Evaluation of the Infant at Risk for Neurodevelopmental Disability

C D Molteno, M C Thompson, S S Buccimazza, V Magasiner, F M Hann

Background. Infants with neurodevelopmental abnormality need to start therapy early, and because of this they should be detected as soon as possible. Currently, no widely accepted method of early evaluation exists.

Objectives. To assess and compare, in terms of predicting neurodevelopmental outcome at 1 year of age: (*i*) a perinatal risk rating (PRR); (*ii*) the Dubowitz Neurological Assessment (DNA); and (*iii*) the Infant Neuromotor Assessment (INA).

Design and setting. A prospective neurodevelopmental follow-up study on graduates from the Groote Schuur Hospital (GSH) neonatal intensive care unit (NICU).

Subjects. A cohort of 130 consecutive NICU graduates were selected according to high-risk criteria.

Outcome measures. Each infant was examined at term gestational age on the DNA before discharge, and a PRR was allocated. Study infants were seen again at 18 weeks of age when an INA was done, and at 1 year of age a Griffiths Developmental Assessment and full neurological examination was carried out.

Results. All of the 130 infants assessed at term were seen at 18 weeks. Thereafter 5 were lost to follow-up and 2 died. The outcome for the remaining 123 is known.

Conclusions. Prediction of a normal outcome at 1 year of age was 96% on the DNA and 98% for the PRR, but for an abnormal outcome they predicted only 56% and 42%, respectively. The INA done at 18 weeks predicted a normal outcome at 1 year in 99% of cases if 3 or less abnormal signs were present and an abnormal outcome in 82% of cases with 4 or more abnormal signs. Based on these findings a protocol for follow-up of these high-risk infants is suggested.

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Department of Psychiatry, University of Cape Town
C D Molteno, MD, PhD, FCP (SA)

Department of Paediatrics and Child Health, University of Cape Town
M C Thompson, MB ChB, DCH (SA)
S S Buccimazza, MD, FCP (SA)
V Magasiner, MSc (Physio) (SA)
F M Hann, FCP (SA)

An increase in the survival rate of very-low-birth-weight (VLBW) infants has been documented.[1] The fact that most VLBW infants who survive do not develop major disabilities[2] renders routine neurodevelopmental intervention unnecessary. Nevertheless there is a need to target those infants likely to experience developmental disabilities so that they can benefit from early intervention. Scant resources must be focused on those with long-term needs. In order to do this, a reasonably efficient and reliable method of infant assessment is required.

The aim of this study was to evaluate a perinatal risk rating (PRR), the Dubowitz Neurological Assessment (DNA)[3] and the Infant Neuromotor Assessment (INA)[4] separately and sequentially using a cohort of neonatal intensive care unit (NICU) graduates. It was hoped that this would offer a realistic prognosis to parents and would target early intervention where necessary.

MATERIALS AND METHODS

A prospective follow-up study involving graduates from the Groote Schuur Hospital NICU was conducted. A cohort of 130 consecutive NICU graduates was selected according to the high-risk criteria listed in Table I. Each infant was examined with the DNA[3] before discharge at term gestational age (as assessed by the Ballard score), and scored according to deviant items as described by Molteno et al.[5] The infants were classified as follows: (i) no deviant signs; (ii) 1 deviant sign; (iii) 2 - 3 deviant signs; (iv) 4 or more deviant signs.

Each infant was also allocated a PRR (Table I). The level of risk was assigned according to the highest risk event in the perinatal course. Each infant had at least one cranial ultrasound examination.

After discharge the infants were seen at 18 weeks of age (corrected), and the INA was carried out. This assessment was also scored according to deviant items.[4] The cohort was seen again at 1 year corrected age, at which time the infants were assessed by neurological examination and the Griffiths Scales of Mental Development (GSMD).[6]

For the purposes of analysis, an infant was considered abnormal if there were clinical signs of cerebral palsy (defined

Table I. Perinatal risk rating

1. Birth weight 1 000 - 1 499 g; RDS; asphyxia neonatorum; symptomatic hypoglycaemia; recurrent apnoea
2. Birth weight 750 - 999 g; IVH grades I & II; BPD, HIE without seizures
3. Birth weight < 750 g; IVH grades III & IV, PVL or SCL; seizures
4. Syndromes associated with mental handicap; major CNS abnormality

RDS = respiratory distress syndrome; IVH = intraventricular haemorrhage;
BPD = bronchopulmonary dysplasia; HIE = hypoxic ischaemic encephalopathy;
PVL = periventricular haemorrhage; SCL = subcortical leucomalacia.

as a non-progressive disorder of movement or posture) or mental retardation (defined as a Griffiths corrected developmental quotient less than 70).

Data analysis

Data were recorded and analysed using Epi Info. Sensitivity, specificity and predictive values[7] were calculated for each assessment modality in order to evaluate their clinical usefulness. The positive predictive value indicates the ability of the assessment to predict abnormal outcome.

