Research Article

Usefulness of Serum Prolactin in Differentiating Epileptic and Pseudoseizures in Children

Om Shankar Chaurasiya, Parul Gupta, Anil Kaushik, Rajesh Yadav

Department of Pediatrics, M.L.B. Medical College, Jhansi

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Abstract:

Transient hyperprolectinemia has been reported to follow unprovoked seizures. This study was conducted in 90 children aged 1-18 years of age. The study comprised of four groups: Group-1 consisted of children with epilepsy which was further subdivided into GTCS, CPS and SPS. Group-2 comprised of children having febrile convulsions. Group-3 comprised of children suffering from non-epileptic paroxysmal events like breath holding spell, syncope and pseudoseizures or conversion reaction. Group-4 consisted of children who served as controls. Blood sample was collected within two hours of the event in all the groups. The exact interval between the event and the collection of blood sample was noted. Serum prolactin level was estimated by ELISA technique. In the present study, significant elevation of serum prolactin level was observed only in the Group-1 (28.77$\pm$15.49ng/ml) as compared to controls (9.53$\pm$2.45ng/ml) and the highest levels were observed in children with GTCS. Maximum elevation of prolactin was seen within 15 to 30 minutes post ictally. As the prolactin levels become normal after two hours of post ictal period, the test looses its significance.

Key Words: Serum Prolactin, Seizure.

Introduction:

Prolactin is secreted from the anterior pituitary gland and is inhibited by tubero-infundibular dopamine neurons in the arcuate nucleus of the hypothalamus. Abnormal electrical discharge passing through the hypothalamus may disrupt the normal functioning. Generalized neuronal discharge of a seizure stimulates the hypothalamus either directly through specific neurotransmitter changes (decrease in GABA and dopaminergic system) or through the release of other substances, thereby, causing increase in serum prolactin level during epileptic form of seizures. Acute changes in serum prolactin levels which occurred following some of the seizures may be useful in differentiating epileptic seizures from non epileptic seizures.

This study was undertaken to know whether elevated serum prolactin levels following a seizure may be used to differentiate epileptic seizure from other paroxysmal disorders of childhood.

Material and Methods:

The present study was conducted on 90 children between 1-18 years of age. They were divided into four groups after taking detailed history and their examination.

Group I included children with epilepsy. These children had an provoked seizure at the time of admission. This group was further subdivided into patients with Generalized Tonic Clonic Seizure (GTCS), Complex Partial Seizures (CPS) and Simple Partial Seizures (SPS).

Group II comprised of children with typical febrile seizures. Children with doubtful diagnostic features of febrile seizures,developmental or neurological abnormalities,prolonged seizures of more than 10 minutes and focal seizures were excluded.

Group III comprised of children with non epileptic paroxysmal events e.g. breath holding spell, syncope, night terror, pseudoseizures etc.

Group IV (control) comprised of children admitted for reasons other than fever or seizure. They were free from any known metabolic or endocrine disease and in whom the exclusion criteria were not applicable.

Exclusion criteria: Children with any metabolic disturbance, infective central nervous pathology, developmental, structural or neurological abnormalities, or patients on drugs known to alter prolactin levels (like phenothizine, haloperidol, metoclopramide, opiates, cimetidine, imipramines, fluoxetine, verapamil) were not included in the study.

Blood sample was collected within two hours of the event in all the groups and the exact interval between the event and collection of blood was noted. One milliliter of blood was taken & serum was separated by centrifugation at room temperature and

Corresponding Author: Dr. Om Shankar Chaurasiya, Department of Pediatrics, M.L.B. Medical College, Jhansi - 284128
Phone No.: +91 9532376316
E-mail : chaurasiyaom@yahoo.co.in

tested withcommercially available kits (UBI Magiwel prolactin quantitative, HP-201 kit) using ELISA technique which provides quantitative estimation of prolactin in serum. In children, the normal values are less than 15ng/ml. Neonatal prolactin concentrations are high, but fall to adult levels by three months of age. Levels were considered high if values were greater than 23 ng/ml or two times more than the base line value.

Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented as Mean ± SD (Min-Max). Significance is assessed at 5 % level of significance. Student unpaired *t-test* was used to find the significance of study parameters on continuous scale between two groups.

