NEUROLOGICAL PROBLEMS

Neonatal Seizures

Guidelines For Management

The incidence of neonatal seizures in babies born at term is 0.7-2.7 per 1000 live births and is probably higher in the preterm population. Few are idiopathic in aetiology therefore prompt recognition and treatment of the underlying cause is vital.
A clinical seizure is a sudden, paroxysmal depolarisation of a group of neurones that results in a transient alteration in neurological state. This may involve abnormal motor, sensory or autonomic activity with or without a change in conscious level. Seizures may be subtle and difficult to identify and apnoea and bradycardia may, for example, be the only outward sign.

Classification.

Evans and Levine (1998) suggest the following adapted from Volpe (1995):

Subtle	Eyelid fluttering, eye deviation, fixed open stare, chewing, sucking, tongue thrusting,cycling, boxing, tachycardia, BP instability and apnoea.
Clonic	Rhythmic jerking, consciousness usually preserved. Focal, multifocal or generalised. Often correlate with a structural lesion.
Myoclonic	Rapid, isolated jerks. Rare in neonatal period and usually indicates diffuse cerebral disease. Focal, multifocal or generalised.
Tonic	Extension of upper and lower limbs accompanied by pronation of arms and clenching fists. Often less than a minute and seen most commonly in the first 24 hrs of life following an hypoxic- ischaemic insult.

Principles of Management:

1. Resuscitation and supportive measures.
2. Assessment and treatment of the underlying cause.
3. Anticonvulsant therapy.

1. Resuscitation and supportive measures:

Airway- clear and maintain the airway.
Breathing- provide adequate oxygenation, mechanical ventilation if necessary.
Circulation- site an iv cannula, volume support if indicated.

Check the blood sugar and correct hypoglycaemia urgently
Ensure appropriate monitoring: saturations, ECG and blood pressure. Early cerebral function monitoring should be considered but should not delay anticonvulsant treatment unduly.

2. Assessment and treatment of the underlying cause:

The initial aim is to identify those conditions which are correctable thus removing the root cause of seizure activity.

History: family history, pregnancy (growth, infections, drugs, diabetes, ?fitting in utero), birth (hypoxia, trauma).

Examination: birth weight and head circumference, congenital abnormalities, signs of congenital infection, neurological abnormalities.

Investigations:

glucose (BM and lab)
urea and electrolytes, calcium, magnesium — **Mandatory and**
blood gas — **urgent blood tests**
blood culture.

Further investigations may be modified according to history but all babies should have a cranial ultrasound and a LP should be seriously considered .

Blood: clotting, LFTs
amino acids, ammonia
congenital infection screen
cardiac enzymes if HIE possible

CSF: MC&S
Protein and glucose
Consider lactate, glycine and herpes PCR

Urine: toxicology
amino acids and organic acids
reducing sugars

Others: Cranial US
MRI (see protocol)
EEG (see protocol)

Diagnosis	**Presentation**	**Treatment**
Hypoxic-ischeamic injury	Term baby with a history of extensive resuscitation. Seizures usually within 24 hrs	See guidelines for HIE
Intracranial causes	Preterm infant: fits occur 24-72 hrs following IVH Term infant: HIE as above, antenatal cerebral infarction / bleed	
Infection	Consider meningitis, herpes encephalitis, CMV, toxoplasmosis.	Treat for sepsis (see protocol), consider acyclovir
Hypoglycaemia	Likely IUGR or infant of diabetic mother. ? galactosaemia, glycogen storage disease. Hypoglycaemia may be the result rather than the cause of seizures.	10% dextrose, 2 ml/kg IV bolus, repeat after 10 minutes if BM < 2.5 (see hypoglycaemia protocol)
Hypocalcaemia (correct for albumin)	Sick infant, IUGR, infant of diabetic mother, high phosphate intake, maternal diet low in Vit D, exchange transfusion.	10% calcium gluconate, 1-2 ml/kg IV over 5-10 minutes with ECG monitoring
Hypomagnesaemia	Rare but may co-exist with hypocalcaemia	50% magnesium sulphate 0.2 ml/kg IV
Hyponatraemia	Infants with reduced urine output e.g. RDS, HIE or preterm infants with high renal losses +/- diuretics. Seizures unlikely if serum sodium > 125 mmol/l	Correct hyponatraemia, fluid restrict, appropriate supplementation
Hypernatraemia	Usually result of dehydration, rarely inappropriate intake.	Rehydrate, decrease sodium intake
Inborn errors	Consanguinous parents, metabolic acidosis, seizures difficult to control, worse with introduction of feeds. Consider maple syrup urine	Whilst investigating stop milk feeds,ensure adequate calorie intake as IV dextrose, correct acidosis

