Original articles

Effect of neonatal periventricular haemorrhage on neurodevelopmental outcome

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SUMMARY All 56 infants born between 23 and 28 weeks' gestation admitted to this hospital in 1981 were examined for periventricular haemorrhage with cerebral ultrasonography. Haemorrhage was diagnosed in 34 (61%)—12 (22%) had germinal layer haemorrhage, 18 (32%) had intraventricular haemorrhage, and four (7%) had intracerebral haemorrhage. The two year outcome of survivors with and without periventricular haemorrhage was compared to determine the effect on neurodevelopment. Only three (16%) of 19 infants with normal scans or germinal layer haemorrhages had evidence of major disability but nine (75%) of 12 infants with intraventricular or intracerebral haemorrhage had major disability. The mental and psychomotor performance on the Bayley scales of infant development was also significantly worse in the latter group. All three survivors with intracerebral haemorrhage had major disability. The continuation of life support treatment for extremely preterm infants who are at very high risk of severe handicap is a matter of increasing concern in neonatal intensive care. Our results show that if extensive periventricular haemorrhage, in particular intracerebral haemorrhage, occurs in this gestational group, extreme pessimism is warranted.

A number of studies have shown an adverse relation between the severity of neonatal periventricular haemorrhage and subsequent neurodevelopmental outcome.^{1–6} There are, however, at least three published reports^{7–9} that have failed to show this. In most studies there was a selection of 'high risk' infants for the diagnosis of periventricular haemorrhage usually by computed tomography; those included had either a clinical suspicion of haemorrhage^{1 5 7} or were considered to have certain risk factors, including male sex, birth asphyxia, multiple gestation, congenital malformation, and assisted ventilation.^{4 6} It is known, however, that in nearly half the very low birthweight infants with periventricular haemorrhage this is not suspected clinically,¹⁰ thus introducing an inherent selection bias to these previous studies. All except three studies^{6–9} included many more mature infants of over 28 weeks' gestation with relatively little attention being focused on the extremely preterm infant with a gestational age of 28 weeks or less. Some studies have been small,^{1 7} with none or very few

survivors with the more severe grades of haemorrhage,^{1 2 8} and survivors without periventricular haemorrhage were not included for comparison.^{1 4 5 7} The attrition rate at follow up exceeded 10% in all except two studies^{2 3} and in only one study did all the children reach 2 years of age at assessment.⁵

In the present study, all extremely preterm infants born between 23 and 28 weeks of gestation, who were admitted to the Queen Victoria Medical Centre in 1981, were studied for periventricular haemorrhage. The outcome at 2 years of age in the survivors was reported to determine the effect of haemorrhage on their neurodevelopment.

Patients and methods

Fifty six infants of between 23 and 28 weeks of gestation consecutively admitted to this hospital during 1981 were studied by cerebral ultrasonography or necropsy, or both. An obstetric estimate of gestation was available for most infants; this was

calculated from the first day of the last maternal menstrual period and confirmed either by an early ultrasound measurement of the fetal crown-rump length or by clinical bimanual palpation of the uterus in the first trimester by an experienced obstetrician.¹¹ The paediatric assessment of gestation was relied on only in those few instances in which the obstetric assessment was unavailable.

Cerebral ultrasound studies were performed using a portable, real time scanner (Toshiba SAL 20) fitted with either a 3.5 MHz or 5 MHz linear array transducer.¹⁰ The first study was performed as soon as possible after admission and repeated once or twice weekly. The mean number of scans done was three, (range, one to seven). Ultrasound findings were described according to the site of visible haemorrhage. Germinal layer haemorrhage was restricted to the germinal matrix only. Intraventricular haemorrhage referred to any amount of intraventricular blood with or without dilation, and intracerebral haemorrhage referred to any intracerebral extension.

