycaemia at <2.6 mmol/l.

As the primary purpose of our investigation was not to determine a safe limit for neonates born to diabetic mothers, we cannot give a recommendation for such a limit in these circumstances. In Sweden we now use the lower limit of 2.2 mmol/l for the diagnosis of neonatal hypoglycaemia in term babies (Swedish Paediatric Association, 1997), and we have found no evidence to suggest that neonates born to diabetic mothers would tolerate lower blood glucose concentrations than healthy mothers.

Vascular ring: an important cause of severe upper airway obstruction

EDITOR.—We report three neonates with upper airway obstruction (UAO), who were exposed to acute life threatening events due to a delay in making a correct diagnosis. Chest x-ray, echocardiogram, bronchoscopy and barium swallow were normal or inconclusive. Magnetic resonance imaging (MRI) revealed

vascular ring in these cases.

Case 1

A girl, born at term by caesarean section (3.9 kg birthweight) developed grunting immediately after birth. She was admitted to the special care baby unit with a diagnosis of UAO. Chest x-ray, barium swallow, echocardiogram and bronchoscopy were normal. She was discharged at 10 days of life with persistent stridor without airway compromise or feeding difficulties. She was readmitted eight days later, and was intubated and ventilated for worsening stridor. A chest x-ray revealed bilateral pulmonary oedema. She developed frequent hypoxic episodes and had two cardiopulmonary arrests, both of which were managed successfully. She had seizures and was then referred to intensive care unit. On arrival she was shocked, had biphasic wheeze, and a combined respiratory and metabolic acidosis (capillary blood gas pH 6.75, pCO₂ 27.5 kPa, pO₂ 28.7 kPa and a base deficit of 15). A chest x-ray showed bilateral diffuse shadowing with extensive air bronchogram. The echocardiogram was normal and bronchoscopy showed a slight swelling into the lumen on the right side 2 cm above the carina with some tracheomalacia. Attempts to wean her from respiratory support were unsuccessful. MRI showed a double aortic arch verified by preoperative angiography. She was successfully extubated after surgery.

Case 2

A boy born at term (3.3 kg birthweight) developed stridor from day 2 of life. He was discharged with a diagnosis of laryngomalacia. The stridor persisted and he was readmitted at 5 weeks of age for bronchitis requiring ventilation. Extubation attempts over two weeks were unsuccessful. Chest x-ray, echocardiogram, and laryngoscopy were normal. He was referred to intensive care; on arrival he was shocked, with the arterial blood gas showing mixed respiratory and metabolic acidosis (pH 7.07, pCO₂ 11 kPa, pO₂ 9.6 kPa and a base deficit of 15). Chest x-ray was normal and an echocardiogram showed a right sided aortic arch with a possibility of a smaller left aortic arch. MRI confirmed the diagnosis of vascular ring, which was verified by preoperative aortogram. He was extubated successfully four days later.

Case 3

A girl born at 34 weeks of gestation (2.5 kg birthweight) remained well until 6 days of life when she developed apnoea and cardiac arrest requiring prolonged cardiopulmonary resuscitation. She was intubated and ventilated. She developed seizures. Chest x-ray was normal and computed tomography scan of the head showed features suggestive of global ischaemia. She failed four extubation attempts because of stridor and recessions. Direct laryngoscopy showed that the cords were slightly oedematous. At 3 weeks of age, she was transferred to intensive care. Bronchoscopy was normal and she was extubated the following day but reintubated two days later for respiratory distress. MRI showed a double aortic arch confirmed by preoperative aortogram. She made an uneventful recovery after surgery.

