

## Serum prolactin for differentiating epileptic seizures in children

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### Abstract

**Background** Serum prolactin level has been used as a marker to differentiate epileptic from non-epileptic seizures in adults. Electroencephalogram (EEG) examination is the primary diagnostic tool used to assess seizures. However, EEGs are quite difficult to perform in children and have sensitivity of only 50%-55%, with 96% specificity.

**Objective** To assess the diagnostic potential of serum prolactin level as an alternative tool for children for differentiating between epileptic and non-epileptic seizures.

**Methods** This diagnostic study was performed between January 2013 and December 2013. Thirty patients aged 3 months to 15 years with seizures and without fever who visited the Emergency Department of Arifin Ahmad Hospital, Pekanbaru, Riau, were included. Blood specimens were collected within 2 hours after seizure. Subjects underwent serum prolactin measurements and EEG examinations.

**Results** Fifteen subjects had normal EEGs and 15 subjects had abnormal EEGs. Post-ictal serum prolactin levels were significantly higher in the epileptiform EEG group. The mean serum prolactin levels were 23.78 (SD 21.86) ng/mL and 10.57 (SD 5.62) ng/mL in patients with epileptic and non-epileptic patients, respectively. Using a prolactin cut-off point of 17.2 ng/mL, serum prolactin had a 73.3% sensitivity and 93.3% specificity for differentiating between epileptic and non-epileptic seizures.

**Conclusion** Our findings suggest that serum prolactin level increases after an epileptic seizure, but not after a non-epileptic seizure. Post-ictal prolactin elevation within 2 hours may be useful in differentiating epileptic seizures from non-epileptic seizures. [Paediatr Indones. 2015;55:273-6].

**Keywords:** prolactin, EEG, epileptic seizures

Epilepsy is one of the most common neurological diseases, affecting 50 million people worldwide. It is defined as a susceptibility to recurrent seizures without precipitating factors. Epileptic seizures result from abnormal excessive or synchronous discharge in the brain.<sup>1</sup> The prevalence of active epilepsy is approximately 1%, but 8 - 10% of the population has at least one seizure during their lifetime. Worldwide, it is estimated that 10.5 million children under 15 years have active epilepsy, representing about 25% of the global epilepsy population. Of the 3.5 million people who develop epilepsy annually, 40% are younger than 15 years, and more than 80% live in developing countries.<sup>2</sup>

The sensitivity of EEG in the diagnosis of epilepsy is 50-55%, while the specificity is 96%.<sup>3</sup> Therefore, EEG in epileptics may yield results which are normal, non-pathognomonic, or inconclusive. The EEG examination is difficult to perform in children, and quite expensive.<sup>4</sup> In addition, not all hospitals or health facilities have EEG equipment and not all pediatricians have been trained to read EEGs. Therefore, we looked for cost-effective alternatives

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such as changes in serum hormones associated with seizures that affect brain function and metabolism.<sup>5</sup> Trimble was the first to show that tonic-clonic seizures increase serum prolactin, while epileptic psychogenic seizures did not.<sup>6</sup>

Studies have shown elevated prolactin (PL) levels after an epileptic seizure.<sup>7-10</sup> On the basis of these findings, elevated prolactin levels following a seizure may be used to differentiate epileptic from non-epileptic seizures. Prolactin release from the pituitary is controlled by the hypothalamus via a prolactin inhibitory factor now believed to be dopamine.<sup>6</sup> Presumably, during a generalized tonic-clonic seizure and most complex partial seizures, which originate in the temporal lobe, the spread of electrical activity from the ventromedial hypothalamus and medial temporal structures leads to release of a specific prolactin regulator into the hypophyseal portal system, and consequently an increase in prolactin.<sup>11-14</sup> Thereafter, there is a progressive decline in prolactin release because of diminished electrical discharges and depletion of prolactin storage. Therefore, elevated serum prolactin levels may be helpful in distinguishing epileptic from non-epileptic seizures.<sup>11-16</sup>

The purpose of this study was to determine the diagnostic potential of serum prolactin levels as an alternative diagnostic tool for children with seizures, in order to distinguish between seizure types, by comparing serum prolactin sensitivity and specificity to EEG results.

## Methods

This study was performed between January 2013 and December 2013. We enrolled 30 children after taking a detailed history and performing a physical examination. The patients were aged 3 months to 15 years, and all of them had seizures without fever. They visited the Emergency Department of Arifin Ahmad Teaching Hospital, Pekanbaru, Riau. Exclusion criteria were any metabolic disturbances, central nervous system infection, or consumption of drugs known to alter prolactin levels. Written informed consent was obtained from parents before enrollment and the study protocol was approved by Ethics Committee of Riau University. Subjects provided blood specimens

(2 mL) at presentation. Serum prolactin levels were quantitatively assessed by an enzyme-linked fluorescence immune assay (ELFA) method. Blood specimens were collected within 2 hours after seizure. Subjects also underwent EEG examinations which then read by neurologist. Statistical analyses were performed to assess for possible associations between variables.

## Results

Thirty patients who met the criteria for the study were included. The sample consisted of 14/30 boys and 16/30 girls. The mean age of study subjects was 48.13 (SD 40.47) months, ranging from 6 to 138 months. General seizure type was most common, in 25/30 subjects. Partial seizure type was seen in 5/30 subjects. The causes of seizures were idiopathic (26/30) or symptomatic (4/30). Abnormal neurological status was seen in 5/30 subjects, while 25/30 subjects had normal neurological status (**Table 1**).

