Brain-orientated intensive care treatment in severe neonatal asphyxia

Effects of phenobarbitone protection

N W SVENNINGSEN, G BLENNOW, M LINDROTH, P O GÄDDLIN, AND H AHLSTRÖM

Department of Paediatrics, Units of Neonatology and Neurology, University Hospital, Lund, Sweden

SUMMARY The effect of applying brain-orientated neonatal intensive care for term infants with severe neonatal asphyxia was studied. Such treatment included protective phenobarbitone administration together with assisted ventilation and other measures to counteract postasphyxial cerebral oedema and any abrupt changes in blood pressure and oxygenation. The mortality rate and incidence of long-term sequelae were reduced appreciably, resulting in a 0–1 year mortality rate of 14% (previously 50%) and an incidence of neurodevelopmental handicap at 18 months of 17% (previously 50%). It is important in the management of infants with severe asphyxia at birth to avoid blood pressure fluctuations and to control neuronal epileptic activity by the use of barbiturates and early ventilator treatment.

Some reports have shown that the long-term prognosis of infants who respond rapidly to resuscitation after neonatal asphyxia may not be as bad as might have been expected from the initial condition of the baby and the course of the disease. However, the more severely asphyxiated infant with inadequate respiration and abnormal motor activity after resuscitation eventually develops apnoeic spells and convulsions, and such infants have a high mortality rate and incidence of cerebral handicaps. Consequently in any baby with severe asphyxia the risk of serious handicap is high. As the chance of handicap cannot be predicted it is difficult to decide to what extent resuscitative efforts should be applied. Mortality rate and incidence of long-term neurodevelopmental handicaps probably vary according to the practice followed by the individual hospital—for example, when to start and when to stop resuscitation. The increasing use of mechanical ventilation in many neonatal units has accentuated this problem as the doctor in charge has to decide if such treatment should be started.

The aim of our study was to evaluate the advantages of early administration of phenobarbital in high dosage combined with vigorous treatment of shock and ventilatory support in term infants with severe neonatal asphyxia.

We studied 35 term (37 to 42 weeks’ gestation) newborn infants with severe neonatal asphyxia treated in our neonatal intensive care unit during the 6-year period 1973 to 1979. During the first 3 years (May 1973 to October 1976) 16 infants (group A) were treated conservatively (treatment A). During the second 3 years (November 1976 to October 1979) 19 infants (group B) were treated in accordance with our special intensive care protocol (treatment B). Any infant with a CNS congenital malformation, other lethal malformation, or a chromosomal disorder was excluded from the study.

Criteria.

Severe neonatal asphyxia

This was considered present if insufficient respiration and severe hypotonia persisted after more than 30 minutes of intensive resuscitation. Most babies also had had signs of intrauterine asphyxia—such as abnormal fetal heart rate pattern on cardiotachographic registration and a fetal scalp pH below 7·20. Only term infants fulfilling these criteria were studied.
Neonatal management

The following procedures were common to groups A and B. General principles in our neonatal intensive care unit have been given earlier.6 7

All infants were nursed in incubators in a neutral thermal environment with a humidity between 60 and 80%. Umbilical vein and artery catheters were inserted and the catheter position controlled by the use of an x-ray film. Chest and abdomen x-ray examinations were done on days 1 and 2, and thereafter according to the condition of the patient. They included: acid-base balance with arterial blood gas measurements, haemoglobin, platelets, prothrombin, blood glucose, serum electrolytes, C-reactive protein, leucocytes and blood cultures, serum creatinine, and blood urea. Electronic monitoring of heart rate, respiration, and skin temperature was made using SAAB-respimeter (SAAB, Linköping, Sweden) or HP cardiorespirograph (Hewlett-Packard, USA). During the last 2 years of the study transcutaneous oxygen tension (TcPo₂) was measured with a radiometer TcPo₂-meter (Radiometer A/S, Copenhagen, Denmark). In 9 infants in group B arterial blood pressure was measured via the umbilical artery catheter. Fluid balance was calculated by continuous measurements of parenteral and peroral fluid supply and fluid output via stool and urine.

Electroencephalograms were recorded in all infants. In any infant with convulsions, a lumbar puncture to search for signs of meningitis or cerebrospinal fluid haemorrhage with cytological examination8 was also done. Head circumference was watched during treatment.

