Witness Statement Ref. No. 138/3

NAME OF CHILD: Claire Roberts

Name: David Webb

Title: Dr

Present position and institution:

Consultant Paediatric Neurologist, Our Lady's Hospital, Dublin, Ireland

National Children's Hospital, Tallaght, Dublin, Ireland

Previous position and institution:
[As at the time of the child's death]

Consultant Paediatric Neurologist, Royal Belfast Hospital for Sick Children.

Membership of Advisory Panels and Committees:
[Identify by date and title all of those since your Witness Statement of March 2012]

Previous Statements, Depositions and Reports:
[Identify by date and title all those since your Witness Statement of March 2012]

OFFICIAL USE:
List of previous statements, depositions and reports:

Ref:	Date:	
091-008-035	25.04.06	Deposition to the Coroner
WS 138/1	14.03.12	Witness Statement to the Inquiry
WS 138/2	18.09.12	Further Witness Statement to the Inquiry

1. I have been asked to set out my recollection of the circumstances in which I gave advice regarding a dose of Midazolam.

I believe I was contacted about Claire Roberts after the seizure that she had recorded in the Nursing Notes at 3.10 on October 22nd 2012. I believe this contact was made by a Doctor but I cannot recall by whom. I believe I suggested Midazolam as the next option for Claire but I would not have been certain of the dose and would have had to check this by reviewing papers kept in my office. I believe my communication with the Medical staff in relation to this was most likely to have been by phone as I did not attend the ward until sometime later and did not write the dose myself in Claire's notes. I cannot recall for certain the dose that I recommended but I believe this would have been a loading dose of 0.15mg/kg. I believe this because this was the dose recommended in the principle paper describing midazolam use in this situation at the time - Rivera R et al (Crit Care Med 1993;21(7)991-994). There were several other shorter papers recommending a similar bolus dose.

A subsequent article published in 1997 highlighted Midazolam as an effective and safe therapeutic approach for the management of childhood status epilepticus - Lal Koul et al (Arch Dis Child 1997;76:445-448). This article also recommends a loading dose of 0.15mg/kg.

I learned about the value of intravenous midazolam in the management of status epilepticus during my time in Vancouver but I cannot recall whether I personally prescribed it during my time there.

I did not include this detail in my first initial statement as I am not certain that it throws any further light on why Claire was prescribed a bolus dose of 0.5mg of midazolam.

I did not personally check the arithmetic for the calculation of the doses of phenytoin and midazolam prescribed for Claire because this would not have been my normal practice at the time. I understood that doses of parenteral medication in particular were always checked by two members of medical/nursing staff prior to administration and this safety check would have included calculations. My source for this understanding is my experience in working in teaching hospitals since 1985 in Ireland, England and Canada. I believe this policy was and is the standard practice and applies to the administration of medication and not to the grade of person administering the medication. If this was not the standard practice at RBHSC then I did not know that at the time but I would be most surprised to hear that it was not.

The article abstracts which recommend a bolus dose of 0.15mg of Midazolam are attached to this statement.

Rivera R et al (Crit Care Med 1993;21(7)991-994

Lal Koul et al (Arch Dis Child 1997;76:445-448

(2) I acknowledge that several of the expert witnesses have been critical of me for not arranging a CT scan and EEG for Claire Roberts earlier than I had planned.

(a) I wish to state that I have no doubt that if a CT scan had been available – down the corridor - in the Children's Hospital in 1996 I would have arranged it for that Tuesday afternoon. However this was not the case and to arrange a CT scan for Claire involved sending her by ambulance to the Adult Hospital. There was a potential for this procedure to be delayed particularly if there was a backlog of Adult cases awaiting brain imaging at the time or if there was a delay in arranging anaesthetic supervision for the procedure. I was also aware of the published concerns about sending children to an adult facility for emergency investigations. I felt that Claire was in non-

convulsive status epilepticus at the time, which we needed to treat and did not think this was a wise option.

I also felt that her presentation had been triggered by infection – probably a viral illness - and the yield from CT brain in children with infection related encephalopathy is low in the early stages of their illness (Mellor D, Arch Dis Child 1992;67:1417-1419), hence the suggestion that it would be better done the following day. It is correct to say that a CT scan might have detected evidence of cerebral oedema but it is also possible for the CT to appear normal in the early stages of cerebral oedema.

(b) In relation to EEG, I must have felt when I saw Claire first at 2pm on October 22nd that I had sufficient evidence to treat Claire for Non Convulsive Status Epilepticus. Her background history of risk, the description of her presentation and subsequent behaviour and response to diazepam were central to this belief.