Double aortic arch (DAA) is the most common cause of symptomatic vascular ring and usually presents in the neonatal period with wheezing, persistent stridor, tachypnoea, dyspnoea, and dysphagia.¹ A high index of suspicion is necessary as inappropriate investigations and management may delay the

correct diagnosis being made, thereby exposing the patient to life threatening events. A chest x-ray may show abnormal indentation or a deviated trachea due to a prominent right aortic arch, but all our patients had normal chest x-rays. A barium swallow may show the abnormal indentations on the trachea and the oesophagus. Only case 1 had a barium swallow study and this yielded normal results. Echocardiography was reported as normal in case 1 and suggestive of the diagnosis in case 2, while bronchoscopy was normal in cases 1 and 2. MRI is an accurate and non-invasive tool for the assessment of vascular ring² and facilitated a correct diagnosis in all cases. Angiography is also accurate but invasive and associated with a small but significant morbidity and mortality. Angiography was done preoperatively due to the surgeon's preference.

We recommend that in a neonate with persistent UAO, a firm diagnosis must be established before hospital discharge and an MRI scan should now be part of the routine investigation of infants with serious and persistent airway obstruction.

A SHARPLES
Department of Anaesthesia
Royal Manchester Children's Hospital
Pendlebury
Manchester M27 4H

- 1 Silverman FN, Kuhn JP. Vascular rings and great vessel anomalies. In: Silverman FN, Kuhn JP, eds. *Caffey's Pediatric x-ray diagnosis: An integrated imaging approach*. New York: Mosby, 1993:809-27.
- 2 Bisset GS, Strife JL, Kirks DR, Bailey WW. Vascular rings: MRI imaging. *Am J Radiol* 1987;149:251-6.

International replications, anyone?

EDITOR.—Chowrimootoo *et al* recently pointed out that: "fetal copper metabolism is different from that of the adult,...with apparent similarity to Wilson's disease."¹ It is well known that the copper chelating agent D-penicillamine (DPA) leads to a clinical improvement in hepato-lenticular degeneration without common toxic effects. Why, then, we wonder, has the demonstration of an effective mode of prevention of retinopathy of prematurity (ROP) in two randomised trials conducted more than 10 years ago in Hungary,² failed to encourage others to undertake the independent replications needed to verify or refute such a promising approach?

We were surprised by the following statement in a recently published English language text: "there are no data on D-penicillamine administration to neonates."³ This assertion was particularly vexing because one of us

reported on the successful use of DPA for neonatal hyperbilirubinaemia as far back as the 1970s.⁴ DPA has been used extensively in Hungary for treating neonates after pre-clinical laboratory research and data from controlled clinical trials. Frustratingly, no efforts seem to have been made by others to repeat this work.

The Cochrane Collaboration is working hard to break down the language barriers that have left so many non-English speaking medical scientists apparently unheard. Furthermore, we would like to draw attention to a recent Cochrane review which we conducted on the existing evidence from controlled trials on the use of DPA in premature infants with ROP and survival as the outcome measure. The consensus reached was that: "DPA is unlikely to affect survival and may reduce acute ROP among the survivors." Studies to date, it was concluded, "justify further investigation of this drug in a broader population."⁵

English speaking doubters, we suggest, should now take up this challenge.

L LAKATOS
Department of Paediatrics
Könyv County Hospital
H-4043 Debrecen
Bartók
B.u. 2-26
Hungary

D L PHELPS
Children's Hospital
Strong University of Rochester
Box 651
601 Elmwood Avenue
Rochester
NY 14642
USA

J WATTS
Department of Paediatrics
1200 Main Street West
Hamilton
Ontario
Canada L8N 3Z5

- 1 Chowrimootoo GFE, Scowcroft H, Seymour CA. Caeruloplasmin isoforms in Wilson's disease in neonates. *Arch Dis Child* 1998;79:F198-201.
- 2 Lakatos L, Hatvani I, Oroszlan G, et al. Controlled trial of D-penicillamine to prevent retinopathy of prematurity. *Acta Paediatrica Hungarica* 1986;27:47-56.
- 3 Bird H, Morgan AW. D-penicillamine. In: van de Putte LBA, Furst-Williams HJ, van Riel PLCM, eds. *Therapy of systemic rheumatic disorders*. New York: Marcel Dekker, 1998:137.
- 4 Lakatos L, Kovér B, Péter F. D-penicillamine therapy of neonatal hyperbilirubinaemia. *Acta Paediatrica Acad Sci Hungary* 1974;15:77-85.
- 5 Phelps DL, Lakatos L, Watts JL. D-penicillamine to prevent retinopathy of prematurity (Cochrane Reveiw). *Cochrane Library*, issue 2. Oxford:1998.