Intravenous fluids

Intravenous fluids given were 10% glucose, generally with sodium-bicarbonate on day 1–2 (6 mmol/100 ml 10% glucose). Thereafter sodium, potassium, calcium, chloride, and 20% human albumin (AB Kabi, Sweden) were added according to fluid and electrolyte balance. The fluid amounts were 60–80 ml/kg per 24 hours on days 1–2, 80–100 ml/kg per 24 hours on days 2–3, and 100–120 ml/kg per 24 hours thereafter.

Antibiotics

Immediately after resuscitation cephalothin (100 mg/kg per 24 hours) was given. If sepsicaemia was diagnosed, treatment was changed to gentamicin (7 mg/kg per 24 hours) and cloxacillin (100 mg/kg per 24 hours) or carbenicillin (200 mg/kg per 24 hours). Serum concentrations of gentamicin were analysed once or twice a week.

Treatment A.

Intubation and ventilator treatment

If the infant had required endotracheal intubation, this was stopped immediately spontaneous breathing started. For correction of acidosis, sodium bicarbonate 5 ml per estimated kg body weight was given through an umbilical vein catheter at 10 to 20 minutes of age to any infant requiring endotracheal intubation. Ventilator treatment was started only if the baby did not obtain spontaneous respiration or if recurrent apnoeic attacks requiring mask and bag ventilation or severe respiratory insufficiency with hypercarbia (Paco₂ > 9 kPa) later occurred.

Blood transfusion

This was given to any infant with a level of haemoglobin below 140 g/l during the first 48 hours after birth.

Anticonvulsive treatment

If convulsions were recorded, an initial intravenous dose of diazepam (1 mg/kg) was given; for recurrent convulsions phenobarbitone (8 mg/kg per 24 hours in two doses intramuscularly or perorally) was given. If the convulsions did not respond, pyridoxine 100 mg in a single dose was given. If the convulsions still continued lidocaine (4–6 mg/kg per hour intravenously in 5–5% glucose infusion) was added.

Treatment B.

Intubation and ventilator treatment

If the baby had required intubation initially, the baby was extubated as soon as adequate spontaneous breathing had been established. Sodium-bicarbonate (5 ml/kg estimated body weight) and 30% glucose (2 ml/kg) were given via umbilical vein catheter at between 10 and 20 minutes after birth. Ventilator treatment was started after resuscitation if the baby did not show regular spontaneous breathing and adequate muscular tone with vigorous movements, and did not cry within 30 minutes after delivery.

Blood and plasma transfusions

All infants were given fresh frozen plasma within the first hours after delivery and thereafter daily for 3 days postnatally in a dosage of 10–15 ml/kg intravenously. Hypotensive infants in shock or with low haemoglobin concentrations (less than 150 g/l at age 0–24 hours) were given erythrocyte concentrate 10 mg/kg repeatedly. Infants with signs of haemorrhagic disorders (blood oozing from umbilicus or heel pricks) received antifibrinolytic drugs (Cyklokapron) and fresh blood exchange transfusion.

Barbiturate protection

In infants fulfilling the criteria for severe neonatal
asphyxia (vide supra) phenobarbitone treatment was started, generally within 60 minutes of delivery without awaiting clinical signs of convulsions. An initial intravenous dose of 10 mg/kg was given and then 4 hours later treatment with 10 mg/kg per 24 hours in two doses was started.

Brain oedema treatment
Bethametasone was started simultaneously in a dosage of 2 mg intravenously 6-hourly and frusemide in a dosage of 2 mg/kg intravenously 8-hourly. These drugs were tailed off over 48 to 96 hours.

Anticonvulsive treatment
If convulsions still occurred despite phenobarbitone intravenous diazepam (1–2 mg/kg) was administered. If convulsions still persisted lidocaine was given in an initial dose of 2 mg/kg intravenously, and thereafter 4–6 mg/kg per hour, tailed off over 24 to 36 hours.

Drug level monitoring
Serum concentration of phenobarbitone was measured 24–48 and 72–96 hours after starting treatment. On day 4 the treatment was tailed off over 4–6 days until the serum concentration was below 125 μmol/l (3 mg/100 ml) before the baby was taken off the ventilator. In infants receiving diazepam the serum concentration of diazepam and N-desmethyldiazepam was measured before the baby was taken off the ventilator.

Treatment with phenobarbitone was continued beyond the neonatal period, generally for 4 to 6 months, if an infant showed clinical signs of convulsions. In such infants the serum concentration of phenobarbitone was kept between 50 and 80 μmol/l (1·2 and 1·8 mg/100 ml).