On my second visit to the ward after 3pm the description of Claire's definite seizure since I had last seen her in many ways reinforced my belief that seizures were central to Claire's presentation and needed to be treated.

At 5pm I would have felt that it was hard to justify trying to request an out of hours EEG at this point as it made sense to continue Claire on anti-convulsant therapy for the moment in any event. At 5pm I believe I was beginning to feel that encephalitis was higher on the differential than a recurrence of Claire's underlying epilepsy and hence the decision to start Acyclovir and Cefotaxime. If Claire had encephalitis she was very likely to have seizures as part of this presentation and it made sense to continue to treat her for seizures in that context.

It was my belief at the time that the standard practice in smaller units in particular was to treat the child and arrange an EEG for the next working day. I am sure I gave consideration to requesting an EEG on the Tuesday afternoon but I would have been very conscious of the workload of the EEG department particularly in the absence of the second technician on maternity leave. The single technician available at the time was providing an EEG service to the entire province and was dealing with children and families who had often waited weeks and longer for an EEG. If I had asked her to "bump a child off her list" at such short notice this would inevitably put her in a conflict situation.

It is easy with hindsight to suggest that I should have demanded an emergency EEG but at the time I decided to stick to what I considered was the standard practice. I would have considered it unreasonable to expect one technician to provide an emergency service for the entire province. EEG technicians were and are a very valuable resource and experienced technicians are and were very scarce. I had just completed my first year at RBHSC and certainly did not want to jeopardise my relationship with our only technician at the time.

This statement is true to the best of my knowledge and belief

Signed  Date October 2012

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Display Settings: Abstract

Crit Care Med. 1993 Jul;21(7):991-4.

Midazolam in the treatment of status epilepticus in children.

Rivera R, Segnini M, Baltodano A, Pérez V.

Intensive Care Unit, National Children's Hospital, San José, Costa Rica.

Abstract

OBJECTIVE: To determine the efficacy and safety of **midazolam** given as a continuous infusion in the treatment of status epilepticus in children.

DESIGN: Prospective, open study.

SETTING: Pediatric intensive care unit.

PATIENTS: Twenty-four children with seizures, in whom three repeated intravenous doses of 0.3 mg/kg of diazepam, 20 mg/kg of phenobarbital, and 20 mg/kg of phenytoin failed to bring the episode under control.

INTERVENTIONS: All patients received a bolus of **midazolam** (0.15 mg/kg iv) followed by a continuous infusion at 1 microgram/kg/min. The dose was increased every 15 mins until the episode of seizure was brought under control. Time to control seizures, infusion rate, and side-effects were monitored.

MEASUREMENTS AND MAIN RESULTS: The mean age of the patient population was 2.2 yrs (range 2 months to 12 yrs; 14 female and 10 male). In all patients, seizures were controlled in a mean time of 0.78 hrs (range 15 mins to 4.5 hrs). The mean infusion rate was 2.3 micrograms/kg/min (range 1 to 18). None of the patients had clinically important changes in blood pressure, heart rate, oxygen saturation, or respiratory status attributable to the use of **midazolam**. The mean time to full consciousness for patients after stopping the infusion was 4.2 hrs (range 2 to 8.5).

CONCLUSION: Midazolam is an effective and safe drug to control refractory seizures in children with status epilepticus.

Comment in

Advances in the management of refractory status epilepticus. [Crit Care Med. 1993]

Midazolam and status epilepticus in children. [Crit Care Med. 1994]

PMID: 8319479 [PubMed - indexed for MEDLINE]

MeSH Terms, Substances

LinkOut - more resources

Continuous midazolam infusion as treatment of status epilepticus

Roshan Lal Koul, Guru Raj Aithala, Alexander Chacko, Rajendra Joshi, Mussalem Seif Elbualy

Abstract

In a tertiary referral centre, midazolam infusion was tried as treatment for 20 children with status epilepticus over a period of two years. The mean age of the children was 4.07 years. Twelve children with refractory status epilepticus had received intravenous or per rectal diazepam and intravenous phenytoin/phenobarbitone or both before midazolam was given (0.15 mg/kg bolus followed by 1–5 µg/kg/min infusion). Eight children required only midazolam to control the established status epilepticus. The seizures were controlled in 19 children. The mean time required for complete cessation of seizures was 0.9 hours. The mean infusion rate required was 2.0 µg/kg/min. All children had regained full consciousness by a mean of 5.1 hours after discontinuation of midazolam treatment. No metabolic derangement or compromise of vital functions was noted in any of the children. Midazolam infusion is thus an effective and safe therapeutic approach for the management of childhood status epilepticus.

