RESEARCH ARTICLE

LEVELS' INFLUENCE OF IFN-γ AND IL-10 IN CHILDREN WITH EPILEPTICUS STATUS

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ABSTRACT

Background. Seizures are a common clinical manifestation in the emergency room. Nearly 5% of children aged under 16 years. Seizures are important as a sign of neurological disorders. Members of interferon are widely studied with seizures and epileptogenesis is interferon-γ. In a study by Choi in 2011, a study of seizures in humans showed that the condition of status epilepticus increased levels of interferon-γ which is quite high compared to patients not status epilepticus seizures. In response to the aftermath of the seizure, Interferon-γ system induces the formation of IL-10 acts as an anti-inflammatory agent that aims to put an end to the action of Interferon-γ.

Objective. To know role of Interferon-γ and IL-10 in children with status epilepticus.

Methods. This research using cross sectional design with recruiting 30 study sample consisted of 15 children in the seizure group SE and 15 children in the group without SE seizures. Measured levels of IFN-γ and interleukin-10 by ELISA. Results were analyzed with the Mann-Whitney and corelation Spearman to see the relationship levels of IFN-γ and IL-10 in children with status epilepticus with SPSS-23.

Results. The results showed significant differences between groups SE and convulsive seizures non SE ;IL-10 (p = 0.000) and IFN-γ (p = 000).

Conclusion. There are significant correlation between the levels of IFN-γ and IL-10 with status epilepticus.

Keywords: Levels of IFN-γ and IL-10, Child, status epilepticus

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INTRODUCTION

Status epilepticus is a seizure that lasts longer, generally more than 30 minutes. Status epilepticus in children is a life-threatening urgency with the risk of neurological sequelae. The longer the seizure lasts, the more difficult to stop it, the greater the complications that can occur. Therefore, the treatment of generalized seizures are more than 5 minutes is to stop the seizures and preventing seizure that lasts a long time or status epilepticus.[1,2] The incidence of SE in children ranges from 10-58 per 100,000 per year in children aged 1-19 years or about 31,600 children under the age of 18 years in the United States per year. Higher incidence has been reported in infants aged less than 1 year ranged -156 135.2 per 100,000 infants per year. Annual incidence of SE in children in developing countries about 20 per 100,000 populations per year.[3] Various conditions of trauma to the brain, such as Neurotrauma, infection, and perinatal injury, can trigger inflammation in the brain. These conditions are risk factors for the development of seizures, and can initiate a cascade of chronic inflammatory process in the central nervous system.The immune system is actually designed to protect the host from external and internal threats. Cytokines are generally synthesized and secreted in response to the presence of antigen stimuli. End this abnormal cytokine expression has been observed in patients with seizures and experimental animals with seizures. Some research suggests that the production and release of cytokines is regulated by the immune system and these cytokines may improve brain damage when acting as a mediator seizures.[6] the immune system is actually designed to protect the host from external and internal threats. Cytokines are generally synthesized and secreted in response to the presence of antigen stimuli. End this abnormal cytokine expression has been observed in patients with seizures and experimental animals with seizures. Some research suggests that the production and release of cytokines is regulated by the immune system and these cytokines may improve brain damage when acting as the mediator seizures. Members of the interferon are widely studied with seizures and epileptogenesis is interferon-γ. In the study by Choi in 2011, a study of seizures in humans showed that the condition of status epilepticus increased levels of interferon-γ which is quite high compared to patients not status epilepticus

seizures. As a response after the seizure, the system Interferon-γ induces the formation of IL-10 which act as anti-inflammatory agents that aims to put an end to the action of interferon-γ, a lot of research has been done to look at the relationship between seizures with both interleukin above, but with disciplined research varies.[7]

The condition of status epilepticus is a state of emergency due to the seizure of time can cause a variety of short-term risks and long-term adverse, even dangerous. A predictor or a specific biomarker capable of predicting the risk of seizures prolonged or repeat seizures in children who suffer from seizures may be a diagnostic tool that helps. The balance between the levels of interferon-γ and IL-10 is said to be important in the onset of seizures. High levels of interferon-γ and low levels of IL-10 have an impact on the more risky the child has seizures were longer, or recurrent seizures.[8,9]

Research in Indonesia about the role of IL-10 in the previous seizures conducted by Andi et al. in 2013 that showed decreased levels of IL-10 in patients with febrile seizures compared to controls. But they have never been no research on Interferon-γ on the status epilepticus seizures in Indonesia. Therefore, this study was conducted as one study that aims to see an increase in interferon-γ levels in pediatric patients with convulsive status epilepticus.This aim fo this study to know correlation of IL-10 and IFN-γ with status epilepticus in children.

