Original Article

Circulating Prolactin and Cortisol Levels in Diagnosis of Pseudo - Seizures

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A controlled prospective study of 52 cases of seizure disorder was carried out with a view to study the clinical patterns and to establish objective parameters for the diagnosis of pseudo-seizures. Clinical diagnosis of the seizure-type was made by a neurologist. EEG and CT Scan of head were done at basal levels and at 5 min, 20 min, 1 hour and 24 hours after the seizure. Forty cases were males and 12 were females. Their ages ranged between 18 to 40 years (mean 27 years). Ten cases had generalized, 18 complex partial, 8 simple partial and 20 cases had pseudo-seizures. Basal serum prolactin levels ranged between 5-22 ng/ml (mean 10.0 ng/ml) in patients and 6-22 ng/ml (mean 11 ng/ml) in controls. Serum prolactin rose to significantly high levels in generalised and complex partial seizure cases. There was rise of cortisol levels in 14 out of 18 cases of pseudo-seizure but there was no rise of serum prolactin in them. Serum prolactin and cortisol levels provide a useful tool in the diagnosis of pseudo-seizures.

Keywords : *Pseudo - Seizure, Prolactin (PRL)*

Seizures pose a serious problem to the patient and to those concerned with him. In many situations, transient alteration in sensorium may mean disaster. A wrong diagnosis means prolonged useless toxic therapy and unnecessary restriction in the profession of the individual. Clinical observation is seldom available. Eye witness account may be misleading. Electroencephalography, computed tomography and magnetic resonance image of the brain provide useful tools but may not be diagnostic. Hormonal studies which provide an objective parameter are so far unavailable. Clemens[1] demonstrated that stimulation of medial hypothalamus led to a rise in serum prolactin (PRL) in rats. Velasco [2] demonstrated spread of seizure discharges to mesocortical structures. A change in circulating hypothalamico-hypophyseal hormones is therefore expected after an epileptic seizure.

Several clinical studies have demonstrated the above mentioned presumption to be true. A rise in PRL after generalised seizures, after complex partial seizures and after simple partial seizures have been demonstrated [3,4,5]. This study was undertaken in a service hospital to assess PRL levels in seizure patients after an attack of seizure.

Material and Methods

The material of this study consisted of 52 consecutive patients admitted for management of seizures. Cases with metabolic abnormalities or abnormal CT scan were excluded. Pregnant women, nursing mothers or patients on drug affecting PRL secretion were not included in the study. The seizure type was classified according to criteria of International League Against Epilepsy[6]. There were 40 males and 12 females. Their age ranged from 18-40 years with a mean of 27 years. They were matched with 50 normal individuals who were spouses, friends or relatives of patients. All controls were examined to exclude any condition that would alter their endocrine status.

Prolactin Assays . Basal blood samples for prolactin assay were drawn in the morning in the fasting state. In the event of a seizure occurring, samples were drawn at 5 min, 20 min, 1 hour and 24 hours after the ictus. Serum prolactin levels were determined in ng/ml by double antibody radio-immune assay performed with a commercial kit.

Cortisol Assays. Blood samples were drawn as for prolactin. Cortisol was estimated in 20 patients with pseudo-seizures and in 18 controls.

Results

Basal serum prolactin levels ranged between 5-25 ng/ml with a mean of 10± 4.8 ng/ml in tests and ranged between 5-22 ng/ml with a mean of 11.1 ± 4.4 ng/ml in controls. Twenty cases were on anti-convulsants and 32 were on placebo. No difference in PRL levels between the two groups was seen. Six cases were on phenobarbitone in various schedules. No difference was found in PRL levels in male and female patients. Five cases had generalised tonic-clonic seizures. Serum PRL levels are shown in the Table. It can be seen that 20 min after an attack of generalised seizure, PRL rose to 37 ± 6.8 ng/ml. This was significantly above the basal levels (P<.01). Thirteen cases had complex partial seizures and serum PRL levels rose to maximum level 20 min after the seizures. It can be seen from the Table that PRL levels rose to a mean of 35 ± 4.7 ng/ml. The mean difference from the basal values was statistically significant (P<.001). The maximum PRL levels in these cases were comparable with simple partial seizures in which PRL levels rose to a mean of 18.2 ± 5 ng/ml. This level was above the basal level but in no case the rise was above 25 ng/ml. The serum PRL levels did not rise after pseudo-seizures. In 18 controls, cortisol levels ranged betweem 150-650 nmol/litre while immediately after pseudo-seizure a rise of 2-3 times the basal levels was seen in cortisol levels without a concomitant rise in serum prolactin in 20 cases of pseudo-seizures.

Serum Prolactin (ng/ml) in Seizures
(Mean ± SD)

Type of Seizure	5 Mins	20 Mins	1 hr	24 hrs	Basal	P Value
Generalised (n=5)	16.2 ± 7.4	37± 6.8	14± 7	15± 7	10± 4.8	P<0.01
Complex Partial (n=13)	16.2± 6.8	35± 4.7	10.8± 3.4	10.5± 4.4	12± 4.6	P<0.001
Simple Partial (n=6)	12± 5.2	18.2± 5	15± 3.4	12.3± 2.9	11± 4	P<0.05
Pseudo-seizures (n=20)	9.4± 4.4	11.1± 3.4	12.9± 4.7	8.8± 3	10± 5	NS

Discussion

The diagnosis of epilepsy rests on historical data only. In circumstances where history is dubious, the diagnosis becomes extremely difficult. Serum PRL provides an objective parameter which may help in different cases. In this study basal levels of PRL in controls and test subjects were comparable. Several factors are known to cause change in PRL levels. Phenobarbitone has been reported to increase basal PRL levels in males[7]. Five males and one female in this study were on phenobarbitone but they did not show a rise in basal PRL level. No comment is possible due to smallness of the sample size. All 5 cases of generalised tonic-clonic seizures showed a significant rise in PRL levels 20 minutes after seizure. This agrees with the result of earlier studies[6]. Definite cases of complex partial seizures and those with minor attacks only were not included in this study. All cases who had major attacks showed significant elevation in PRL levels after the seizure. This finding is in agreement with the earlier studies. Several studies [3,6] reported less rise in PRL after complex partial than after generalised tonic-clonic seizure. But these studies included cases which had aura or minor attacks only. By stereotactic recording of EEG, Wyllie[5] demonstrated that if the seizure discharges travelled upto amygdaloid

nucleus only, the rise in PRL was marginal. Further spread to hippocampus and hippocampal gyrus is necessary for significant rise in PRL levels. Serum PRL levels 20 minutes after simple partial seizures rose to statistically significant levels. This finding is at variance with the other study[6] which showed no rise in PRL after simple partial seizures. In a given case of simple partial seizure, the rise of PRL is not considered diagnostic per se. Further, marginal rise in PRL indicates partial spread of seizure discharges to limbic structures. In all cases of pseudo-seizures, there was no rise of PRL levels after the "seizure". Muscular activity during seizure caused increased plasma cortisol level without rise in PRL. This has been reported earlier[3,10]

Result of this study indicates that diagnostic rise in serum PRL is seen 20 minutes after generalised tonic clonic and complex partial seizure. In the absence of a competent observer, serum PRL and cortisol levels, provide an objective parameter of diagnostic importance. Simultaneous measurements of plasma cortisol levels provide additional information.

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