Sedating the wheezy child

Sir,

We read with interest the report on the bronchodilator effect of inhaled ipratropium bromide in wheezy toddlers.¹ In their study Hodges *et al.* sedated all wheezy children with chloralhydrate.

Although sedating a wheezy child may be a safe practice in units in which repeated measurements of respiratory function are made and if necessary ventilation instituted, in the absence of such facilities sedation of wheezy children is not recommended as it may suppress respiratory drive and lead to carbon dioxide retention and anoxia.²

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Professor Milner and co-workers comment:

We do not recommend giving strong sedatives to babies with acute severe respiratory problems. The babies we studied were not critically ill but they were still wheezy. Currently sedation is a prerequisite for lung function assessment in young children; this may to some extent modify their breathing pattern but on none of several hundred occasions in which we have given chloralhydrate did we notice any adverse effect.

We should like to point out that the dose of ipratropium bromide given in the legend to the Figure should read 250 µg and not 25 µg.

Oral chlormethiazole in childhood epilepsy

Sir,

Intravenous chlormethiazole (Heminevrin) has found a useful place in the management of status epilepticus since the first report of its use.¹ Although its use orally in status epilepticus has been reported,² there appears to have been no report of its long-term use in the management of difficult cases. Three children are reported, refractory to other anticonvulsants, who responded well to oral chlormethiazole.

Case 1

A 2-year-old child presented with an acute encephalopathy leaving her with severe epilepsy which failed to respond to doses of carbamazepine, sodium valproate,

phenytoin, or phenobarbitone. Her electroencephalogram (EEG) was characterised by seizure activity particularly in the left hemisphere; she had a tendency to right-sided clonic seizures and had a right-sided hemiparesis. She was admitted aged 3 years weighing 13.8 kg in status epilepticus which failed to respond to intravenous diazepam, lignocaine, L-dopa, or steroids either singly or in combination. Intramuscular paraldehyde produced only a temporary response. Intravenous chlormethiazole was begun at 20 ml per hour with good effect, but when the rate was reduced the convulsions reappeared. She was therefore started on oral chlormethiazole mixture 100 mg increasing to 300 mg 4 times a day as the infusion was stopped. She was eventually stabilised on 200 mg 3 hourly during the day and 400 mg at night, as 6 hourly dosage led to some fitting. Apart from some fits at night she was well controlled on a combination of chlormethiazole at this dosage and phenobarbitone 15 mg 3 times a day. Two months later she underwent corpus callosal section with some improvement in control and could be weaned off the chlormethiazole after 4 months' treatment. There were no side effects apart from temporary diarrhoea and vomiting which settled spontaneously. Haematological and biochemical values remained normal throughout.

Case 2

A 5-year-old girl with a history of left-sided seizures from age 6 weeks, of unknown aetiology, developed generalised convulsions at age 16 months. These proved difficult to control responding only poorly to phenytoin, sodium valproate, clonazepam, carbamazepine, primidone, and imipramine either singly or in combination. She was markedly developmentally delayed. Her EEG showed abnormal background of delta and beta activity with frequent sharp and slow wave complexes particularly over the right hemisphere.

She was readmitted with a 48-hour history of frequent convulsions interspersed with a semi-conscious state. Her weight was 14.7 kg and she was receiving carbamazepine 200 mg 3 times a day, sodium valproate 200 mg twice a day, and 400 mg at night. Intravenous diazepam and phenobarbitone failed to control her convulsions without rendering her totally unconscious. On substituting intravenous chlormethiazole her convulsions came under control and she was subsequently weaned on to oral chlormethiazole mixture, 360 mg 3 to 4 hourly, 540 mg at night with good control. She has remained on chlormethiazole in combination with carbamazepine and sodium valproate, and her epilepsy has been well controlled with only an occasional convulsion although her fits start again if she misses a dose of chlormethiazole. She has now been on this combination for 5 months and awaits surgical management in the near future. Her haematological and biochemical values remain normal.

Case 3

The patient, one of triplets, developed hydrocephalus and porencephaly secondary to intraventricular haemorrhage; she subsequently developed ventriculitis and shunt colonisation. This was eventually controlled, but she developed infantile spasms and myoclonic seizures,

occurring up to 20 times a day, in bursts with several hours between. Her EEG, at age 1 year, showed high voltage delta theta waves, spikes and sharp waves, with a tendency to periodicity. She failed to respond to benzodiazepines, sodium valproate (maximum serum level 940 nmol/l), carbamazepine, or corticosteroids. When chlormethiazole 75 mg was given as a single dose each day the seizures stopped, without sedation or side effects. She weighs 9 kg and is also receiving clonazepam 0.2 mg twice a day and sodium valproate 200 mg twice a day.

None of the children has experienced any of the common side effects of chlormethiazole such as fever, headache, respiratory depression, bronchorrhoea, sneezing, hypotension, or changes in heart rate^{2,3} although Case 1 had a transient gastrointestinal upset which settled spontaneously without stopping treatment.

These were undoubtedly difficult cases and under the circumstances it was felt justifiable to continue the use of a drug which had not yet been recommended for use in young children. Although control was not perfect in Cases 1 and 2 the parents were pleased with the response. Case 3 has been free of fits for 4 months and is showing evidence of rapid developmental advance.

Addiction and withdrawal reactions have been reported after high dosage regimens⁴ but were not a problem in Case 1. Sedation was a problem in none.

Chlormethiazole has been reported to have a short half-life, about 50 minutes in two early studies^{1,5} although in young healthy adults without alcoholism the half-life after an oral dose was 6 hours using a more sensitive method.⁶ Pharmacokinetic studies have not been carried out in the paediatric age group, but our impression was that effective anticonvulsant action diminished after 4 hours in the two older children. This short half-life means the drug can easily be tailored to each patient's needs.

The long duration of action in Case 3 has not been explained.

Oral chlormethiazole may be a useful adjunct in the management of difficult cases of childhood epilepsy.

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