ISSN NO. 2320-5407

Journal homepage: http://www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH

RESEARCH ARTICLE

"STUDY OF SERUM PROLACTIN LEVELS & ELECTROLYTE PANEL IN PATIENTS WITH NEW ONSET SEIZURES"

Priyanka Parihar[1], Peeyush Yadav[2*], Dr.Rashmi Ranka[3], Dr.G.G.Kaushik[4]

1. PG. Student, Department of Biochemistry, J.L.N Medical College, Ajmer. Rajasthan,India.
2. Senior Demonstrator, Department of Biochemistry, J.L.N Medical College, Ajmer. Rajasthan,India.
3. Senior Professor, Department of Biochemistry, J.L.N Medical College, Ajmer. Rajasthan,India.
4. Professor & Head, Department of Biochemistry, J.L.N Medical College, Ajmer. Rajasthan,India.

Manuscript Info

Manuscript History:

Received: 18 April 2015
Final Accepted: 25 May 2015
Published Online: June 2015

Key words:

Prolactin, Seizure, Epilepsy

Corresponding Author

Peeyush Yadav

Abstract

Background: Epilepsy is a group of long-term neurological disorders characterized by epileptic seizures [3]. Prolactin in serum transiently increased in early epileptogenesis. Serum Prolactin levels are elevated following generalized motor seizures in approximately 90% of cases, and following complex partial seizures in about 70% of cases. The body electrolytes sodium (Na^+), potassium (K^+), calcium (Ca^{2+}), and magnesium ($Mg2^+$) and the level of some trace elements play a vital role in seizure condition to develop.

Aim: To evaluate the role of prolactin and electrolytes (sodium, potassium, calcium & magnesium) levels in types of seizures & to differentiate true seizures from non epileptic seizures.

Patients & Methods: Study includes 50 patients of new onset seizure & 50 controls. Serum Prolactin was estimated using ELISA method & serum electrolytes were also estimated. Data were compared by using 't' test. Pearson's correlation was done to see the changes among the markers.

Results: Only patients with Generalized Tonic-Clonic Seizure & Complex Partial Seizures had highly raised Prolactin. A decrease in Sodium, Calcium, Magnesium levels & nearly normal Potassium levels were found in all types of seizures except pseudo seizures in which electrolytes (Na^+,K^+,Ca^{2+},Mg^{2+}) showed no significant change.

Conclusion: Prolactin estimation can be a useful biomarker to differentiate Epileptic seizures from Pseudoseizures.

Introduction

A Seizure is a paroxysmal event due to abnormal, excessive, hypersynchronous discharges from an aggregate of central nervous system (CNS) neurons. Seizure is defined as an "involuntary alteration of behaviour with or without loss of consciousness accompanied by an abnormal electrical discharge in the brain." These seizures are episodes that can vary from brief and nearly undetectable to long periods of vigorous shaking. Epilepsy (from the Ancient Greek, meaning "to seize, possess, or afflict") is a group of long-term neurological disorders characterized by epileptic seizures[3].Seizures can be partial and generalized. The difference between the two is of loss of consciousness. In partial cases a focal point of the brain is affected. In generalized seizures the impulses comes out from both sides of the brain at the same time. Partial seizures may generalize; start from one site in the brain and spread to involve the whole brain. There are mainly four types of seizures-

1. **Generalized Tonic-Clonic Seizure (GTCS) -** A grand mal seizure - also known as a generalized tonic-clonic seizure - features a loss of consciousness and violent muscle contractions. Grand mal seizure is caused by abnormal electrical activity throughout the brain. Most of the time grand mal seizure is caused by epilepsy.
2. **Focal or Partial Seizure (FS) -** also called **partial seizures** and **localized seizures** are seizures which affect initially only one hemisphere of the brain. Partial seizures are split into two main categories:
   a. **Simple Partial Seizure** are seizures which affect only a small region of the brain, often the temporal lobes or hippocampi. People who have simple partial seizures retain consciousness.
   b. **Complex Partial Seizure (CPS)** is an epileptic seizure that is associated with unilateral cerebral hemisphere involvement and causes impairment of awareness or responsiveness i.e. alteration of consciousness.
3. **Status epilepticus (SE) -** It is an epileptic seizure of greater than five minutes or more than one seizure within a five minute period without the person returning to normal between them. Status epilepticus is a life-threatening condition particularly if treatment is delayed.
4. **Psychogenic non-epileptic seizures (PNES) -** Also known as non-epileptic attack disorders (NEAD), are events superficially resembling an epileptic seizure, but without the characteristic electrical discharges associated with epilepsy. PNES are triggered by psychological problems, and frequently occur in conversion disorder.

