

Short report

Serum prolactin during status epilepticus

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SUMMARY The serum concentration of prolactin is frequently increased after single epileptic seizures and has therefore been used as a method to differentiate between hysterical attacks and epileptic seizures. We determined plasma prolactin concentrations in fifteen patients with status epilepticus. Seven patients had absence status, five complex partial and three generalised tonic-clonic status epilepticus. Prolactin levels were normal in all patients which indicates that, in contrast to single seizures, status epilepticus is not associated with an increase in serum prolactin.

The prolactin secretion after epileptic seizures has been studied extensively.¹⁻⁹ Seventy to 90% of complex partial and generalised tonic-clonic seizures are accompanied by transient elevations of serum prolactin concentrations, whereas this is less frequent and less pronounced after seizures with brief or no impairment of consciousness.^{3,5,7,8-11} Absences and myoclonic seizures are not followed by a rise in prolactin levels,^{1,2} nor are pseudo-epileptic seizures.^{1,3,6,10} Prolactin appears to be released at the onset of the seizure, reaching a peak elevation within 20 minutes after the attack.^{5,11} The prolactin concentration in plasma obtained within 30 minutes after a seizure is therefore often used to differentiate between epileptic and non-epileptic events. This clinical practice is based on previous studies where prolactin has been determined almost exclusively after single seizures. The paucity of information on prolactin release during prolonged epileptic manifestations prompted this study of serum prolactin in status epilepticus.

Patients and methods

Patients

Fifteen adult patients (nine male, six female) with status epilepticus, were studied. Ages ranged from 31 to 79 years. In three patients, the status was the first manifestation of

epilepsy. Twelve of the patients had a previous history of epilepsy ranging from a few weeks to 72 years, and eleven patients were under continuous treatment with anticonvulsant drugs (table). Thirteen of the patients, including all with nonconvulsive status epilepticus, had their status verified by ictal EEG recordings. Patients with focal ictal EEG seizure activity and impaired consciousness without convulsions were classified as cases of complex partial status according to the criteria of Mayeux and Lueders.¹³

Nonconvulsive status with generalised EEG seizure activity was designated as absence status. If the generalised discharges were rhythmic spike waves at 3 Hz, the status was classified as a typical absence status. Patients with generalised seizure activity other than 3 Hz spike waves were classified as having atypical absence status in accordance with the classification by Gastaut.¹⁴ One patient had a typical and six had atypical absence status. A previous status episode in one of the patients (patient 5) with atypical absence status has been described earlier.¹⁵ Five patients with ictal EEG recordings had complex partial status and one generalised tonic-clonic status. The seizures in the latter patient appeared to be secondary generalised from a frontal focus. Two further patients were included despite the absence of ictal EEG recordings. Both had been patients at the Department of Neurology at Södersjukhuset for many years. They had clinically typical generalised tonic-clonic status observed at the hospital.

The status was terminated by the intravenous administration of 5 to 10 mg of diazepam in fourteen patients or 1 mg of clonazepam in one patient. All patients had a prompt initial clinical and electroencephalographic response to the therapy.

Methods

An ictal blood sample for determining prolactin was taken from each patient from an antecubital vein either during the

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Table Serum prolactin concentrations in fifteen patients with status epilepticus

Patient	Drug therapy (mg/day)	Type of status	Duration of status at ictal blood sample (hours)	Prolactin concentration ($\mu\text{g/l}$)	
				Baseline	Ictal
1	carbamazepine (400) ethosuximide (500) phenobarbital (15)	Typical absence	7	12	6.6
2	carbamazepine (400)	Atypical absence	6	3.8	3.1
3	—	Atypical absence	6	11	1.0
4	carbamazepine (1000) valproate (1500)	Atypical absence	24	2.0	2.0
5	carbamazepine (200)	Atypical absence	4	2.0	6.0
6	—	Atypical absence	20	7.0	8.0
7	carbamazepine (700) phenobarbital (100)	Atypical absence	6	14	6.0
8	—	Complex partial	120	110*	7.0
9	—	Complex partial	2	21	20
10	phenytoin (300)	Complex partial	30	14	2.0
11	carbamazepine (800)	Complex partial	10	—†	1.0
12	carbamazepine (400)	Complex partial	5	<0.1	<0.1
13	phenytoin (300)	Generalised tonic-clonic	4	10	4.0
14	carbamazepine (1200) phenytoin (200) clonazepam (4) phenobarbital (100)	Generalised tonic-clonic	4	2.0	2.0
15	valproate (1800) carbamazepine (300) primidon (125) phenobarbital (50)	Generalised tonic-clonic	6	—†	18

*After administration of 300 mg of thioridazine daily.