Follow-up examinations. Sono-encephalogram and skull transillumination as well as neurological evaluation were made before discharge from the neonatal unit.

At 5–6, 9–10, and 14–18 months neurodevelopmental examinations were performed in all babies. Ophthalmological examination and audiometric tests (at 10–18 months) were also performed in all.

Statistical methods. The χ² test has been used for group comparisons.

Results
Table 1 gives details of the infants. There were 16 group A and 14 group B infants with early neonatal asphyxia at delivery. In addition 5 group B infants with late neonatal asphyxia are presented separately. They had sudden cardiac arrest and apnoea several hours postnatally after a clinically apparently symptom-free period. All were term infants. One in group A and 2 in group B were small for gestational age. The boy/girl distribution was 12/4 and 12/7. Instrumental or caesarean section delivery had been made in 8 of 16 infants in group A and in 10 of 19 infants in group B.

Among the infants with early neonatal asphyxia 10 in group A and 7 in group B were inborn (that is delivered in the maternity hospital in Lund). During period A another 4 and during period B another 2 term infants with severe perinatal asphyxia did not respond to resuscitation and died shortly after delivery. These 6 infants were not included in the study. In our inborn population the total incidence of severe early neonatal asphyxia was 1·1 per thousand (14 of 12 653 liveborn infants) during period A and 0·8 per thousand (9 of 10 519 liveborn infants) during period B.

The degree of asphyxia as evaluated by Apgar score is also shown in Table 1. The mean Apgar score of infants in groups A and B with early asphyxia at delivery was not appreciably different, whereas group B infants with late neonatal asphyxia had only slightly reduced Apgar scores. In group A 10 (62%) of 16 infants were treated with intermittent positive pressure ventilation (IPPV). In these infants IPPV was started at a mean age of 8·5 hours

<table>
<thead>
<tr>
<th>Group</th>
<th>Early asphyxia (n=16)</th>
<th>Late asphyxia (n=5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>3366</td>
<td>3168</td>
</tr>
<tr>
<td>Range</td>
<td>2380–4100</td>
<td>1970–4430</td>
</tr>
<tr>
<td>Gestational age (weeks)</td>
<td>Mean</td>
<td>39·7</td>
</tr>
<tr>
<td>Range</td>
<td>37–42</td>
<td>37–42</td>
</tr>
<tr>
<td>Small for gestational age (&lt;2 SD)</td>
<td>Boys: girls</td>
<td>1:2:4:9:5</td>
</tr>
<tr>
<td>Mode of delivery</td>
<td>Vaginal: vertex*</td>
<td>14 (6)</td>
</tr>
<tr>
<td></td>
<td>Breech</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>Caesarean section</td>
<td>2</td>
</tr>
</tbody>
</table>

Table 1 Clinical data of 35 infants with severe neonatal asphyxia

- *Vacuum extraction, forceps instrumental delivery in brackets.
- NS not significant.
Table 2  Clinical data of 5 group B infants with late neonatal asphyxia

<table>
<thead>
<tr>
<th>Sex</th>
<th>Birthweight (g)</th>
<th>Gestational age (weeks)</th>
<th>Delivery</th>
<th>Apgar score</th>
<th>Neonatal asphyxia</th>
<th>Age at which respiratory and cardiac arrest took place (hours)</th>
<th>Age at which IPPV started (hours) and duration</th>
<th>Symptoms</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>M</td>
<td>3180</td>
<td>41</td>
<td>Caesarean section (ablation placentae)</td>
<td>9-9-9</td>
<td>13 (5 days)</td>
<td>Persistent fetal circulation. No convulsions</td>
<td>Normal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>F</td>
<td>4020</td>
<td>40</td>
<td>Vertex</td>
<td>7-5-5</td>
<td>2 (6 days)</td>
<td>Neononin aspiration. No convulsions</td>
<td>Normal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>4150</td>
<td>40</td>
<td>Breech</td>
<td>8-10-9</td>
<td>2 (3 days)</td>
<td>Meconium aspiration. Convulsions at 4 hours</td>
<td>Died day 3 (anoxic encephalopathy and meconium aspiration syndrome)</td>
<td>Normal</td>
<td></td>
</tr>
<tr>
<td>F</td>
<td>2940</td>
<td>39</td>
<td>Vertex</td>
<td>9-10-10</td>
<td>48 (10 days)</td>
<td>Group B streptococcal sepsis.</td>
<td>Infantile spasms. Moderate psychomotor retardation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>3120</td>
<td>37</td>
<td>Caesarean section</td>
<td>9-9-9</td>
<td>9 (21 days)</td>
<td>Persistent fetal circulation.</td>
<td>Normal</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(range 1 to 18). In group B 11 (87%) of 14 infants were treated with IPPV starting early according to treatment B criteria at a mean age of 0-9 hours (range 0-5 to 4) after birth. The delay in starting IPPV in some group B infants was mainly related to transportation of outborn infants. In the 3 infants not treated with IPPV in group B, sufficient spontaneous ventilation and oxygenation had been established at arrival in the neonatal intensive care unit. Despite starting earlier, IPPV was not continued significantly longer in group B than in group A. The 5 group B infants with late neonatal asphyxia were started on IPPV after resuscitation because they fulfilled our criteria for severe neonatal asphyxia. Their clinical data and diagnoses are shown in Table 2.