Prolactin (PRL), also known as luteotropic hormone or luteotropin, released from the pituitary is controlled by the hypothalamus via a PRL inhibitory factor, now believed to be dopamine. PRL is secreted from the pituitary gland in response to eating, mating, estrogen treatment, ovulation, and nursing. It is secreted in a pulsatile fashion in between these events. It also plays an essential role in: metabolism; regulation of the immune system; and pancreatic development.PRL levels may be of some use in distinguishing epileptic seizures from PNES. The serum PRL level usually rises following an epileptic seizure. PRL elevation in serum following seizure has been considered a potential candidate for a surrogate marker.

Electrolyte abnormalities may affect many organs and tissues, including the brain. Acute and/or severe electrolyte imbalances frequently cause seizures and these seizures may be the sole presenting symptom. Seizures are especially common in patients with sodium imbalance, hypocalcaemia and hypomagnesaemia. Successful management of patient seizures begins with the establishment of an accurate diagnosis of the underlying electrolyte disturbance, because rapid identification and correlation of the disturbance is necessary to control seizures and prevent permanent brain damage [10]. Several reports suggested that the body electrolytes sodium (Na^+), potassium (K^+), calcium (Ca^{2+}), and magnesium (Mg^{2+}) and the level of some trace elements play a vital role in seizure condition to develop.

It is therefore, of prime importance to correctly diagnose new onset seizures, so as to treat it specifically. Keeping in view the above aim, the study was carried out to evaluate the role of prolactin and electrolytes (sodium, potassium, calcium & magnesium) levels in types of seizures & to differentiate true seizures from non epileptic seizures.

MATERIALS AND METHODS

Fifty cases of new onset seizures of age group 20-50 yrs. of either sex were included in the present study. Patients suspected to have new onset seizures presented within 2 hrs. of ictus. All were randomly recruited from the O.P.D. of Department of Medicine in Jawahar Lal Nehru Medical College & Associated Group of Hospitals, Ajmer. Excluded from this study were those who have presented after 2 hrs. of seizure, who have taken any intramuscular injections just prior to coming to the hospital, patients with known epileptic on or off treatment or known renal or endocrine disorder and Pregnant women. Fifty normal healthy (age and sex matched) subjects served as a control group. Detailed information of the study was given to each patient and consent of all subjects was taken to attend this study. After the baseline evaluation, the subjects were divided into two main groups: normal healthy subjects (n = 50) & subjects of new onset seizures (n = 50). A positive EEG is the gold standard for establishing the diagnosis of epilepsy and for evaluating seizure type and syndrome. Venous blood sample was drawn from anticubital vein of each subject by using aseptic precautions and subjected for following estimations. Serum was analyzed for quantitative estimation of Prolactin by ELISA Method, Sodium and Potassium by Flame photometry, Calcium by OCPC End point Colorimetric Method, Magnesium by Colorimetric Titan Yellow Method. The values were expressed as mean and standard deviation (mean±SD). Pearson's correlation analysis was performed to assess the association between the various test parameters. A p value <0.05 was considered to be significant.

RESULTS

New onset seizure patients were further sub-divided into five groups according to type of seizure: patients with GTCS (n=19), FS (n=12), CPS (n=9), SE (n=6), PNES (n=4).