Results:

The present study was undertaken to find out the usefulness of serum prolactin in distinguishing the true epileptic seizures from pseudoseizures and other non epileptic paroxymal events.

There were 30 children (17 males and 13 females) in Group I and 20 cases each in group II, III and IV (Table I).

Group I contained 15 cases of GTCS, 8 cases of CPS and 7 cases of SPS. Group II had 20 cases of Febrile convulsions. Children with non epileptic paroxysmal events (Group III) consisted of 7 children with breath holding spell, 5 with syncope and 8 cases had pseudoseizures.

Group I had highly significant increase in prolactin levels after seizure episode than the control group ($p<0.0001$). Rise in serum prolactin level was not significant in group II & III as compared to group IV (Table II).

The mean serum prolactin level in children with GTCS was 35.06 ± 14.26 ng/ml, with range of 11.80-56.45 ng/ml; in CPS, the values were 28.3 ±12.94 ng/ml with the range of 8.45-48.50ng/ml, while in SPS the mean value was 13.74±6.92ng/ml in the range of 7.50-26.75ng/ml. On statistical analysis, the levels were found to be significantly higher in children with GTCS ($p<0.0001$). The levels were also elevated in CPS but were not significant. In SPS the levels were significantly increased than the controls ($p<0.05$; Table III).

Table I: Distribution of cases according to sex in all the groups.

Group	No. of Cases	Mean ± SD	Male	Female
I	30	8.7± 3.5	17	13
II	20	3.21± 0.7	12	8
II	20	7.87± 3.1	11	9
IV	20	7.21± 2.1	10	10

Table II: Serum prolactin level in different groups

Variables	Mean±SD Range	No. of Cases	*t*-value	*d.f.*	*p*-value
Group I	28.77±15.49	30			
	7.5-56.75		5.49	48	<0.0001**
Group IV	9.53±2.45	20			
	5.75-17.45				
Group II	11.25±3.14	20			
	6.75-17.45		1.93	38	0.0609
Group IV	9.53±2.45	20			
	5.75-17.45				
Group III	8.74±2.64	20			
	5.45-14.25		0.98	38	0.3328
Group IV	9.53±2.45	20			
	5.75-17.45				

Table III: Comparison of serum prolactin levels in subdivisions of Group I.

Variables	Mean±SD Range	No. of Cases	*t*-value	*d.f.*	*p*-value
GTCS	35.06 ± 14.26	15			
	11.80-56.45		7.89	33	<0.0001**
Control	9.53 ± 2.45	20			
	5.75-13.75				
CPS	28.73 ± 12.94	8			
	8.45-48.50		0.78	26	0.4409
Control	9.53 ± 2.45	20			
	5.75-13.75				
SPS	13.74 ± 6.92	7			
	7.50-26.75		2.39	25	0.0246*
Control	9.53 ± 2.45	20			
	5.75-13.75				

*Significant ($p<0.005$), **Highly significant ($p<0.0001$)

Serum prolactin level was found to be significantly elevated after epileptic attacks. Elevated levels were observed in 12 out of 15 (80.0%) cases of GTCS, 5 out of 8 (62.50%) cases of CPS and 2 out of 7 (28.5%) cases of SPS.

Elevation in serum prolactin level after the seizure was observed upto 90 minutes of post ictal duration, but was more marked when the post ictal duration was < 30 minutes. In the Group I with post ictal duration of < 30 minutes, the mean serum prolactin level was 33.16 + 14.6Ing/ml and with post ictal duration of > 30 minutes, the mean value was 20.04 + 6.75 ng/ml. In the Group II, these values were 11.84 + 2.74 ng/ml and 11.14 + 2.52 ng/ml respectively, and in

Table IV: Serum prolactin level in three groups in relation to post ictal duration (<30 minutes vs.>30 minutes)

Variables		Group I (n=30)	Group II (n=20)	Group III (n=20)
Post ictal duration < 30 min	Mean± S.D.	33.16 ± 14.61 (n=19)	11. 84± 2. 74 (n=12)	9.05 ± 3. 17 (n=9)
Postictal duration > 30 min	Mean± S.D	20.04± 6.75 (n=11)	11.14 ± 2.52 (n=8)	8.46± 2.89 (n=11)
	t-value	10.092	0.939	0.756
	d.f.	28	18	18
	p-value	<0.0001**	0.3	0.4

** Highly significant (p<0.0001)

the Group III, these values were 9.05 + 3.17 ng/ml and 8.46 + 2.89ng/ml respectively. Statistical analysis revealed that the values were highly significant (p<0.001) only in the group I and not significant in group II & III (p>0.3, >0.4 respectively; Table IV).