(*Arch Dis Child* 1997;76:445–448)

Keywords: status epilepticus; refractory; midazolam

Status epilepticus is a medical emergency that requires prompt intervention. The term is applied to situations in which seizures occur so frequently that complete recovery between fits does not take place.[1] A more substantive definition is continuous seizures lasting for 30 minutes or longer or recurrent seizures occurring with impairment of consciousness between seizure activity.[2] Status epilepticus is more common in childhood, and the reported death rate varies between 3 and 20%.[3] Prolonged seizure activity itself produces irreversible cerebral damage, independent of accompanying hypoxia, acidosis, and consequent biochemical derangements. The excessive metabolic demands of continuously firing neurones leading to depletion of essential nutrients is currently thought to be the most important factor leading to cell death during continuous seizures.[4] Although the majority of children who suffer continuous seizures respond to intravenously administered diazepam and phenytoin sodium, some require other modalities of treatment including general anaesthesia, which could lead to serious adverse effects.

Midazolam is a recently developed water soluble benzodiazepine, commonly used as a preanaesthetic agent with remarkable anticonvulsant action.[5] It has been shown to have a wide margin of safety and a broad therapeutic index. Furthermore, it diffuses rapidly across the capillary wall into the central nervous system and can be mixed with saline or glucose solutions to allow its administration as a continuous infusion.[6]

Subjects and methods

Twenty children suffering from status epilepticus admitted to the paediatric ward from November 1993 to November 1995 were included in this study. Eleven were already taking various antiepileptic drugs.

Status epilepticus was diagnosed according to the criteria of Engel, namely continuous seizures for 30 minutes or longer or several seizures occurring with impairment of consciousness between seizure activity.[2] Refractory status epilepticus was the diagnosis if the seizures continued, despite at least two doses of diazepam intravenously or rectally in succession followed by phenytoin sodium/phenobarbitone or both 20 mg/kg given over 30 minutes as an infusion, or failure to respond to the latter alone or in combination. The duration of status before midazolam therapy was approximate, based on the history obtained from the patient's attendants and the referring physician's notes. Electroencephalography (EEG) was not used for the diagnosis. It was, however, performed after the seizures had been controlled to monitor the electrical suppression of seizure discharge. Continuous EEG monitoring was not available. However, it was used to diagnose non-convulsive status epilepticus at onset. All children underwent computed tomography scanning of the brain and other relevant investigations.

All 20 children received intravenous midazolam at 0.15 mg/kg as a bolus followed by a constant infusion starting at 1 µg/kg/min up to 5 µg/kg/min increasing by 1 µg/kg/min every 15 minutes until complete control of seizures was achieved. The optimum rate of infusion at which seizure control was achieved was maintained for a period of 24 hours. Subsequently the midazolam infusion rate was gradually decreased (by 1 µg/kg/min every two hours) until tapering was completed.

Variables such as age, weight, sex, history of seizures, underlying diseases, and the time required for control of seizures were carefully recorded for each patient. Vital parameters

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Table 1 Type, duration, and control of status epilepticus