TABLE-1

No. of patients with raised prolactin level in various types of seizures

Type of Seizure	No. of patients (n=50)		No. of patients with raised levels of Prolactin	
	Number	Percentage	Number	Percentage
GTCS	19	38%	10	52.6%
FS	12	24%	03	25%
CPS	09	18%	07	77.7%
SE	06	12%	02	33.3%
PNES	04	08%	00	0%

Fig.-1 : No. of patients with raised prolactin level in various types of seizures

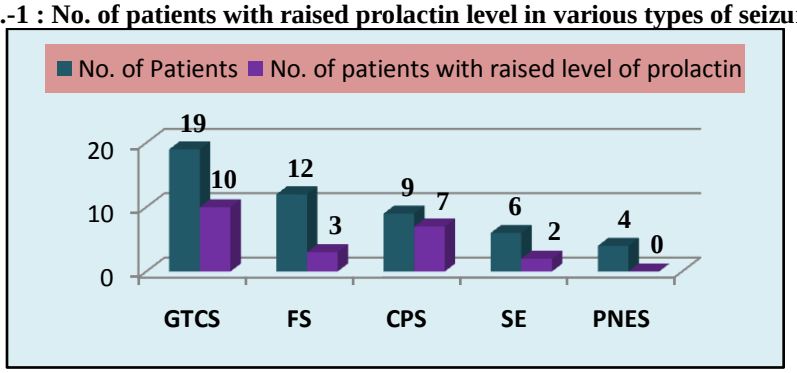
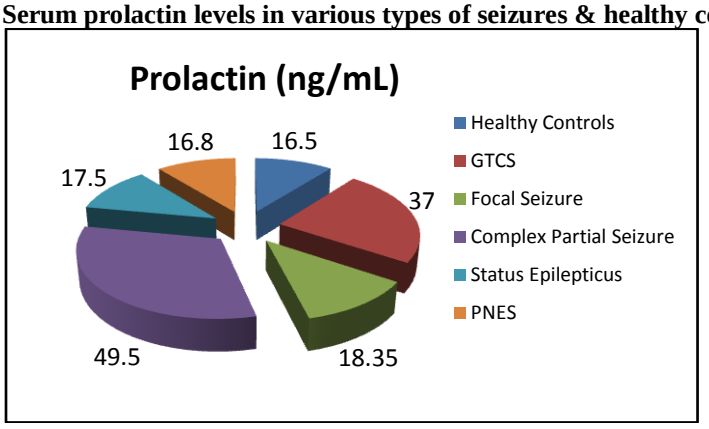


TABLE-2

Serum prolactin levels in various types of seizures & healthy controls

	Healthy Controls (n=50)	GTCS (n=19)	FS (n=12)	CPS (n=9)	SE (n=6)	PNES (n=4)
Prolactin (ng/mL)	16.5±6.75	37.0±3.0	18.35±2.56	49.5±4.39	17.5±2.8	16.8±3.4
p value by t-test		p<0.0001 (HS)	p=0.35 (NS)	p<0.0001 (HS)	p=0.56 (NS)	p=0.97 (NS)

Fig.-2: Serum prolactin levels in various types of seizures & healthy controls



In GTCS & CPS patients, the increase of Prolactin was observed statistically highly significant (p<0.0001) when compared with healthy controls. Our study confirms that serum Prolactin increases after generalized & complex seizures. The increase of Prolactin was observed statistically non-significant (p>0.0001) in FS, SE & PNES patients, when compared with healthy controls.

TABLE-3
LEVELS OF SERUM ELECTROLYTE PANEL IN VARIOUS TYPES OF SEIZURES & HEALTHY CONTROLS

PARAMETER	HEALTHY CONTROLS (n=50)	GTCS PATIENTS (n=19)	FS PATIENTS (n=12)	CPS PATIENTS (n=9)	SE PATIENTS (n=6)	PNES PATIENTS (n=4)
SODIUM (mmol/L)	138.0±2.5	132.0± 0.75	135±1.0	133±3.0	129±1.0	137.0±1.25
POTASSIUM (mmol/L)	4.5±0.5	4.3±0.5	4 .4±0.2	4.2±0.45	4.0±0.12	4.3±0.20
CALCIUM (mg/dL)	10.0±0.5	8.3±0.1	8.8±0.2	8.8±0.2	7.8±0.12	9.8±0.22
MAGNESIUM (mg/dL)	1.9±0.12	1.5±0.07	1.65±0.062	1.8±0.12	1.3±0.07	1.8±0.05