Discussion:

Epilepsy is the commonest neurological condition of the childhood. It is often confused with other frequently occurring non epileptic paroxysmal disorders of the childhood. Acute changes in the pituitary hormone levels, which occur following some of the seizures can help in differentiating epileptic seizure from pseudoseizure and febrile seizure. The most predictable post ictal changes are increased serum cortisol levels and serum prolactin levels. Because of the normal diurnal variation in serum cortisol levels and the relative delay in the post ictal elevations of serum cortisol, serum prolactin level is more useful as diagnostic measure of epileptic seizure. In the present study, significant elevation of serum prolactin level was observed only in children of Group I (28.77±15.49 ng/ml) as compared to control (9.53 ± 2.45 ng/ml). Serum prolactin levels were higher in GTCS (35.06 ± 14.26 ng/ml) and CPS (28.73 ±12.94 ng/ml) as compared to SPS (13.74 ± 6.92 ng/ml).

Similar observations were also made by many other workers showing increase in serum prolactin levels post ictally especially after GTCS. Abbott et al (1980) had demonstrated that elevation of serum prolactin level is not due to a non specific response to stress but probably indicates an alternation in the hypothalamic neurotransmitter activity during the seizure.

Collinas et al (1983), Rao et al (1989) and Graf et al (1988) had also reported similar results, but Lusic et al (1999) had found confounding results in patient with seizure and syncopal attacks.

An elevation of serum prolactin can be taken as a predictor of epilepsy. A non elevation of prolactin is not predictor of epilepsy and hence does not rule out the diagnosis of epileptic seizure as non elevated levels were seen in up to 20% of GTCS, 38% CPS and 72% of SPS.

Sperling & Wilson (1986) found that complex partial seizures were associated with bilateral limbic ictal discharges and had a significant rise in the serum prolactin concentration. Cases which did not exhibit a rise in serum prolactin levels, ictal discharges probably originate in the frontal and supplementary motor cortex without involving the limbic system. It has been suggested that when ictal discharges spread from the medial temporal area to the hypothalamic nuclei, they also lead to an alternation in consciousness. This probably explain why more cases of GTCS and CPS had elevated levels of prolactin. In SPS the decreased intensity and spatial involvement, probably accounts for the decreased incidence of prolactin elevation.

Culebras et al (1987) have studied the response of prolactin to seizures and to stress and reported that stressed patients had significantly less elevated prolactin levels, suggesting that neurogenic stimuli responsible for post ictal release of prolactin is independent of stress mechanism.

Wyllie et al (1984) reported marked prolactin elevation above three times of baseline at 15 or 30 minutes post ictally in 80% GTCS, 43% of CPS and 10% of SPS. Bauer et al (1989) found significant rise in serum prolactin level in 88% of GTCS, 78% of CPS and 22% of SPS. Observation of the present study are at par with the above studies. Zelnik et al (1991) observed significantly higher prolactin levels in the epileptic group (26.5 ±3.3 ng/ml) as compared with children with febrile seizures (13.2± 1.0 ng/ml), fever (11.2 ± 0.9 ng/ml), syncope (7.3 ± 0.9 ng/ml) and the control group (7.9 ± 0.6 ng/ ml). Pritchard et al (1985) reported a two fold increase in prolactin level following

true epileptic seizures, but no significant change occurred after pseudo epileptic attacks.

Kurlemann et al (1992) studied serum prolactin level in cerebral and psychogenic seizures in childhood and adolescence. A more than 2 to 3 fold prolactin increase of the baseline value occurred almost always after grandmal seizures, and regularly after complex partial seizures, but no hyperprolactenemia was observed after psychogenic seizures.

Malkowicz et al (1995) reported that seizure occurring after longer seizure free interval showed robust prolactin responses. After shorter seizure free interval prolactin response was reduced.

As Shown in table III, children with febrile seizure had higher prolactin levels than children with non epileptic events and controls, but the levels were still with in the normal range. Similar results were also observed by Zelnik et al (1991) and Dirik et al (1996).