Mortality. As shown in Table 3 the total mortality (at age 0-12 months) was significantly lower in group B (14%) than in group A (50%). In group A 5 infants died in the neonatal period with anoxic encephalopathy at necropsy examination. Cerebral oedema in 3 of these infants, and intraventricular haemorrhage in the remaining 2 were major additional findings. Postnatal deaths occurred at 1 3/2, 3, and 3 1/2 months of age in group A and at 7 and 11 months of age in group B infants. These 5 infants all had severe anoxic encephalopathy with cortical-cerebral atrophy at necropsy. All had shown clinical symptoms of severe cerebral sequelae—that is convulsions, retarded psychomotor development, and tetraplegia or hemiplegia.

Handicaps in surviving infants. As shown (Table 4) the higher survival rate in group B did not result in

Table 3  Mortality rate

<table>
<thead>
<tr>
<th>Group A</th>
<th>Group B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early asphyxia (n=16)</td>
<td>Early asphyxia (n=14)</td>
</tr>
<tr>
<td>Liveborn infants</td>
<td>16 (10)</td>
</tr>
<tr>
<td>Mortality 0-28 days</td>
<td>5 (4)</td>
</tr>
<tr>
<td>Mortality 28 days–1 year</td>
<td>3 (3)</td>
</tr>
<tr>
<td>Total mortality</td>
<td>8 (50%)</td>
</tr>
<tr>
<td>P-value</td>
<td>\textless{}0.05</td>
</tr>
</tbody>
</table>

No of infants treated with IPPV shown in brackets.

Table 4  Handicap rate in infants after severe neonatal asphyxia and surviving the first year of life

<table>
<thead>
<tr>
<th>Group A</th>
<th>Group B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early asphyxia (n=16)</td>
<td>Early asphyxia (n=14)</td>
</tr>
<tr>
<td>Survivors at 1 year</td>
<td>8 (50%)</td>
</tr>
<tr>
<td>Neurodevelopmental sequelae in survivors</td>
<td>4 (50%)</td>
</tr>
<tr>
<td>CP</td>
<td>1</td>
</tr>
<tr>
<td>CP+PMR</td>
<td>1</td>
</tr>
<tr>
<td>CP+PMR+convulsions</td>
<td>2</td>
</tr>
<tr>
<td>PMR+convulsions</td>
<td>—</td>
</tr>
<tr>
<td>Rate of handicap</td>
<td>4 (50%)</td>
</tr>
<tr>
<td>In survivors</td>
<td>4 (50%)</td>
</tr>
<tr>
<td>P-value</td>
<td>\textless{}0.05</td>
</tr>
</tbody>
</table>

CP = cerebral palsy, PMR = psychomotor retardation.
an increased rate of neurodevelopmental handicaps (17%) compared with group A (50%). On the contrary in relation to the total number of infants the incidence of normal survivors after early severe asphyxia was 71% in group B compared with only 25% in group A (P < 0.01). In infants with early neonatal asphyxia at birth the following handicaps were found:

**Group A**
One infant had moderate diplegia only, one hemiplegia with moderate psychomotor retardation, and 2 infants severe dyskinetic cerebral palsy, and convulsive disorders (infantile spasms in one case).

**Group B**
One infant had severe tetraplegia and psychomotor retardation, and one infant with moderate psychomotor retardation had hemiconvulsions at age 2 years.