All patients with GTCS & CPS showed statistically highly significant decrease in levels of sodium, calcium, magnesium & non-significant change in levels of potassium. All patients with SE showed highly significant decrease in levels of sodium, calcium, magnesium & nearly normal level of potassium. All FS patients showed statistically highly significant decrease in levels of sodium, calcium, magnesium & non-significant change in levels of potassium. All patients with PNES showed a statistically non-significant change in Electrolytes levels.

DISCUSSION

It has been estimated that 1.5% to 0.5% of persons in any population will have a seizure at some time. Partial seizures, with or without secondary generalization, are the most common seizure type, followed by generalized tonic-clonic seizures. A seizure occurs when a portion of the brain becomes overly excited or when nerves in the brain begin to fire together in an abnormal fashion. Seizure activity can arise in areas of the brain that are malformed from birth defects or genetic disorders or disrupted from infection, injuries, tumors, strokes, or inadequate oxygenation. Seizures are controllable with medication in about 70% of cases [5]. Prolactin release from the pituitary is controlled by the hypothalamus via an inhibitory factor, now believed to be a dopamine [6]. Prolactin is released during periods of significant stress. Serum levels are elevated following generalized motor seizures in approximately 90% of cases, and following complex partial seizures in about 70% of cases [2]. It has been hypothesized that ictal epileptic activity in the mesial temporal structures may propagate to the hypothalamus, altering the hypothalamic regulation of prolactin release. In GTCS, there is presumed spread of electrical activity from the ventromedial hypothalamus, leading to release of a specific PRL regulator into the hypophyseal portal system. Most CPS originates 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[19]. 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 prolactin. In our study, the increase of Prolactin in GTCS & CPS patients was observed statistically highly significant ($p<0.0001$) when compared with healthy controls. Our findings are consistent with Trimble, Collins WCG et.al. who in separate studies found that elevation of prolactin level is much higher in GTCS and CPS than in partial seizures or PNES.

In FS, the decreased intensity and spatial involvement probably account for the decreased occurrence of prolactin increase. The increase of Prolactin was observed statistically non-significant when compared with healthy controls. Our observation is in agreement with Sperling MR et. al.; who also observed that in focal seizures, decreased occurrence of prolactin elevation was due to the decreased intensity and spatial involvement.

PNES or Pseudoseizures do not affect serum PRL levels. In our study, the increase of Prolactin in FS, SE & PNES patients was observed statistically non-significant ($p>0.0001$) when compared with healthy controls. This goes in accordance with the reports of Abbot RJ et.al., Torbjorn Tomson et.al., who found that all patients with SE had ictal prolactin levels within normal range and there was no increase from baseline values. All patients who presented with PNES had nearly normal PRL levels. Serum PRL level estimation has been considered one of the methods to be used for differentiation of true seizures from PNES. Our findings were in agreement with the findings of Collins WCG et.al., Singh UK et.al., Kurlemann G et.al., who in separate studies found that serum PRL levels are significantly raised after true seizure but not after PNES.

Nerve cells between discharges normally have a negative charge internally due to the active pumping of positively charged sodium ions out of the cell. Discharge or firing of the nerve cell involves a sudden fluctuation of the negative charge to a positive charge as ions channels into the cell open and positive ions, such as sodium, potassium, and calcium, flow into the cell. Both excitatory and inhibitory control mechanisms act to allow appropriate firing and prevent inappropriate excitation of the cell.