Thirty three (59%) infants were discharged from hospital; one of these died shortly afterwards and one was lost to follow up. Thirty one (97%) of the long term survivors were assessed at the corrected age of 2 years, apart from one infant who was assessed at 1 year but died shortly before the 2 year assessment. At the Growth and Development Clinic children were given clinical, neurological, and psychological assessments by a multidisciplinary team.¹² The Bayley scales of infant development were administered which included a mental developmental index and a psychomotor developmental index. Major disability was defined as cerebral palsy of any type or severity, blindness, sensorineural deafness, developmental delay (mental developmental index more than 2SD below the mean), epilepsy, and hydrocephalus necessitating ventriculoperitoneal shunting.

Results

The mean birthweight of the 56 extremely preterm infants was 938 g (range 567 to 1378 g). Thirty four (61%) had periventricular haemorrhages; 12 (22%) had germinal layer haemorrhages, 18 (32%) had intraventricular haemorrhages, and four (7%) had intracerebral haemorrhages. The number of infants, mean birthweight, and incidence of periventricular haemorrhage at each week of gestation are shown in Table 1. There was no significant difference in birthweight, gestation, sex, Apgar scores at 1 and 5 minutes, or the requirement and duration of assisted ventilation between those infants with and without periventricular haemorrhage or those with no

Table 1 Incidence of periventricular haemorrhage

Gestation (wks)	No of infants	Birthweight (g) Mean (SD)	Incidence of periventricular haemorrhage No (%)
23	3	724 (142)	3 (100)
24	7	708 (97)	4 (57)
25	9	871 (44)	6 (67)
26	9	900 (161)	4 (44)
27	18	990 (178)	11 (61)
28	10	1164 (292)	6 (60)
Total	56	938 (205)	34 (61)

periventricular haemorrhage or germinal layer haemorrhage and intraventricular or intracerebral haemorrhage (Table 2).

Table 3 shows that six of the 31 survivors (19%) had cerebral palsy, six (19%) had developmental delay, two (6%) had blindness (one had cortical blindness and one had retrolental fibroplasia), two (6%) had epilepsy, and one had posthaemorrhagic hydrocephalus requiring ventriculoperitoneal shunting. Three children had more than one major disability. Eight of the 12 children with major disabilities were considered to have severe or moderate functional handicap. Therefore, of the 56 infants born at 23 to 28 weeks' gestation, 24 (43%) died, eight (14%) survived with a serious functional handicap, one (2%) was lost to follow up, and 23 (41%) were considered to be developing within the normal range.

There was no significant difference between those survivors with disability and infants without disability in respect of birthweight (mean (SD) 959 (238) g v 943 (233) g) or gestation (mean SD 26.4 (1.8) weeks v 26.7 (1.2) weeks). The number of survivors with and without periventricular haemorrhage and the incidence of major disability in the respective groups are shown in Table 4. Only one (9%) of the

Table 2 Perinatal data

Perinatal factors	No periventricular haemorrhage ± germinal layer haemorrhage	Intraventricular ± intracerebral haemorrhage
Birthweight (g). Mean (SD)	985 (252)	893 (192)
Gestation (wks) Mean (SD)	26.6 (1.3)	25.5 (1.7)
Male sex No (%)	8 (42)	8 (62)
Apgar score Mean (SD)		
1 minute	5.6 (2.1)	5.6 (2.4)
5 minutes	7.4 (1.8)	7.2 (2.1)
Assisted ventilation No (%) infants	18 (84)	11 (92)
Duration (days)	16 (13)	23 (21)

Table 3 *Survivors with major disability*

Gestation (wks)	Birthweight (g)	Periventricular haemorrhage	Cerebral palsy	Mental developmental index	Other disabilities	Functional handicap
23	580	ICH	Quadriplegia	<50	—	Severe
25	909	IVH	Quadriplegia	<50	—	Severe
26	1019	IVH	Quadriplegia	72	—	Severe
28	1287	—	Quadriplegia	<50	Blind, epilepsy	Severe
24	695	ICH	Hemiplegia	83	—	Mild
25	847	IVH	Hemiplegia	85	—	Mild
27	870	ICH	—	—	Blind (RLF)	Severe
27	1125	IVH	—	79	Hydrocephalus	Nil
28	1285	GLH	—	77	Epilepsy	Mild
23	730	IVH	—	63	—	Moderate
27	1259	GLH	—	67	—	Moderate
28	904	IVH	—	67	—	Moderate

ICH=intracerebral haemorrhage; IVH=intraventricular haemorrhage; GLH=germinal layer haemorrhage; RLF=retrolental fibroplasia.