RESULTS

One hundred and thirty infants who met criteria for the GSH follow-up programme formed the cohort.

The characteristics of the cohort are shown in Table II. Eighty per cent were preterm infants, with a mean birth weight of 1 172 g and a mean gestational age of 34 weeks. The remainder of the cohort comprised term infants who suffered perinatal hypoxia. The morbidity parameters are shown.

Table II. Characteristics of the cohort — morbidity (N = 130)

Birth weight (mean) (g)	1 439 (range 580 - 3 400)
Gestational age (mean) (wks)	34 (range 26 - 42)
Preterm	98 (80%)
Weight (mean) (g)	1 172 (range 580 - 2 300)
Gestation (range) (wks)	26 - 36.8
Sex	65 male (53%)
Ventilated	4 days (25%)
	(range 1 - 21 days)
Oxygen required	8 days (56%)
	(range 1 - 99 days)
BPD	6 (5%)
Apnoea	15 (12%)
NEC	7 (6%)
Seizures	9 (7%)
Cranial ultrasound	
IVH	
Gr II	13 (11%)
Gr III (shunt)	2 (1.6%)
Gr IV	2 (1.6%)
PVL	4 (3.3%)
SCL	2 (1.6%)

BPD = bronchopulmonary dysplasia; NEC = necrotising enterocolitis;
IVH = intraventricular haemorrhage; PVL = periventricular leucomalacia;
SCL = subcortical leucomalacia.

On Dubowitz assessment (Table III) 72% of the cohort was normal (0 or 1 deviant sign) and 7% had 4 or more deviant signs. On PRR 42% were at low risk, 55% medium risk and 3% high risk for developmental problems.

Of the 130 infants, 3 died after 18 weeks but were known to be abnormal (2 had cerebral palsy (CP) with mental retardation

Table III. Characteristics of the cohort — assessemnt at term gestational age (N = 123)

	No.	%
Dubowitz		
0 - 1 deviant	88	72
2 - 3 deviant	26	21
4 or more deviant	9	7
Perinatal risk rating		
1	51	42
2	53	43
3	15	12
4	4	3

Table IV. Predictive values for normal outcome at 1 year

	PPV (%)	NPV (%)	Sensitivity (%)	Specificity (%)
PRR	42	98	80	90
DNA Group 2[†]	56	96	50	97
DNA Group 1[*]	26	99	90	77
INA Group 2[†]	82	99	90	98
INA Group 1[*]	25	99	90	76

* Group 1: Normal v. suspect + abnormal.
† Group 2: Normal + suspect v. abnormal.

and the third was an infant with Down syndrome). A further 2 died during infancy with their neurodevelopmental status unknown at the time of death. Five children left the area before they reached 1 year of age. Contact was maintained with their families and none appeared to have a disability. Of the remaining 120 infants, 112 were assessed on the GSMD and neurological examination and 6 were assessed at home on a developmental screening test. Two other infants, both with known CP, were unable to complete a formal Griffiths assessment but underwent neurological examination. For the analysis of outcome, data were used from the 120 infants evaluated after 1 year of age (112 Griffiths, 6 screened at home and 2 CP) plus the 3 deaths where the developmental status was known.

By 18 weeks of age 6 infants were diagnosed as having CP and 5 were developmentally delayed. A further 25 infants had 2 or 3 deviant signs on INA at this age and were regarded as suspect. Eighty-seven infants (71%) were normal.

At 1 year of age, 111 infants (90%) were normal, 3 infants were developmentally delayed (1 global delay, 2 specifically motor delay) and 6 infants had CP. Three infants had died (2 CP, 1 Down syndrome). There were 8 infants with CP in total over the 12-month period, only 2 of whom had a developmental quotient (DQ) above 70. Five infants had an abnormal DNA as well as a high PRR and 7 of the 8 were abnormal at their 18-week assessment. Other than the infants with CP, only 1 infant in the cohort had a DQ less than 70.

The PRR was grouped as follows: 1 - 2 = low risk, 3 - 4 = high risk.

The DNA was evaluated as follows: 0 - 1 deviant signs = normal, 2 - 3 deviant signs = suspect, 4 or more deviant signs = abnormal.

For analysis and evaluation of the best predictive value the DNA was grouped in two ways: (i) normal v. suspect + abnormal; and (ii) normal + suspect v. abnormal.

Analysis (Table IV) showed that the best predictive values for outcome at 1 year of age on the DNA were obtained using group 2, and were 96% for negative predictive value (NPV)

and 56% for positive predictive value (PPV). The PRR had a NPV of 98% (i.e. more than 98% of infants with a PRR < 3 and/or a DNA with less than 4 deviant signs will be normal at 1 year of age).