Sodium is the major extracellular cation. A loss of sodium from body results in a decrease of extracellular fluid volume affecting circulation, renal function and nervous system. Complications of severe and rapidly evolving hyponatremia include seizures, usually generalized tonic–clonic. Seizures generally occur if the plasma sodium concentration rapidly decreases to <115 mEq/L; they represent an ominous sign and also a medical emergency, as they are associated with high mortality [17]. The decreased levels of Sodium in GTCS, CPS, FS and SE patients was observed statistically highly significant ($p<0.0001$) when compared with healthy controls while in PNES the decrease was statistically non- significant. Our observation is in agreement with Rajesh Padhi et.al., who found that Hyponatremia is a common electrolyte disturbance occurring in critically ill patients.

Potassium is major intracellular cation. Its concentration in plasma determines neuromuscular & muscular irritability. Unlike other electrolyte alterations, hypokalemia or hyperkalemia rarely causes symptoms in the CNS, and seizures do not occur. Changes in the extracellular potassium level (serum levels) have predominant and profound effects on the function of the cardiovascular and neuromuscular systems. Thus severe potassium abnormality may provoke fatal arrhythmias or muscle paralysis before CNS symptoms appear [7,17]. Increase or decrease in potassium levels can cause muscle weakness, muscle cramps, muscle twitching, low blood pressure, respiratory failure, paralysis and the muscle breakdown disorder called rhabdomyolysis; but seizures rarely occur. The decreased levels of potassium in GTCS, CPS, FS, SE and PNES patients was observed statistically non-significant when compared with healthy controls. Our findings were in agreement with Gennari & Riggs.

Calcium is the most abundant and one of the most important minerals in the human body. Approximately 99% of body calcium is found in bones. A decrease in albumin level causes a decrease in serum calcium. Hypocalcemia is defined as a plasma calcium level of <8.5 mg/dl or an ionized calcium concentration <4.0 mg/dl. Seizures may occur without muscular tetany in patients with hypocalcemia. Seizures occur in 20–25% of patients with acute hypocalcemia as a medical emergency, and in 30–70% of patients with symptomatic hypoparathyroidism[8,13]. The decreased levels of calcium in GTCS, CPS, FS and SE patients was observed statistically highly significant ($p<0.0001$) when compared with healthy controls while in PNES the decrease was statistically non- significant. Our results are in consistence with Riggs, Mrowka et al. , Kline et al., who in separate studies found that Generalized tonic–clonic, focal motor, and (less frequently) atypical absence or akinetic seizures can occur in hypocalcemia and may be the sole presenting symptom.

Magnesium is the second most abundant intracellular cation of the human body after potassium, being essential in great number of enzymatic and metabolic processes. Symptoms do not appear unless Mg^{2+} decreases to <1.2 mg/dl, and they may not correlate well with serum ionized Mg^{2+} levels. The primary clinical findings are neuromuscular irritability, CNS hyperexcitability, and cardiac arrhythmias. Seizures, usually generalized tonic–clonic, can occur in neonates and adults in association with severe hypomagnesemia, at levels <1 mEq/L [17]. The decreased levels of magnesium in GTCS, CPS, FS and SE patients was observed statistically highly significant ($p<0.0001$) when compared with healthy controls while in PNES the decrease was statistically non- significant. This goes in accordance with the study of Weisleder P et.al, who concluded that Hypomagnesemic seizure is a consequence of renal magnesium wasting.

Acute and/or severe electrolyte imbalances frequently cause seizures, and these seizures may be the sole presenting symptom. Seizures are especially common in patients with sodium disorders, hypocalcaemia, and hypomagnesaemia [12].

CONCLUSION

Our study indicates highly raised serum Prolactin levels, only in patients with Generalized Tonic-Clonic Seizure & Complex Partial Seizures. The levels of serum Electrolytes (sodium, magnesium, calcium) decrease in various types of seizures except PNES in which electrolytes (sodium, magnesium and calcium) showed no significant change while potassium remains nearly normal in all types of seizures. Prolactin estimation can be a useful biomarker to differentiate Epileptic seizures from PNES. The serum PRL level usually rises following an epileptic seizure while it remains unchanged in PNES. Hyperprolactinemia has been considered a potential candidate for a surrogate marker in seizures. Seizures often represent an important clinical manifestation of electrolyte disturbances. Seizures are more common in patients with hyponatremia, hypocalcemia, and hypomagnesemia. Successful management of seizure patients begins with the establishment of an accurate diagnosis of the underlying electrolyte disturbances. For that reason, complete serum chemistry, including measurements of electrolytes, especially sodium, calcium, and magnesium, should be part of the initial diagnostic workup in adult patients with seizures.

