Letters to the editor

'Audit of the use of chloral hydrate as an acute treatment for childhood seizures'

SIR–For some years oral chloral hydrate has been used for the acute management of seizures at The David Lewis Centre (Alderly Edge, Cheshire, UK), a residential school for children with severe epilepsies, and The Royal Manchester Children's Hospital (Pendlebury, Manchester, UK), a tertiary children's neurology service. Chloral has been used either as pre-emptive medication (medication given between seizures to prevent deterioration of seizure control) or rescue medication (medication given acutely to control epileptic activity) for children with poorly controlled seizures.

We reviewed the literature pertaining to the use of chloral hydrate for seizure disorders. We then studied the effectiveness of chloral in the acute management of seizures by reviewing the notes of patients who had received chloral hydrate for this indication. Patients were identified from a search of pharmacy records at each of the above named institutions. Their clinical notes and prescription charts were then examined, and a pro forma giving patient details, event description, dosage, and outcome was recorded for each episode.

Data were collected on 40 episodes for 16 patients (five females, 11 males; age range 7mo–18y, median 11y), eleven from The David Lewis Centre and five from The Royal Manchester Children's Hospital. All patients had severe drug resistant epilepsies, with 13 having cryptogenic generalized epilepsy, two with symptomatic generalized epilepsy, and one with symptomatic partial epilepsy.

The reasons for administration of chloral as oral rescue medication fell into two main categories. Most often it was used for accelerating seizure clusters to avoid progression to status epilepticus (22/40 episodes). In addition, chloral was prescribed where caregivers or clinicians with a close familiarity with the pattern of an individual child's epilepsy felt there was 'frequent non-convulsive epileptic activity' manifesting as bouts of reduced alertness, drooling, occasional myoclonic seizures etc. (13/40). Chloral was used on three of 40 occasions for documented non-convulsive status epilepticus, and twice for slow recovery from a prolonged seizure. Chloral hydrate was used as first-line rescue medication in 24/40 episodes. Examples of first-line use of chloral were recorded in all categories, except for non-convulsive status epilepticus.

The dose of chloral hydrate used varied between 10 and 30mg/kg. The total number of doses given for the different categories of clinical situation also varied. The most frequently given number of doses was a single dose for seizure clusters or frequent non-convulsive epileptic activity (18/40 episodes). Where more than one dose was given in an episode the most common scenario was for four doses to be given at 6 hourly intervals over 24 hours (11/40 episodes). The interval between multiple doses varied between 4–6 hours.

In 28 of the 40 episodes presumed acute, epileptic activity was successfully curtailed with chloral. In 19 of these episodes, chloral hydrate was the only rescue medication required. In the remainder, chloral was effective after first-line alternative rescue treatment had been used, usually buccal midazolam. In 12 episodes, additional rescue treatment was required after the first dose of chloral, usually diazepam and/or paraldehyde. Significant side-effects were experienced in 3/40 episodes, including vomiting and over-sedation.

Four case reports refer to the use of chloral hydrate in the management of seizures: (1) Powell and Rosenbloom[1] recorded two children with 'life threatening seizures'. Both were given chloral hydrate at dosages of up to 30mg/kg after treatment with intravenous diazepam had failed. In both cases the administration of chloral hydrate resulted in a decrease in seizure activity. (2) Lampl et al.[2] detailed the use of chloral hydrate in five adult patients with drug resistant status epilepticus. All five patients were treated with 30mg/kg chloral hydrate given rectally. Seizures were controlled between 5 and 12 minutes after the administration of chloral. (3) Pranzatelli and Tate[3] considered the use of chloral hydrate as a regular medication in patients with progressive myoclonic epilepsy. They reported four patients aged between 14 and 35 years with progressive myoclonic epilepsy who were already taking antiepileptic drugs. In addition to their daily drug regime, patients were given 500–1000mg of chloral hydrate between two and six times a day. In all patients, myoclonic seizures were reduced and all reported an improvement in quality of life as a result. The expected side-effect of sedation was less marked than anticipated. (4) Kršek et al.[4] reported the successful treatment of a 5-week-old female with Ohtahara syndrome (early infantile epileptic encephalopathy) with chloral hydrate after failure of standard antiepileptic drug therapy. Within 24 hours of initiation of chloral hydrate therapy (58mg/kg/day) there was no further seizure, and this was maintained over a 7 month follow-up period.