In order to evaluate the usefulness of the INA the infant outcome was grouped in the following two ways: (i) normal (0 - 1 deviant signs) v. all abnormalities (2 or more deviant signs); and (ii) normal plus suspect (0 - 3 deviant signs) v. abnormal (4 or more deviant signs).

The highest predictive values were obtained using group 2. The INA at 18 weeks of age is 99% predictive of normal outcome (NPV) at 1 year of age if 3 or fewer abnormal signs are present. The PPV of abnormal outcome of the INA at 18 weeks is 82% if 4 or more abnormal signs are present.

DISCUSSION

A number of scoring methods for identifying infants at risk for poor neurodevelopmental outcome have been proposed. Most of the early methods focused on specific complications that occurred during the perinatal period.[8] Subsequently a more global view was adopted, based on the amount of intensive care required.[9] A more direct approach assessed the potential effect of insults on the central nervous system by focusing on mechanisms of brain injury such as hypoxia, hypoglycaemia and hyperbilirubinaemia.[10]

The Neonatal Medical Index (NMI) of Korner et al.,[11] combining birth weight and neonatal complications in a single score, aims at predicting the mental and motor development of low-birth-weight, preterm infants up to 3 years of age, while the Neonatal Health Index (NHI) developed by Scott et al.[12] is a measure of neonatal health based on the length of hospital stay adjusted for birth weight, standardised to have a mean score of 100 and a standard deviation of 16.

The majority of studies on prediction deal specifically with low-birth-weight or preterm infants. For clinical practice, a

system should include both VLBW and term asphyxiated infants.[5] Molteno et al.[5] developed a perinatal risk rating based on the neonatal clinical course and ultrasound findings. This rating, which is simple to apply and is applicable to both preterm and term infants, was used in the present study. As in the original study, we found it to have a high NPV but only a moderate PPV.

Allen and Capute[13] used a method with items drawn from a number of sources to evaluate the outcome of VLBW infants. They found a good correlation between neonatal examination and neuromotor status at 1 year, but prediction of mental retardation was less accurate. They concluded that although an abnormal examination could not be used to diagnose handicap in preterm infants, it identified a group of high-risk infants who should be carefully monitored during infancy and childhood.

Early neonatal neurological examinations were designed for use in either preterm or term infants, but not both. However, Dubowitz et al.[14] developed an examination that could be used for preterm as well as full-term neonates. They did not quantitate the items collectively or give a single score but looked at the number of deviant signs, showing that the greater the number of deviant signs, the greater the likelihood of later abnormality. Molteno et al.[5] developed objective criteria for assessing deviant items on the Dubowitz examination and showed predictive validity in terms of neurodevelopmental outcome. The latter study[5] provided the method for evaluating deviant items used in this study. The Dubowitz Neonatal Neurological Assessment was accurate in predicting normal outcome in infants with 0 or 1 deviant sign, but it was less successful in detecting abnormal infants.

A number of tests of infant motor development have been described. These include the Milani-Comparetti Motor Development Screening Test,[15] the Chandler Movement Assessment of Infants Screening Test,[16] the Infant Motor Screen,[17] the Infant Neurological International Battery[18] and the Alberta Infant Motor Scale.[19] All these tests have been criticised and none have been generally accepted for clinical use. The INA was developed for screening infants referred to the follow-up clinic at Groote Schuur Hospital. It is easily mastered by both medical and allied professionals and can be completed within 10 - 15 minutes.[4] The INA was used in the present study and its predictive validity was confirmed.

In conclusion, we have shown that the DNA is useful in screening high-risk infants for potential neurological abnormalities. The use of a PRR can be equally accurate, is in fact far less time consuming, and can be assessed by any staff member. The limitation of the PRR is that an ultrasound examination of the newborn brain is required. We have also shown that at 18 weeks the INA is a sensitive screening examination for infants at risk, and that this assessment can be used effectively at community-based clinics. Infants showing 4 or more deviant signs at 18 weeks of age should be referred to

a tertiary care centre for neurodevelopmental therapy and further follow-up. In a rural or secondary-level hospital infants can be screened with the DNA at hospital discharge. In a tertiary-level hospital the PRR is sufficient.

RECOMMENDATIONS

At discharge we recommend that: (i) if PRR is low (1 or 2) or the DNA is normal (0 - 1 deviant sign), then the infant can be followed up in the community; (ii) if PRR is high (3) or if the DNA is abnormal (4 or more deviant signs), then the infant should be seen at 18 weeks of age for an INA; and (iii) if PRR = 4, then the infant should be referred immediately for neurodevelopmental therapy and follow-up.

At 18 weeks we recommend that: (i) if INA is normal (0 - 1 deviant sign), then discharge from follow-up; (ii) if INA is abnormal (4 or more deviant signs), then refer for NDT and follow-up at multidisciplinary developmental clinic; and (iii) if INA is suspect (2 - 3 deviant signs), then see at 6 - 9 months for a repeat INA.

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