Role of cisapride in preterm infants

EDITOR.—Enriquez *et al* provided evidence that cisapride given to preterm infants was beneficial and free of side effects.¹ A study of similar design, based in our unit, was halted by the Medicines Control Agency (MCA) because of the possible risks of prolonged QT intervals.² It is therefore interesting to note that the publication of Enriquez's study coincides with an update from the MCA. This states that cisapride is contraindicated in preterm infants up to the age of 3 months.³

We recently undertook a survey of 367 neonatologists in the UK and Ireland to ascertain the prevalence of cisapride prescriptions in preterm infants and the indications for its use.⁴ Almost 70% of those surveyed responded to the questionnaire. The results showed that 85% of respondents continue to actively prescribe cisapride in their units while only 5% have stopped using it because of the risk of QT interval prolongation. The predominant indication for use was for gastrointestinal reflux (87%), but around 50% of respondents also used it for feed intolerance, gastric stasis, and intestinal dysmotility.

Our survey shows that cisapride is still widely prescribed for preterm babies in the UK and Ireland. We urgently need clear risk: benefit data from randomised controlled trials. We suggest that the best way to clarify the role of cisapride in the care of preterm infants is by a large multicentre randomised controlled trial which investigates gut motility and oesophageal reflux, and includes serial ECG monitoring and pharmacokinetic studies. We are concerned that without such a trial cisapride will continue to be widely used, perhaps placing infants at unnecessary risk.

J S CRAIG
B G MCCLURE
Department of Child Health
The Queen's University of Belfast
Institute of Clinical Science
Belfast BT12 6B9
T R J TUBMAN
Royal Maternity Hospital
Belfast BT12 6BB

- 1 Enriquez A, Bolisetty S, Patole S, Garvey PA, Campbell PJ. Randomised controlled trial of cisapride in feed intolerance in preterm infants. *Arch Dis Child* 1998;79:F110-13.
- 2 Craig JS, Tubman TRJ, McClure BG. Cisapride treatment for preterm infants. *Pediatr Res* 1998;44:426.
- 3 Committee on safety of Medicines/Medicines Control Agency. *Current Problems in Pharmacovigilance* 1998;24:11.
- 4 Craig JS, Tubman TRJ, Millia BG. Survey of cisapride usage in preterm infants in UK and Ireland. *Pediatr Res* 1998;44:425.

Correction

In the correspondence section of the January issue, the letter by Dr Skelton *et al* contained an error. The abbreviation LVH had inadvertently been printed as left ventricular haemorrhage. This should have read left ventricular hypertrophy. We apologise for this error. (*Arch Dis Child* 1999;80:80).



Neonatal hypoglycaemia after diabetic pregnancy

T H H G KOH

Arch Dis Child Fetal Neonatal Ed 1999 80: F252
doi: 10.1136/fn.80.3.F252

Updated information and services can be found at:
<http://fn.bmj.com/content/80/3/F252.1.full.html>

These include:

References

This article cites 5 articles, 3 of which can be accessed free at:
<http://fn.bmj.com/content/80/3/F252.1.full.html#ref-list-1>

Email alerting service

Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
<http://group.bmj.com/group/rights-licensing/permissions>

To order reprints go to:
<http://journals.bmj.com/cgi/reprintform>

To subscribe to BMJ go to:
<http://group.bmj.com/subscribe/>