There is no previous report of the use of chloral for the termination of accelerating seizure clusters and frequent non-convulsive epileptic activity, or in the treatment of non-convulsive status epilepticus.

In both The David Lewis Centre and The Royal Manchester Children's Hospital, chloral is only used for children with frequent breakthrough seizures and a high risk of status epilepticus. Chloral is initially prescribed where more conventional treatments, e.g. benzodiazepines, have been ineffective. For some children, chloral is then given first-line because clinicians, parents, and caregivers feel it has been the most effective option of those available. This may have increased the likelihood of chloral being successful and contributed to the high number of episodes where chloral was given first-line.

The decision to use pre-emptive or rescue treatment with chloral was made by clinicians or caregivers who were very familiar with an individual child's pattern of epilepsy. This was especially the case for clusters of seizures and frequent non-convulsive epileptic activity where previous experience had suggested that alternative or non-treatment would lead to deterioration towards status epilepticus. Whether chloral was given pre-emptively or as rescue treatment for these episodes is unclear without concomitant electroencephalogram monitoring. Chloral may be beneficial either because of a direct antiepileptic effect or because of an indirect mechanism, e.g. alterations in arousal. In this highly selected group of children, the clinicians and caregivers involved felt that tailored use of chloral was effective on 70% of occasions, and chloral continues to be prescribed for some children.

Doses given were generally lower than in the few previous reports, although repeat doses were given for individual episodes, again, according to previous experience with

individual patients. The lower doses may explain the few recorded adverse effects reported in this study. Some side-effects, e.g. drowsiness, may be under-reported in patients' medical records, as this is a reaction common to most emergency rescue medication and a post-ictal child is often drowsy. The literature suggests that chloral hydrate is a relatively safe drug. The main side-effect is over-sedation; additionally, gastric irritation may result in nausea and vomiting. High doses may result in respiratory depression, hypotension, and cardiac arrhythmias, and coma is associated with high blood levels of trichlorethanol.[1] There has also been a report of cardiac arrhythmia at a dose of 70mg/kg.[5]

Given the paucity of published reports of experience in its use, it is of interest that chloral is used for this clinical indication in childhood epilepsy. There may be other examples where potentially useful and long-standing clinical practice in individual institutions is inadequately disseminated. This retrospective review suggests that chloral can be helpful for individual children, and that for some it is the drug of first choice as rescue treatment. Our observations should be treated cautiously until more rigorous prospective data is available.

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'Ictus emeticus in a prolonged frontotemporal seizure secondary to a brain tumour'

SIR–Ictal vomiting or ictus emeticus is frequently seen in children suffering from idiopathic occipital epilepsies, including those with early onset, benign childhood occipital seizures (Panayiotopoulos syndrome),[1] and photosensitive occipital lobe epilepsy.[2] In contrast to the cases described in adults, this clinical manifestation appears to be exceptional in symptomatic epilepsy of infancy, and these differences suggest that the pathophysiologic mechanisms underlying vomiting may be age related.[3]

The purpose of this observation is to describe the clinical video-electroencephalogram (video-EEG) and neuroimaging features of a child who experienced a prolonged frontal seizure with prominent late ictal retching and nausea.

A 5-year-old right-handed male was admitted to our paediatric outpatient clinic with a history of recurrent episodes consisting of involuntary myoclonic jerking of the head, tongue deviation to the left side, difficulties in speech, and uncontrolled clonic movements affecting the left upper limb without secondary generalization. Consciousness was fully preserved. There was no somatosensory aura preceding the attacks. Although these episodes had occurred 10 times over the last month, a precise diagnosis and treatment had not been established. The child was born after an uneventful pregnancy and delivery, and had normal development. There was no family history of epilepsy or neurological disease. Physical and neurological examinations were normal.