Table 4 *Periventricular haemorrhage and major disability*

	No of survivors	No (%) with major disability
No periventricular haemorrhage	11	1 (9)
Periventricular haemorrhage	20	11 (55)
Germinal layer haemorrhage	8	2 (25)
Intraventricular haemorrhage	9	6 (67)
Intracerebral haemorrhage	3	3 (100)

survivors with no periventricular haemorrhage had a major disability compared with 11 (55%) of survivors with periventricular haemorrhage ($P<0.05$, Fisher's exact test). There is an apparent trend between the gradation of periventricular haemorrhage and incidence of disability. When survivors with no periventricular haemorrhage or germinal layer haemorrhage were compared with those with intraventricular or intracerebral haemorrhage the incidence of major disability among those with lesser or no haemorrhage (three of 19 (16%)) was lower than those with more severe haemorrhage (nine of 12 (75%)) ($P<0.01$, Fisher's exact test). The former group also had significantly higher mental developmental index scores (mean (SD) 74 (19) v 65 (17), $P<0.02$) and psychomotor developmental index scores (mean (SD) 97 (24) v 88 (20), $P<0.01$) compared with the latter group.

Discussion

The incidence of periventricular haemorrhage in this study is higher than in previous reports.¹⁻⁶ It is known, however, that the risk of periventricular haemorrhage is in inverse proportion to gestation,¹³ and the present study comprised a much more preterm population. We found a similar incidence of 60% in a previous study carried out in infants who were 1250 g or less at birth.¹⁴

The incidence of major disability in survivors is higher than that found in two previous studies. These also carried out routine real time cerebral ultrasonography on an entire preterm population but reported the outcome of survivors at 1 year of age;^{2,3} all infants under 33 to 34 weeks were included, their birthweights ranged up to 2500 g, and none were below 27 weeks.

The present study showed that the incidence of major disability of extremely preterm children at 2 years of age was significantly higher after intraventricular and intracerebral haemorrhage. Both mental and psychomotor development were also delayed significantly in the latter group, similar to the findings in a previous study of more mature preterm infants in which a selected group with intraventricular haemorrhage was compared with a matched control group.¹⁵

Only one infant without periventricular haemorrhage had major disabilities, and these were multiple and severe. He was one of the most mature and heavier infants in the study (28 weeks and 1287 g), his Apgar scores at birth were 4 at 1 and 6 at 5 minutes, and he required ventilation for only two days. The cause of his disability is unknown. We have previously documented that in a very low birthweight population 50% of children found to have cerebral palsy at 2 years did not require assisted ventilation in the neonatal period and 93% had a 5 minute Apgar score greater than 4.¹⁶

The continuation of life support treatment for extremely preterm infants who are at very high risk of severe handicap is a matter of increasing concern to members of both the medical profession and the public.^{17,18} It will probably be possible to identify which of these extremely preterm infants are so hopelessly brain damaged that intensive care can, with parental consent, be withdrawn ethically. Our results show that if intracerebral haemorrhage

occurs in this gestational group, extreme pessimism is warranted. Larger numbers and a longer follow up, however, are required before a definitive approach to their neonatal management can be suggested. Certainly there are case reports of only minor disability after intracerebral haemorrhage in more mature infants.^{19 20} They are important and disturbing reminders of our very limited ability to predict the outcome for an individual infant despite increasing knowledge about the epidemiology of neonatal complications. Theoretically, it would seem that the preterm brain, while in a relatively 'plastic' state, might be able to compensate for severe damage more effectively.²¹ Recent advances in neuroradiological techniques (position emission tomography²² and nuclear magnetic resonance²³) may make it possible not only to relate neurodevelopmental outcome to structural damage of the neonatal brain but also to functional and ischaemic lesions.

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