REFERENCES

1. Abbot RJ, Browning M, Davidson DLW(1980).“Serum Prolactin And Cortisol Concentrations After Grand Mal Seizures”:J Neurol Neurosurg Psychiatry;43:163-7.
2. Belton NR, Alms RE, Millichap JG(1967). “Serum prolactin & creatine phosphoinase activity in epilepsy” :Neurology;17:1073-6.
3. Chang BS, Lowenstein DH (2003). "Epilepsy":N. Engl. J. Med. 349 (13): 1257–66.
4. Collins WCJ, Lanigan O, Callaghan N(1983). “Plasma prolactin concentrations following epileptic & pseudoseizures”: J Neurol psychiatry;46:505-8.
5. Eadie, MJ (2012). "Shortcomings in the current treatment of epilepsy.":Expert Review of Neurotherapeutics 12 (12): 1419–27.
6. Frantz AG(1978).” Prolactin.” N Engl J Med;298:201-207.
7. Gennari FJ. (1998).” Hypokalemia”: New England Journal of Medicine 339:451–458.
8. Gupta MM. (1989).” Medical emergencies associated with disorders of calcium homeostasis”. Journal of Associated Physicians of India37:629–631.
9. Kline CA, Esekogwu VI, Henderson SO, Newuton KI. (1998).” Non-convulsive status epilepticus in a patient with hypocalcemia”: Journal of Emergency Medicine 16:715–718.
10. Kunze K. (2002).” Metabolic encephalopathies”. Journal of Neurology 249:1150–1159.
11. Kurlemann G, Heyen P,Menges EM(1992). “Serum prolactin after cerebral and psychogenic seizures in childhood and adolescence”:klin padiatr;204:105-4.
12. Luis Castilla-Guerra, Mar´ıa del Carmen Fern´andez-Moreno, Jos´e Manuel L´opez-Chozas,and Ricardo Fern´andez-Bola˜nos;(2006). “Electrolytes Disturbances and Seizures”: Epilepsia, 47(12):1990–1998.
13. Messing RO,Simon RP.(1986).“Seizures as manifestation of systemic disease”.NeurologyClinics4:563-584.
14. Mrowka M, Knabe S, Klinge H, Oden P, Rosenow F. (2004).”Hypocalcemic generalized seizures as manifestation of iatrogenic hypoparathyroidism months to years after thyroid surgery”. Epileptic Disorders 6:85–87.
15. P Weisleder, JA Tobin, JF Kerrigan(2002). Journal of child Neurol January; vol.17 no. 1 59-6.
16. Rajesh Padhi, Baikuntha Nath Panda, Snehalata Jagati & Subhas Chandra Patra (2014).“Hyponatremia in critically ill patients”: Indian journal of critical Care Med. 18(2): 83–87.
17. Riggs JE (2002).” Neurological manifestations of electrolyte disturbances”. Neurology Clinics 20:227–239.
18. Singh UK, Jana UK(1994).“Plasmaprolactin in epilepsy and pseudoseizures”:Indian pediatr;31:667-9.
19. Sperling MR, Wilson CL(1986). “The effects of limbic and extralimbic electrical stimulation upon prolactin secretion in humans”:Brain res.;371:293-297.
20. Torbjorn Tomson (1989). “Serum prolactin during staus epilepticus” ; journal of neurology,neurosurgery and psychiatry;52:1435-37.
21. Trimble MR(1978).”Serum prolactin in epilepsy and hysteria”, BMJ;2;1682.