A video-EEG study was performed after partial sleep deprivation. The EEG revealed normal background activity and focal irregular slow waves and sharp-and-slow wave complexes involving the right central, anterior, and mid-temporal electrodes. After 30 minutes of recording, the child noted left facial clonic twitches and deviation of the mouth to the left side. Immediately, he experienced forced head-turning toward the left, elevation of the right arm, and tonic posturing with rhythmic clonic jerks of the left arm and head. Consciousness was preserved and although speech was not fluent he was able to speak intelligibly. The head slowly returned to the midline and the clonic jerks of the left arm ceased. Subsequently, when the seizure appeared to be ending, he became unresponsive and experienced salivation and oro-alimentary automatisms. Two minutes later, the child was pale and nauseous and overt retching without expulsion of gastric contents developed (ictus emeticus). This was followed by chewing and swallowing automatisms which persisted for several minutes up to the end of event. The seizure lasted 10 minutes. The patient remained mildly confused for several minutes and had postictal paresis of the left arm for about one hour.

The ictal EEG showed a focal discharge of paroxysmal fast activity, and repetitive spikes and rhythmic sharp waves arising from the right central area which spread rapidly over the mid-line and the contralateral rolandic region. While the ictal discharges predominated in the right hemisphere there was a gradual progression of seizure activity to the right temporal region. The seizure stopped abruptly and a diffuse postictal slowing and generalized decrement of background activity was observed. Magnetic resonance imaging of the brain disclosed a right frontal lesion compatible with a malignant brain tumour. Over the following days the tumour was resected and histopathological examination revealed a low grade astrocytoma. Two years later the patient remains seizure-free and is being treated with carbamazepine.

Ictal vomiting is a common symptom in seizures arising from the occipital lobe in children. Some investigations have suggested that this clinical manifestation in childhood epilepsy is more likely due to activation of non-dominant limbic or insular structures. Thus, Guerrini and colleagues[4] demonstrated that vomiting can be a late ictal phenomenon in occipital seizures due to propagation of the epileptic activity to the temporal lobe. They proposed that the inferior longitudinal fasciculus is the more possible anatomic pathway connecting both cerebral structures. By contrast, ictal vomiting is rare in adults and appears to be associated with complex partial seizures originating in the non-dominant temporal lobe.[5–7] Nevertheless, to our knowledge, this phenomenon has not been previously proven in frontal seizures. Indeed, Kotagal and coworkers[8]

have recently analyzed 149 seizures from 42 patients, 28 with mesial temporal lobe onset and 14 with frontal lobe origin, and observed that retching and vomiting never occurred in frontal complex partial seizures. In our patient, the onset of ictal discharges involved the primary motor cortex and spread rapidly to the supplementary motor area. The seizure activity remained localized for minutes in the frontal lobe but the occurrence of oro-alimentary automatisms, retching, nausea, and scalp EEG changes indicated a late right temporal lobe involvement. Unfortunately, the lack of intracranial recordings prevents an accurate description of the route followed by the ictal epileptiform discharges. However, it could be hypothesized that seizure activity arises in the primary motor area is propagated to the supplementary motor area and, finally, spreads to the temporal lobe through the cingulate gyrus.

In general, the description of vomiting during a seizure in children has been related to benign types of epilepsy. Panayiotopoulos syndrome and photosensitive occipital lobe epilepsy are some of the conditions more frequently associated with emetic symptomatology.[1,2] Our description suggests that ictal vomiting may occur in symptomatic frontal epilepsy and, therefore, a benign aetiology should not be automatically assumed when this clinical feature is presented during seizures in children. It is clear that the video-EEG recording demonstrated firmly that vomiting was an ictal epileptic manifestation. Otherwise, in our case, the occurrence of salivation, nausea, and retching may have been interpreted as a postictal state. This fact emphasized that late gastrointestinal and autonomic manifestations due to temporal activation may occur in frontal epilepsy, particularly in abnormally long-lasting seizures in infants.

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