No	Age	Sex	Diagnosis	Previous antiepileptic drugs	Status: Type	Status: Duration (minutes)	Status: Antiepileptic drugs received to control	Midazolam: Rate (μg/kg/min)	Midazolam: Cessation of seizures (minutes)	Midazolam: Side effects	Outcome
1	2 months	M	Acute purulent meningitis	Nil	GTC	40	DZP PR, IV, PHT IV	1	15	Nil	No recurrence
2	10 years	M	Idiopathic epilepsy	SVA, VGB, LTG, PHT, ETH	GTC	45	DZP PR, IV	1	30	Nil	No recurrence
3	10 years	F	Idiopathic epilepsy	—	GTC	30	PHT IV	1	15	Nil	No recurrence
4	4 years	F	Neurological degeneration	SVA	Partial motor/MYO	300	DZP PR	2.5	50	Nil	Several
5	1 year	M	Postencephalitic sequelae	PHT, PHB	GTC	180	DZP IV (3)	2.5	60	Nil	No recurrence
6	2 months	M	Cerebrovascular accident	SVA, PHT	GTC	120	DZP IV	1.5	25	Nil	No recurrence
7	6 months	M	Acute purulent meningitis	—	GTC	45	DZP IV, PHT IV	1.5	25	Nil	No recurrence
8	8 months	M	Acute purulent meningitis	—	Partial motor	60	DZP IV, PHB IV	1	25	Nil	No recurrence
9	5 years	M	Chronic encephalitis	SVA, CLZ	GTC, MYO	1440	DZP PR, IV, PHT IV	5	220	Nil	Lost to follow up
10*	3 years	M	Idiopathic epilepsy	CBZ	MYO, T	90	DZP IV	2	40	Nil	No recurrence
11	3 years	M	Idiopathic epilepsy	—	MYO, astatic	30	DZP PR	1	10	Nil	Recurred twice
12	13 years	M	Cerebrovascular accident	—	GTC	40	DZP IV	2	60	Nil	No recurrence
13*	4 years	M	Idiopathic epilepsy	CBZ, SVA, CLZ	MYO, T	120	DZP PR (2)	2	25	Nil	No recurrence
14	9 years	F	Idiopathic epilepsy	SVA, CBZ	Complex partial	65	PHT IV	2	30	Nil	No recurrence
15	3 years	F	Acute meningoencephalitis	—	Complex partial	60	PHT IV	2.5	50	Nil	No recurrence
16	6 months	M	Cerebral dysgenesis	PHB, PHT, SVA	GTC	720	DZP PR, PHT IV	5	240	Nil	Recurred twice
17	3 years	M	Idiopathic epilepsy	SVA, PHT	GTC, MYO	120	PHT IV	2	60	Nil	No recurrence
18	7 years	M	Idiopathic epilepsy	SVA, PHT	GTC	45	PHT IV	2	60	Nil	No recurrence
19	2 years	F	Acute meningoencephalitis	—	GTC	30	PHT IV, PHB IV	1	15	SpO_2 90%	No recurrence
20	2.5 years	M	Acute meningoencephalitis	—	GTC, dystonic	60	PHT IV, PHB IV	1.5	25	SpO_2 90%	No recurrence

GTC = generalised tonic-clonic; T = tonic; MYO = myoclonic; IV = intravenous; PR = per rectum; DZP = diazepam; PHT = phenytoin sodium; PHB = phenobarbitone; SVA = sodium valproate; CBZ = carbamazepine; VGB = vigabatrin; LTG = lamotrigine; ETH = ethosuximide; SpO_2 = oxygen saturation; * Lennox-Gastaut syndrome status.

including respiratory rate, heart rate, and blood pressure were documented. The oxygen saturation of each child was monitored continuously by pulse oximetry.

The children were also monitored for the development of adverse effects of benzodiazepines including hypotension, hypoxia, and respiratory depression. In order to exclude electrolyte and metabolic disturbances as a cause of the seizures, blood samples were taken on admission and at 24 hours to measure circulating sodium, potassium, calcium, glucose, and magnesium concentrations.

Results

Of the 20 children with status epilepticus admitted to our high dependency care unit, 15 were boys (table 1). The mean age was 4.07 years (range 2 months to 13 years). Eleven children had a history of seizures and were already taking antiepileptic drugs, which included various combinations of sodium valproate (n = 9), carbamazepine (n = 3), phenobarbitone (n = 2), phenytoin sodium (n = 6), clonazepam (n = 2), ethosuximide (n = 1), vigabatrin (n = 1), and lamotrigine (n = 1). Eight children had idiopathic epilepsy, three acute purulent meningitis, three acute meningoencephalitis, and the remainder had various vascular or degenerative lesions of the brain.

The type of status presented in the children as follows: generalised tonic-clonic (n = 13), partial seizure status (partial motor (n = 2), complex partial (n = 2)), myoclonic astatic (n = 1), and Lennox-Gastaut status (myoclonic + tonic; n = 2). Myoclonic seizures were seen as a combination of myoclonus with generalised tonic-clonic status in three others. Twelve patients had refractory status epilepticus (table 2). Their seizures continued for more than 30 minutes after administration of diazepam, followed by phenytoin sodium/phenobarbitone or both intravenously. Eight children being followed up in the outpatient department who were on various antiepileptic drugs were given midazolam infusion alone.

Table 2 Drugs given before midazolam in refractory status epilepticus

Drug	No of cases
Diazepam	12
IV	9
PR	7
Combined	3
Phenytoin	11 (2 with phenobarbitone)
Phenobarbitone	3 (2 with phenytoin)

IV = intravenous; PR = per rectum.