	disease, urea cycle deficits, non-ketotic hyperglycinaemia	
Pyridoxine deficiency	Seizures unresponsive to anticonvulsant therapy, may be a family history	Trial of pyridoxine 50-100 mg IV with EEG monitoring. Acute hypotonia, apnoea with a flat EEG may follow
Drug withdrawal	Maternal history	See withdrawal protocol
Drug toxicity	Theophylline, local anaesthetics	
Idiopathic	Benign familial epilepsy	

3 Anticonvulsant therapy:

In the case of the actively fitting child anticonvulsants should be commenced after resuscitation and following treatment of any immediately correctable metabolic abnormality such as hypoglycaemia. Levene suggests treatment should commence if clinical or electrical seizures are occuring 3 or more times every hour or are lasting > 2 minutes but it may be appropriate to treat even if seizures are less frequent than this. Unless continuous EEG monitoring is available selection of an infant to treat with anticonvulsants depends on the identification of clinical seizures which may not be obvious (see seizure classification above).

Phenobarbitone is the traditional first line anticonvulsant**.** It is successful as a monotherapy in up to 70% of cases if doses of up to 40mg/kg are used (Gilman 1989). A suggested scheme of treatment is as follows:

Phenobarbitone 20mg/kg IV over 10-15 minutes.

↓ If seizures continue after 10-15 minutes

Phenobarbitone 10 mg/kg IV
Repeat if necessary up to a total of 40mg/kg.

If seizures continue ↓

Clonazepam 100mcg/kg IV as a loading dose over 30 seconds.
Follow by 100mcg/kg IV once daily as bolus.

A combination of phenobarbitone and benzodiazepine therapy is highly likely to stop clinical seizures. If not consider **paraldehyde** 200-400 mcg/kg PR. Although **phenytoin** might be as effective as phenobarbitone (Painter 1999) it should be avoided due to the risk of cardiac arrhythmia especially in the ischaemic myocardium. A potential approach for the future is the use of benzodiazepine therapy alone e.g. **midazolam** 0.15 mg/kg IV bolus followed by 1-5 micrograms/kg/min IV infusion (LalKuol 1997) or **lorazepam** IV bolus followed by a **midazolam** infusion (Tasker 1998)). **Lignocaine** also has anticonvulsant potential. Trials in neonates are awaited.

The aggressiveness with which therapy is approached in the neonatal period is debatable. On the one hand seizures themselves may cause brain injury (Delgado-Escueta 1982). On the other hand, drugs used to treat seizures may have deleterious effects on development (Swaiman 1991). More controversial still is the criteria used to determine the adequacy of treatment.

In the reality of clinical practice the aim should be to eliminate all or nearly all clinical seizure activity. Elimination of clinical seizures does not guarantee elimination of electrophysiological manifestations and it is possible that electrical seizures may cause brain damage. However, a prerequisite to elimination of all electrographic seizure activity is a means of continuous EEG monitoring. In addition the anticonvulsant doses required may impair ventilatory and cardiac function.

Maintenance:

- Once seizures are controlled further diagnostic evaluation can be undertaken as above.
- Close observation is required for evidence of further fits.
- If further convulsions are thought to be unlikely then anticonvulsants can be stopped. If further convulsions are thought to be likely then maintenance treatment should be continued and then withdrawn gradually with an aim to have the baby on monotherapy.
- Maintenance treatment is usually commenced 12 hours after initial therapy.
- Usually, maintenance treatment is with phenobarbitone at 5-6mg/kg/dose od IV or orally.
- Duration of treatment is a matter for consideration with regard to each individual case but as a general principle if the cause of the seizure was a transient metabolic upset then subsequent seizures are unlikely. If neurological examination and interictal EEG normalise in asphyxiated infant subsequent epilepsy is highly unlikely and anticonvulsants should be stopped.
- Longer-term therapy may be required if there is structural brain pathology or if the baby is neurologically abnormal particularly if there is an abnormal EEG.
- It should be noted that there have long been concerns that long term phenobarbitone may have detrimental effects on neurodevelopment (Diaz). Anticonvulsants should therefore be continued with caution.