In infants with late neonatal asphyxia only 1 of 4 survivors developed abnormally with infantile spasms at age 4 months, later developing slight psychomotor retardation but no seizures. The normal survivors were at least 18 months (range 18 months—6 years) at the last follow-up examination.

**Convulsions and phenobarbitone treatment.** Neonatal convulsions occurred in 87% of group A infants (Table 5). In group B phenobarbitone treatment was started as soon as intensive care treatment had been decided on. Yet in 3 infants convulsions had started before phenobarbitone treatment was instituted and 9 infants had convulsions despite it. However, recurrent neonatal convulsions occurred much more often in group A (63%) than in group B infants (21%).

Convulsive disorders were still present after the neonatal period in 5 of 11 group A infants compared with only 3 of 14 group B infants.

Phenobarbitone serum concentrations were regularly measured in group B infants and the maximum levels obtained are shown in the Figure. Although the initial dose was equal in all cases the maximum level generally obtained on day 2 or 3 differed widely, as did the disappearance rate after stopping phenobarbitone. Apart from these pharmacokinetic peculiarities of phenobarbitone, we noted that in infants with serum concentrations greater than 225 μmol/l (5.2 mg/100 ml) there was invariably a decrease of heart rate below 100 per minute as well as decreased beat-to-beat variability (to less than 5) in infants monitored with a cardiorespirograph. In 6 group B infants blood pressure monitoring showed a decrease of mean arterial blood pressure from 40–50 to 30–35 mmHg within 15 minutes after intravenous phenobarbitone infusion.

**Discussion**

Several experimental studies have indicated that barbiturate can ameliorate the effects of various types of brain hypoxia or ischaemia even when administered in the phase of resuscitation.6–15 This has led to clinical trials of barbiturate therapy after cardiac arrest in adults and these have given contradictory results.11–15 In one report a lower rate of mortality and brain damage was found in the
offsprings of rhesus monkey mothers treated by barbiturate before birth. The present study our aim was to evaluate the outcome of phenobarbitone treatment in the neonatal period as protection against brain lesions in severely asphyxiated newborn infants.

There are several possible mechanisms whereby barbiturate may exert a protecting effect for example by a sedative effect, by a reduced cerebral metabolic rate of oxygen (CMRO\textsubscript{2}) known to follow barbiturate administration, by the anticonvulsant effect per se, by prevention of cerebral oedema and reduction of intracranial hypertension, or by a membrane stabilisation effect. The suggested ability of phenobarbitone to inhibit lipid peroxidation has recently been disproved.

Recent reports indicate that in asphyxiated preterm newborn infants the autoregulation of cerebral blood flow in relation to blood pressure is lost leading to a pressure passive cerebral blood flow. Consequently there is a considerable risk of cerebral haemorrhage due to sudden rise in blood pressure often occurring during infant care (for example, at suctioning, handling, feeding, etc.) or during seizures. In our study 2 infants who died early in the neonatal period actually had cerebral haemorrhage at necropsy in addition to anoxic encephalopathy. For the same reason the risk of ischaemic cerebral lesions due to sudden drop in blood pressure is also high in neonatal asphyxia. From continuous measurements of blood pressure in some babies in our study it was obvious that the rather high barbiturate concentrations obtained ameliorated sudden rapid blood pressure changes—for example during endotracheal tube suctioning or lumbar puncture. In this context animal studies showing that during stress CMRO\textsubscript{2} will increase to about twice the pre-stress value should be taken into consideration. Thus sedation may be crucial in the treatment of seriously ill newborn infants.

It is well known that seizures under certain circumstances may give rise to brain damage. Therefore the anticonvulsant effect of barbiturate per se may also be an important protective factor. Postasphyxial seizures are common after severe neonatal asphyxia, in some reports occurring in more than half of the cases. Furthermore, in these studies several children with neurodevelopmental handicaps initially had had prolonged seizures. In the postasphyxial state convulsions probably have a deleterious effect since CMRO\textsubscript{2} increases if there is impaired circulation and ventilation, finally leading to curetted cerebral energy balance. Furthermore, Wasterlain showed that even short-lasting but recurrent seizures in newborn rats are followed by reduction in brain size and DNA content. Thus it is important to prevent prolonged or recurrent seizures after neonatal asphyxia. Despite early anticonvulsant treatment several group B infants still had seizures. However, recurrent seizures were avoided to a large extent in this group (Table 5).