†Data missing.

end of the status (all twelve patients with nonconvulsive status) or within 20 minutes of its termination. A baseline value was taken at the same time on the following seizure-free day. This was done to control physiological prolactin circadian variations. Prolactin was measured by radioimmunoassay.¹⁶ Normal serum prolactin levels at our laboratory are less than 25 $\mu\text{g/l}$.

Results

Baseline values and ictal levels of serum prolactin for the fifteen patients are shown in the table. All ictal prolactin concentrations were within the normal range. The ictal prolactin level was lower than the baseline value in most patients. Patient 8 had an abnormally high baseline prolactin concentration. This may be explained by the fact that this patient was given 300 mg of thioridazine daily immediately after the status and before the baseline sampling for the treatment of a psychosis. This drug is known to induce hyperprolactinaemia.

Discussion

The clinical features of generalised tonic-clonic status epilepticus are generally easily recognised, and effective treatment is given before EEG verification. This is the evident explanation for the underrepresentation of the convulsive forms of status epilepticus among the thirteen patients with ictal EEG recordings. To

increase the number of patients with generalised tonic-clonic status, we included two patients with clinically indisputable tonic-clonic status epilepticus, despite the lack of EEG verification. Among cases of non-convulsive status, only patients with focal ictal seizure activity were classified as cases of complex partial status. All patients with non-focal seizure activity were designated as absence status. Generalised epileptiform discharges could, however, also represent complex partial status in which the generalised discharges are originating from an epileptic focus.^{13,15} Some of our patients, classified as cases of absence status, may therefore represent complex partial status with secondary generalised EEG discharges.

Seven patients were classified as having absence status. Prolactin secretion after single absence seizures has previously been reported in only a few patients.^{7,12} Serum prolactin has consistently been normal and unchanged from baseline levels. It has been postulated that this is due to the different nature of the epileptic discharge or that there may not be a spread of the paroxysmal activity to hypothalamic neurons in absence seizures.² The lack of effect on serum prolactin, however, may also be due to the short duration of single absences. Thus, the serum levels of prolactin are normal both after short single absences and in connection with absence status epilepticus. Whether or not there is a rise in serum prolactin after absence seizures of intermediate duration remains to be investigated.

Serum prolactin was within the normal range also in all cases of complex partial and generalised tonic-clonic status. It is thus obvious that serum prolactin concentrations cannot be used as a biochemical marker to distinguish between epileptic and non-epileptic attacks in connection with status epilepticus. All our patients, who represent three different types of status epilepticus, had ictal prolactin levels within the normal range and there was no increase from baseline values. To our knowledge, this is the first published systematic study of prolactin secretion during status epilepticus. However, in a study of 23 patients with various seizures, Bye *et al*⁷ included three patients with so called minor epileptic status. The term was used for severe repetitive myoclonic attacks. A significant increase in prolactin concentrations was found in only one of the three patients.

Jackel *et al*¹⁷ studied a patient who had three complex partial seizures in six hours. They found a decreased prolactin response with repetitive seizures. A reduced prolactin release with repeated seizures is consistent with our observations in status epilepticus. Ictal prolactin concentrations were in fact lower than baseline levels in most of our patients, and in thirteen of the patients they were in the lower part of the normal range. Patient 9, who had the highest ictal prolactin concentration, was also the patient with the shortest duration of her status. The length of the seizure is apparently crucial for the prolactin concentration. Previous studies have shown that there is generally no rise in serum prolactin after brief attacks of less than about 30 seconds.¹¹ Our study shows that there is no increase in prolactin levels after protracted seizure activity as in status epilepticus of two hours or more.

Benzodiazepines were given to all patients in order to terminate the status. One may therefore speculate if this may have influenced the prolactin levels. However, diazepam, which was used in fourteen of the fifteen patients, has been shown not to affect serum prolactin concentrations.¹⁸ Furthermore, the prolactin samples were obtained before benzodiazepine treatment in most patients.

The prolactin increase induced by epileptic seizures could be due to the spread of electrical activity to the hypothalamic nuclei resulting in a secretion of prolactin.³ Jackel *et al*¹⁷ suggested that a depletion of stored prolactin by a recent attack may explain the reduced response after the following seizure. Another possible explanation is that repeated or prolonged seizures may activate the dopaminergic system that inhibits the secretion of prolactin from the hypophysis.

Whatever the mechanism may be, it is clear from our observations that plasma concentrations of prolactin in connection with prolonged epileptiform features need to be interpreted with caution, and that values within the normal range do not necessarily imply pseudo-epileptic seizures.

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