Serum Copeptin Level in Children with Febrile Seizures

Samir T. Abdullah, Mohamed H. Mahgoob and Alaa B. Abdelazeem.
Department of Pediatrics, El-Minia Faculty of Medicine

Abstract
Introduction: Febrile seizures occur in 2-5% of children between six months and five years of age and represent the most common convulsive event in childhood. There is a hormone released by the pituitary gland, arginine-vasopressin (AVP), has been shown to be involved in the thermoregulatory response to fever and convulsions. The C-terminal portion of the AVP precursor, copeptin, has been recognized as a robust marker of AVP secretion. Aim of the work: to evaluate the role of serum copeptin in differentiation of febrile seizures from other seizures. Patients and methods: The study was a prospective cross-sectional study, conducted on 20 patients presented with febrile seizures, 20 with epileptic seizures and 20 patients with febrile illness without seizure. Results: Our study was carried on 80 children who were classified into 4 groups; Group I: included 20 patients with FS. Group II: included 20 patients with febrile illness without seizure. Group III: included 20 patients with epileptic seizures. Group IV: included 20 apparently healthy, age and sex matched children as a normal control. They were randomly selected during the period from January 2016 to July 2016. Informed written consents were obtained from the patient's legal guardians before enrollment in the study. Discussion: Copeptin is a 39-amino acid, glycosylated peptide, and the C-terminal part of provasopressin, the precursor of arginine vasopressin (AVP), which is an antidiuretic hormone from the hypothalamus. Copeptin is secreted from pituitary gland together with AVP after hemodynamic and osmotic stimuli. Since AVP is unstable and unfit to be used as a biomarker, copeptin instead used in the place of AVP because of its molecular stability, easier testing methods and faster results. Recommendation: The measurement of serum copeptin is better suited for the diagnosis of FS. Future studies.

Keywords: Serum Copeptin, Febrile Seizures,

Introduction
Febrile seizures (FS) occur in 2-5% of children between six months and five years of age and represent the most common convulsive event in childhood (Fetveit., 2008).

There is a hormone released by the pituitary gland, arginine-vasopressin (AVP), has been shown to be involved in the thermoregulatory response to fever and convulsions (Ohno et al., 2012). The C-terminal portion of the AVP precursor, copeptin, has been recognized as a robust marker of AVP secretion (Nickel et al., 2012).

Aim of The work
To evaluate the role of serum copeptin in differentiation of febrile seizures from other seizures.

Patients and methods
This is a prospective cross-sectional study that included 20 patients presented with febrile seizures (FS) and 20 others with epileptic seizures collected from pediatric emergency department, Children and maternity university hospital, Minia University. They were randomly selected during the period from January 2016 to July 2016. Informed written consents were obtained from the patient's legal guardians before enrollment in the study.

The kit assay Human CPP level in the sample, use Purified Human CPP antibody to coat microtiter plate wells, make solid-phase antibody, then add CPP to wells, Combined CPP antibody which With enzyme labeled,

become antibody - antigen - enzyme-antibody
complex, after washing completely. Add substrate, substrate becomes blue color. At HRP enzyme-catalyzed, reaction is terminated by the addition of a sulphuric acid solution and the color change is measured spectrophotometrically at a wavelength of 450 nm. The concentration of CPP in the samples is then determined by comparing the O.D. of the samples to the standard curve.

Results

Table (1): Comparison of studied laboratory data between four groups.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Febrile seizures group</th>
<th>Febrile without seizures group</th>
<th>Epileptic group</th>
<th>Control group</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HB (g/dl)</td>
<td>10.7 ± 1.3</td>
<td>11.04 ± 0.9</td>
<td>11.1 ± 1</td>
<td>10.9 ± 1.1</td>
<td>0.5</td>
</tr>
<tr>
<td>TLCX Mean±SD</td>
<td>14.5 ± 1.6</td>
<td>14.7 ± 1.4</td>
<td>6.3 ± 1.2</td>
<td>6.1 ± 1.1</td>
<td>0.7 0.001*</td>
</tr>
<tr>
<td>RBG (mg/dl) Mean±SD</td>
<td>77.9 ± 6.6</td>
<td>79.2 ± 5.7</td>
<td>78.9 ± 6.4</td>
<td>79.7 ± 5.8</td>
<td>0.8 0.001*</td>
</tr>
<tr>
<td>CRP (mg/l) Mean±SD</td>
<td>15.6 ± 5.6</td>
<td>14.4 ± 7.7</td>
<td>3 ± 1.5</td>
<td>1.8 ± 5.9</td>
<td>0.6 0.001*</td>
</tr>
<tr>
<td>Na (mg/l) Mean±SD</td>
<td>139.9 ± 3.8</td>
<td>139.5 ± 4.2</td>
<td>139.2 ± 4.2</td>
<td>138.7 ± 4.6</td>
<td>0.6 0.001*</td>
</tr>
<tr>
<td>Ca (mg/l) Mean±SD</td>
<td>9.8 ± 0.9</td>
<td>9.9 ± 0.7</td>
<td>10 ± 0.9</td>
<td>10 ± 0.6</td>
<td>0.2 0.001*</td>
</tr>
<tr>
<td>Serum prolactin (mg/l)</td>
<td>32.5 ± 13.8</td>
<td>13.7 ± 4.1</td>
<td>38.6 ± 4.4</td>
<td>13.5 ± 4.5</td>
<td>0.001* 0.07</td>
</tr>
<tr>
<td>Serum Copeptin (mg/l)</td>
<td>613 ± 164.5</td>
<td>177 ± 119.7</td>
<td>569 ± 120.5</td>
<td>168 ± 61.3</td>
<td>0.001* 0.6</td>
</tr>
</tbody>
</table>

* significant. One way ANOVA test and post-hoc CRP=C-reactive protein, TLC=total leucocytic count, RBG = random blood glucose, Na=corrected sodium, Ca=semin calcium, HB=haemoglobin in blood.

This table shows statistically significant higher CRP and TLC levels in febrile seizure and febrile without seizure groups than in epileptic seizure and control groups. Also statistically significant higher copeptin and prolactin levels in febrile seizure and epileptic groups than in febrile without seizure and control groups.

Discussion

Febrile seizure occurs in a child between the age 6 months and 5 years during an episode of fever, it affects 2% to 5% of children and recurs in 30% (Offringa et al., 2017).

There was significant correlation between serum copeptin level with time elapsed since the episode of febrile seizures (r=-0.91, p=0.001). This was in accordance with the study of Stocklin et al., 2015., who found that, it was an inverse significant correlation between serum copeptin level with time elapsed since the episode of FS. This may be explained by
that, the half-life of copeptin in the peripheral blood is approximately 45-60 min (L’Abate et al., 2013).

The ROC curve analysis of serum copeptin and prolactin for prediction of FS showed that serum copeptin had 97% sensitivity & 70% specificity at a cut-off point >304 pg/ml, while serum prolactin had 90% sensitivity & 60% specificity at a cut-off point >20.8 ng/ml for prediction of febrile seizure episode. So copeptin exhibited an increased overall ability to differentiate between children with FS and controls compared to prolactin (AUC 0.853, 97% vs. 0.757, 90%; p <0.001).

**Recommendation**
The measurement of serum copeptin is better suited for the diagnosis of FS. Future studies, large and wide scale study on a large population with FS to find statistically differences among the simple and complex FS groups with serum copeptin. Further study to compare epileptic & pseudo seizures for the use of copeptin to differentiate in between.

**References**
3. Alehan F, Erol I, Cemil T, Bayraktar N, Ogus E and Tokel K.