Large doses of barbiturate may cause cardiac failure. Besides a moderate bradycardia (85 to 105 beats per minute) and decrease of beat-to-beat variability we noted only a moderate decrease in blood pressure. If cerebral autoregulation is abolished in asphyxiated infants such a decrease in blood pressure could lead to a reduction in brain perfusion and lower cerebral oxygen availability. However, this is counterbalanced by the reduction in CMRO\textsubscript{2} induced by barbiturate.

Barbiturate blood levels varied widely but in all cases levels well above the therapeutic range considered anticonvulsant in older infants (50-120 \textmu mol/l (1-2-2.9 mg/100 ml)) were reached. At levels above 200 \textmu mol/l (4-8 mg/100 ml) no infant had seizures. However, respiratory insufficiency occurred at levels 150-180 \textmu mol/l (3-6-4-3 mg/100 ml). It is possible that the phenobarbitone administration thereby may have prolonged ventilator treatment in some infants. From studies of Jallig it is known that the phenobarbitone half-life in the newborn is long and variable. It was not possible to keep to a fixed treatment schedule as our asphyxiated newborn infants in several cases showed unpredictable pharmacokinetics (Figure). Repeated measurements of serum levels must be done during treatment, and heart rate and blood pressure should be monitored continuously.

Brain swelling is common in asphyxiated newborn infants, and was found in 3 infants at necropsy in our study. In accordance with earlier studies we therefore added steroids and IPPV to our intensive care treatment. The hyperosmotic glucose solution given initially in group B should counteract cerebral oedema more rapidly than steroid treatment which does not reduce intracranial pressure in less than 12 to 24 hours. Eventually the presumed membrane stabilising ability of barbiturate may also help to diminish the brain oedema.

The impact of disturbances in carbohydrate turnover in perinatal asphyxia is unknown. Experimental studies have repeatedly shown that hypoglycaemia reduces resistance to anoxia and seizures in the newborn period. There is experimental evidence implying that blood glucose concentrations considered adequate in physically well infants may be inadequate in cases of asphyxia. Furthermore, it has been claimed that perinatal asphyxia may play a role in early onset of neonatal hypoglycaemia, especially in term infants. On the other hand, experimental studies indicate that the brain lactate
accumulation after anaerobic metabolism may be a deleterious factor, brain lesions being less common in animals starved before experimental hypoxia. However, these studies have dealt with metabolic events before and during the asphyxial period. The consequence of administration of glucose in the resuscitation period in newborns has not been defined. In this context the impending heart failure due to depletion of cardiac glycogen stores must also be considered.

Not only is adequate oxygenation crucial; the Pco₂ level is of considerable importance too. Cerebral blood flow varies directly with the CO₂ tension and it has been shown that slight or moderate hypercarbia will increase the rate of intraventricular haemorrhage in newborn infants. Hyperventilation transiently and quickly lowers the intracranial pressure. In the present study we aimed at and obtained in most cases an arterial Pco₂ level in the range of 2-8 to 4.5 kPa (21 to 33 mmHg) within the first hours of IPPV treatment. As glomerular filtration rate is much lower in neonatal asphyxia diuretics were included in the initial intensive care treatment to avoid fluid overload.

Owing to the fact that we had few patients and were not able to achieve a double-blind design, evaluation of our study should be cautious. However, this brain-orientated intensive care regimen including phenobarbitone protection seemed to improve the outlook for this group of patients in whom the prognosis would otherwise have been bad. Whether this regimen can be used in severely asphyxiated low birthweight infants cannot be decided without further clinical trials. Finally, we want to stress that the resources of a neonatal intensive care unit with experience in assisted ventilation and blood pressure monitoring is necessary for this kind of treatment until further experience is gained.

This work was supported by grants from Margaretha-hemmet, First of May Flower Research Foundation, Jerring Research Foundation, and Swedish Medical Research Foundation grants Nos 29X-4732 and 14X-02872.

References

Brain-orientated intensive care 183


Correspondence to Dr N W Svenningsen, Neonatal Intensive Care Unit, Department of Paediatrics, University Hospital, S-221 85 Lund, Sweden.

Received 24 August 1981
Brain-orientated intensive care treatment in severe neonatal asphyxia. Effects of phenobarbitone protection.

N W Svenningsen, G Blennow, M Lindroth, P O Gäddlin and H Ahlström

Arch Dis Child 1982 57: 176-183
doi: 10.1136/adc.57.3.176

Updated information and services can be found at:
http://adc.bmj.com/content/57/3/176

These include:

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/