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## Serum Prolactin in Seizure Disorders

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*This study aimed to determine the post-ictal prolactin (PL) response in different types of seizures and seizure-like events in children, and correlate with the post-ictal duration. Patients were divided into group I (generalized tonic-clonic seizures, complex partial seizures or simple partial seizures), group II (febrile convulsions) and group III (conditions mimicking seizures). Group IV consisted of 25 controls. Blood was collected within 2 hours of the seizure and PL levels assayed. PL levels were significantly high only within group I; highest and baseline levels were attained within 10 minutes and by 100 minutes respectively. The sensitivity and specificity of elevated PL for epileptic seizures were 64% and 98% respectively. It is concluded that a high prolactin level within 100 minutes of a seizure is suggestive that a generalized or complex partial seizure has occurred.*

**Key words:** Prolactin, Seizures.

An elaborate history and accurate description is necessary for making correct diagnoses of seizures. Uncertainty arises when it has occurred in isolation or the

description is unreliable. The repertoire of seizures is so extensive that even physicians find it difficult to distinguish between seizures and similar conditions(1). Jeavons, *et al*,

demonstrated that 20% of patients being treated as epileptics were not actually so, in a reputed epilepsy clinic in England(2). The coexistence of pseudoseizures with epilepsy is as high as 33%(3).

The adverse effects of anticonvulsant drugs, duration and expense of therapy and social implications, make it essential for accurate diagnosis, before starting treatment. EEG findings may be normal, non-pathognomic or inconclusive. In developed countries, expensive, sophisticated and time-consuming investigations like 24-hr video monitoring, ambulatory EEG, provocative EEG tests and SPECT are used in cases of diagnostic uncertainty. However, they are not always conclusive(4). In India, such modalities are not easily available and hence a cheaper and easily accessible alternative is required.

Studies have shown elevated prolactin (PL) levels after an epileptic seizure(5). The aim of this study was to determine whether PL levels could be used as a single exposure, biochemical marker to differentiate between various types of epileptic seizures, febrile convulsions and seizure-like events in children, and to correlate the levels with the post-ictal duration.

### Subjects and Methods

The study group included seventy-five children, between 6 months to 12 years who were enrolled into three groups, after a detailed history and examination. Group I consisted of patients with generalized tonic-clonic seizures (GTCS), complex partial seizures (CPS) or simple partial seizures (SPS). Group II consisted of typical febrile convulsions. Group III consisted of conditions mimicking seizures (breath holding spells, syncope, pseudoseizures and night terrors). Exclusion criteria were any metabolic

disturbance, infective central nervous system pathology, developmental, structural or neurological abnormality or patients on drugs known to alter PL levels. The controls (group IV) consisted of 25 children admitted for reasons other than fever or seizures and in whom the exclusion criteria were not applicable. Informed consent for inclusion in the study was taken from all subjects.

One ml of blood was collected at presentation, if the seizure had occurred within two hr. The exact interval was noted. Levels of PL were quantitatively assayed using ELISA. Levels were considered high if values were greater than 23 ng/mL, which is the upper limit of normal for all age groups and both sexes(6). The PL level was plotted graphically against the post-ictal duration, for each group. Statistical analysis was performed by one way analysis of variance (ANOVA).

### Results

The mean ages of groups I, II and III, was  $6.8 \pm 4.6$ ,  $2.2 \pm 0.7$  and  $7.5 \pm 3.7$  yrs respectively. There were 15 males and 10 females in groups I and II, and 9 males and 16 females in group III. In the control group the mean age was  $5.8 \pm 2.5$  yrs and there were 12 males and 13 females.

Group I contained 60%(10) GTCS, 20%(5) CPS and 20%(5) SPS. There were 25 febrile convulsions within group II. Conditions mimicking seizures in group III included 48%(12) pseudoseizures, 28%(7) breath holding spells, 16%(4) night terrors and 8%(2) syncope.

It was observed that the post-ictal PL levels were significant high ( $p < 0.05$ ), only within group I (*Table I*). Furthermore, within group I the mean PL values were significantly higher in GTCS (34.46 ng/mL) and CPS (31.60 ng/mL) as compared to SPS (14.20 ng/mL). Eighty percent of GTCS, 60% of CPS

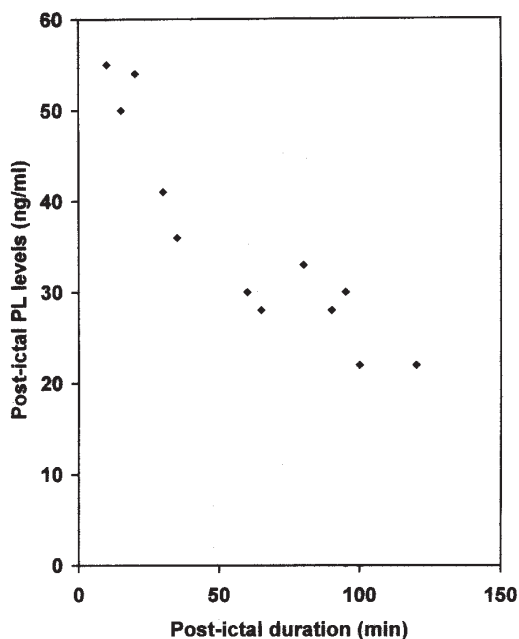
**TABLE I—Prolactin Levels in the Study and Control groups.**

Group	No. of cases (N)	Prolactin levels (ng/ml)		
		Mean	SD	Median
Epileptic seizures (GTCS/CPS/SPS)	25	29.84	14.93	29
Febrile convulsions	25	10.52	7.58	8
Conditions mimicking seizures	25	8.2	5.57	6
Controls	25	10.76	8.97	7

SD: Standard deviation, GTCS: generalized tonic clonic seizures; CPS: complex partial seizures; SPS: Simple partial seizures,  $P < 0.05$  from overall comparison, ANOVA.

and 20% of SPS had elevated levels. The sensitivity and specificity of elevated PL level, as an indicator of an epileptic seizure, was 64% and 98% respectively.