In children with febrile seizures, minor rise in serum prolactin level was found, this is because of non specific response to fever related stress. Petroni et al (1998) had also reported similar results in febrile and true seizures.

In children with conditions mimicking seizures, no rise in the serum prolactin level was observed. Similar results were also observed by Graf et al (1988).

Maximum elevation of prolactin is seen within 15 to 30 minutes post ictally but levels can be assessed up to 90 minutes of post ictal duration. This is significant as it is not always possible to obtain a sample within the period of maximum elevation. As the prolactin levels are normal after two hours of post ictal duration, the test loses its significance and can not be used to differentiate true epileptic event from other events.

Conclusion:

An elevation of serum prolactin can be taken as a predictor of epilepsy. Maximum elevation of prolactin is seen with in 15 to 30 minutes post ictally but levels can be assessed up to 90 minutes of post ictal duration .It is suggestive that GTCS or CPS has occurred.

Bibiliography:

1. Abbott RJ, Browing MCK, Davidson DLW: Serum prolactin and cartisol concentration after grand mal seizures. *Journal of Neural, Neurosurgery and Psychiatry*, 1980; 43(2): 163-167 .
2. Bauer J, Stefan H, Schrell U, Sappke U, Uhlig B: Neurophysiologic principles and clinical value of post-convulsive serum prolactin determination in epileptic seizure. *Psychiatry*, 1989;57(11):457-468.
3. Collins WC, Lanigan O, Callaghan N: Plasma Prolactin concentration following epileptic and pseudoseizures. *Journal of Neural, Neurosurgery and Psychiatry*, 1983;46(6):505-508.
4. Culebras A, Miller M, Bertram L, koch J: Differential response of growth hormone, cortisol and prolactin to seizures and to stress. *Epilepsia*, 1987;28(5):564-570.
5. Dirik E, Sen A, Anal O, Cevik NT: Serum cortisol & prolactin levels in childhood paroxysmal disorder. *Acta Paediartica Japanica*, 1996;38(2):118-120.
6. Graf M, Tatzer E, Weninger M, Groh C, Waldhauser F, Rosenmayr F, Lischka A: Discrimination between epileptic and noon-epileptic seizures using defined prolactin studies. *Wiener klinische Wochenschrift*, 1988; 100(9):656-658.
7. Kurlemann G, Heyen P, Menges EM, Palm DG: Serum prolactin after cerebral and psychogenic seizures in childhood and adolescence-an additional useful method for differentiating the two form of seizures. *Klinsche Padiatric*, 1992;204(3):150-154.
8. Lusic I, Pintaric I, Hozo I, Boic L, Capkun V: Serum prolactin levels after seizure and syncopal attacks. *Seizures*, 1999; 8(4):218-222.
9. Malkowicz DE, Legido A, Jackel RA, Sussman NM, Eskin BA, Harner RN: Prolactin secretion following repetitive seizures. *Neurology*, 1995;45(3Pt-1):448-452.
10. Petroni F, Bensi P, Andreotti M, Russo F, La Placa G: Plasma prolactin in childhood paroxysmal disorders. *Padiatric and Medical Surgical Pediatrics*, 1998 ;20(2):137-138.
11. Pritchard PB, Wannamaker BB, Sagel J, Daniel CM: Serum prolactin and cortisol levels in evaluation of psedoepileptic seizures. *Annals of Neurology*, 1985;18(1):87-89. Article first published online: 7 OCT 2004 DOI: 10.1002/ana.410180115.
12. Rao ML, Stefan H, Bauer J: Epileptic but not psychogenic seizures are accompanied by simultaneous elevation of serum pituitary hormones and cortisol levels. *Neuroendocrinology*, 1989;49(1):33-39.
13. Sperling MR, Wilson CL: The effect of limbic and extralimbic electrical stimulation upon prolactin secretions in humans. *Brain Researcher*, 1986;371(2):293-297.
14. Wyllie E, Luders H, Mac Millan JP, Gupta M: Serum prolactin levels after epileptic seizures. *Neurolagy*. 1984;34(12):1601-1604.
15. Zelnik N, Kahana N, Rafael E, Besner I, Lancu TC: Prolactin and cortisol levels in various paroxysmal disorders in childhood. *Pediatrics*, 1991;88(3):486-489.

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