Fifteen subjects had normal EEGs and 15 subjects had abnormal EEGs. Post-ictal serum prolactin levels were significantly higher in the epileptiform EEG group. The mean serum prolactin levels were 23.78 (SD 21.86) ng/mL in patients with epilepsy and 10.57 (SD 5.62) ng/mL in patients with non-epilepsy. Using a prolactin cut-off point of 17.2 ng/mL, serum prolactin had 73.3% sensitivity and 93.3% specificity (**Figure 1**).

**Table 2** shows that of all the subjects with epilepsy, as many as 11/15 had an increase in prolactin level. However, of the non-epileptic patients, only 1/15

**Table 1.** Characteristics of subjects

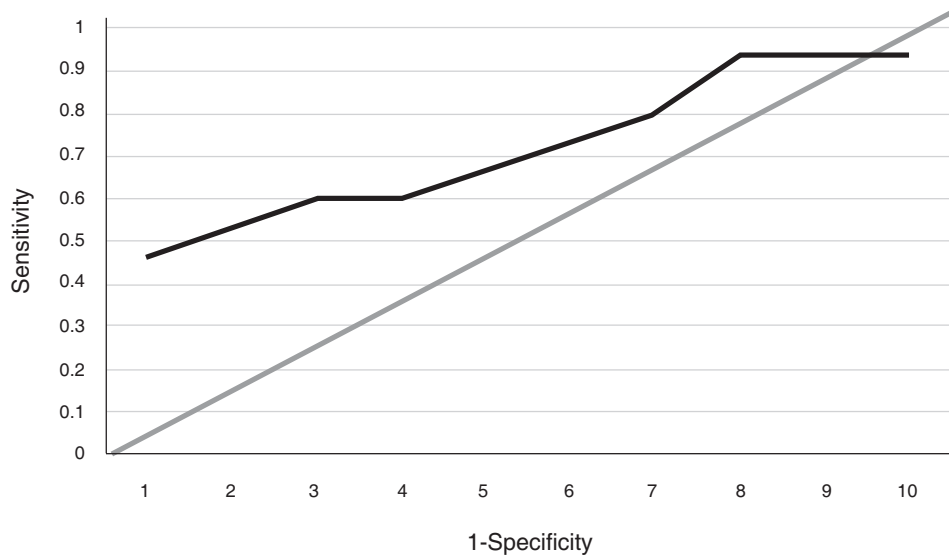
Characteristics	N=30
Mean age (SD), months	48.13 (40.47)
Median age (range), months	30.50 (6-138)
Gender, n	
Male	14
Female	16
Seizure type, n	
General	25
Partial	5
Etiology, n	
Idiopathic	26
Symptomatic	4
Neurological status, n	
Normal	25
Abnormal	5

**Table 2.** Serum prolactin results compared to EEG results

Prolactin level	EEG		P value
	Epileptiform, n (N=15)	Non-epileptiform, n (N=15)	
<17.2 ng/mL	4	14	< 0.001
≥7.2 ng/mL	11	1	

Sensitivity=0.73; specificity=0.93; positive predictive value (PPV)=0.91; negative predictive value (NPV)=0.78; positive likelihood ratio (LR+)=10.42; negative likelihood ratio (LR-) =0.29

and found increased serum prolactin post ictal.<sup>14</sup> Also Alving (1998) studied serum prolactin in subjects aged 13 to 68 years with epileptic seizure or non-epileptic seizure. Blood specimens were taken within two hours after the seizure. They found significantly increased serum prolactin in patients with epileptic seizures.<sup>15</sup> Similarly, Maccoie *et al.* studied children aged 6 months to 5 years who suffered from febrile



**Figure 1.** ROC of serum prolactin

Cut- off point : ≥ 17.2 ng/mL Sensitivity : 73.3 % Specificity : 93.3 % AUC : 78.4 % (CI:0.60-0.96)

had increased prolactin. Chi-square analysis revealed a statistically significant relationship between epilepsy and prolactin, with P value <0.001. The relationship strength parameter used was odds ratio (OR), which was 38.50 (95% CI 3.75 to 395.40) indicating that people with epilepsy may have a 38.50 times likelihood an increase in prolactin compared to non-epileptic patients with seizures. The OR value of 38.50 can also be interpreted as the probability of patients with epilepsy to have increased prolactin to be 97.5% [ $P = OR / (1 + OR)$ ].

## Discussion

Distinguishing between epileptic and non-epileptic seizures may be difficult. Our findings showed that post-ictal serum prolactin levels were significantly higher in patients with epilepsy. Ehsan *et al.* (1996) studied 50 patients with epilepsy aged 6 – 60 years

seizures and epileptic seizures and found that an increase in serum prolactin occurred in those with epileptic seizures.<sup>7</sup>

Our findings suggest that serum prolactin concentration increases after an epileptic seizure; however, it does not tend to increase after a non-epileptic seizure. Post-ictal prolactin elevation may be useful as a prognostic risk factor in children with seizures. This study demonstrates that serum prolactin had a sensitivity of 73.3%, for a cut-off point of 17.2 ng/mL.

In conclusion, examination of serum prolactin levels within two hours after a seizure can be used for screening purposes to distinguish between epileptic and non-epileptic seizures.

## Conflict of interest

None declared.

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