A definite correlation was seen between the post-ictal level and duration only in the cases of GTCS with elevated PL (*Fig. 1*). It was observed that the highest level was



*Fig. 1. Correlation between the post-ictal prolactin (PL) level and corresponding post-ictal duration in cases of generalised tonic clonic seizures.*

attained 10 minutes post-ictally, which was the earliest presentation. A progressive decline in the levels with respect to corresponding increasing post-ictal duration followed. Normal levels were observed in all cases with the post ictal duration more than 100 minutes.

#### Discussion

It was observed that mean PL levels were significantly high only within group I, and were higher in GTCS and CPS as compared SPS. This suggests the possibility of a correlation between the degree of PL elevation and extent of epileptic activity. In GTCS, there is presumed spread of electrical activity from the ventromedial hypothalamus, leading to release of a specific PL regulator into the hypophyseal portal system. This could either be a direct stimulator of PL release or an inhibitor of PL-inhibiting factor(7,8). Dopamine, noradrenaline and gamma-amino-butyric acid (GABA) are considered inhibitory to PL secretion(9).

Most CPS originate in the temporal lobe. It has been demonstrated that electrical activity spreads from the medial temporal structures to the limbic system, even before actual ictal manifestations are seen(7,10). Those cases, not exhibiting a rise in PL, probably originate in the frontal and supplementary motor cortex

### Key Message

- Elevated blood level of Prolactin within a post-ictal time interval of 100 minutes is highly suggestive that a generalized tonic clonic or complex partial seizure has occurred.

without involving the limbic system. Sperling found that only high frequency (>10 Hz), unilateral or bilateral limbic discharges, persisting for more than 20 seconds, spread to subcortical areas. These presumably triggered the ventromedial hypothalamus. Discharges, which were of variable or lower frequency, of shorter duration or did not involve the limbic regions, did not propagate to these areas(10). It has been suggested that when ictal discharges spread from the medial temporal structures to the hypothalamic nuclei, they also lead to an alteration in consciousness. This probably explains why more cases of GTCS and CPS had elevated levels of PL(11). In SPS, the decreased intensity and spatial involvement probably account for the decreased occurrence of PL increase. The definite correlation between PL levels and the post-ictal intervals in GTCS is probably due to the progressive decline of PL release as the electrical discharges diminish.

In typical febrile seizures, sub-clinical electrical activity does not exist since the after-discharges are less intense and transient to project to the ventromedial hypothalamus(12) whereas conditions mimicking seizures completely lack electrical discharges. This accounts for the lack of PL elevation.

The clinical usefulness of post-ictal PL estimation is restricted to the positive diagnosis of epileptic seizures. A positive result is highly suggestive of a GTCS or a CPS having occurred. Since non-elevated levels were seen in up to 20% of GTCS, 40% of CPS and 80% of SPS, it cannot be used exclusively

for differentiation between subtypes of epileptic seizures. However, it can be applied in cases of diagnostic uncertainty between epileptic and non-epileptic events, before having to resort to more sophisticated and expensive investigations.

It was observed that the non-elevated values of PL had a wide range of variability within the significant time frame. If this individual variation is taken into consideration, the predictive value will probably increase. The authors suggest that a ratio between the post-ictal level within the significant time frame and the baseline level attained afterwards should be studied.

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## Spectrum of Congenital CNS Malformations in Pediatric Epilepsy

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*This study was conducted in a tertiary pediatric epilepsy clinic to ascertain the spectrum of development malformations in children, with seizures. Seventy Six Children (0-12 yr) with seizures and CNS malformations based on neuroimaging were included. Observed anomalies included dysgenetic corpus callosum (DCC), lissencephaly, focal cortical dysplasia (FCD), pachygyria, polymicrogyria, heterotopia, schizencephaly, holoprosencephaly, hemimegalencephaly, and phakomatoses like tuberous sclerosis, Sturge Weber syndrome and linear cutaneous nevus syndrome. Seizure semiology varied in all categories. Microcephaly, developmental delay and tone abnormalities were common clinical findings. 60.5% cases presented in infancy. The characteristic EEG features provided a clue to the diagnosis of anomalies like lissencephaly, agenesis of corpus callosum and alobar holoprosencephaly.*

**Key words:** CNS malformations, EEG, Epilepsy, Neuroimaging.

Developmental CNS malformations are a complex group of congenital malformations often presenting with variable neuro-developmental dysfunction and seizures(1).

Computed tomography (CT) scan and magnetic resonance imaging (MRI) have revolutionized our understanding of these malformations, providing a good anatomic