METHODS

Research design

The design of this study was observational analytic cross sectional connect status epileptius with high levels of IFN-γ and IL-10 in children. This study will be conducted in the Department of Pediatrics Saiful Anwar Hospital and Laboratory of Physiology Faculty of Medicine, Brawijaya University.

The samples are blood samples of pediatric patients who have seizures that come in the Intensive Care Unit (ICU) and treated in the Department of Pediatrics Hospital Saiful Anwar Malang. The inclusion criteria for cases of status epilepticus, patients had seizures for 30 minutes or more, or have two or more periods of seizure and between 2 seizures unconscious patient. Examination laboratory: patients willing to be involved in this study with informed concent of

parents, exclusion criteria: patients with severe malnutrition, patients with malignancies, patients with autoimmune diseases, patients' age more than 14 years. Exclusion criteria of patients with malnutrition, patients with malignancy, autoimmune disease patient, patient's age over 14 years. Definition of status epilepticus that is still widely used researchers and clinicians is the definition according to the International League Against Epilepsy, published in 1981, the seizure of more than 30 minutes or two or more seizures in whom seizure patients fail to recover consciousness.

Obtained results of investigations support. In the data levels of IFN-ᵞ and IL-10 normality test (to determine the distribution of normal data or not) by using the Kolmogorov-Smirnov test and variant (to determine the variant data is the same or not). If the distribution of normal data and variants of the same data, then used the unpaired t-test to determine differences in the mean levels of IFN-ᵞ and IL-10 between groups. If you do not qualify (data not normally distributed) done first data transformation. If the new variable transformed normal distribution, then used unpaired t-test. If the new variable transformation result is not normal, the Mann-Whitney test was used to determine differences in IFN-ᵞ and IL-10 between groups. Data were analyzed using a 95% confidence level ($\alpha = 0.05$). The entire technical computerized data processing were analyzed using statistical software product and service solution 23 (SPSS 23). Rated significant if $p < \alpha$. If there are differences continued with subsequent statistical test for Spearman correlation test for abnormal distributed data and Pearson correlation for normally distributed data. This study meaningfully when the value of $p < 0.05$. The entire technical computerized data processing were analyzed using statistical software product and service solution 23 PS (23 PS SPSS).

RESULTS

This study used cross sectional design by recruiting 30 study sample consisted of 15 children in the group seizure with SE and 15 children in the group seizure without SE. Here are the basic characteristics of the study sample. From the characteristics of the study shows that the levels of hemoglobin found significant differences between the two groups of seizure with SE and non SE ($p = 0.048$), whereas for age ($p = 0.172$), gender ($p =$

0.223), leukocytes ($p = 0.182$), RDW ($p = 0.163$) were not significant with $p > 0.05$. The results of data analysis of Spearman correlation test showed that there is a significant correlation between status epilepticus with levels of IFN-γ with $p = 0.000$ as well as the levels of IL -10 with $p = 0.000$.

Table 1. Characeristic of the subject

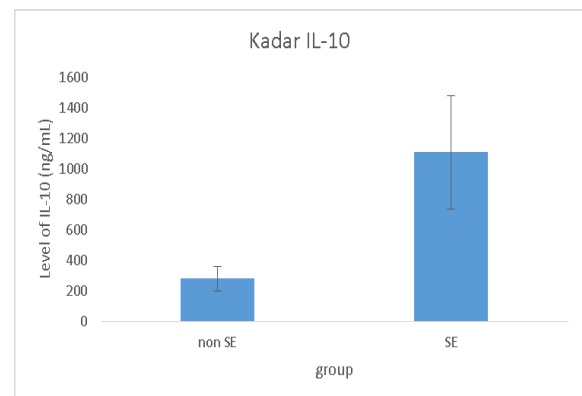| Characteristic of sample	Seizure with SE group (n=15)	Seizure without SE group (n=15)
Age(month), x±SD	23,25±9,4	234,7 ±11,4
Sex		
• Male, n	7 (7/15)	7 (7/15)
• Female, n	8 (8/15)	8 (8/15)
Hemoglobin, x±SD	9,2±2,8	11,5±1,2
leukocyte, x±SD	13622,2±7317,8	9318,9±1759,2
RDW, x±SD	14,0±0,68	13,4±1,04

Figure 1. There are significant correlations between status epilepticus with increased levels of IL-10
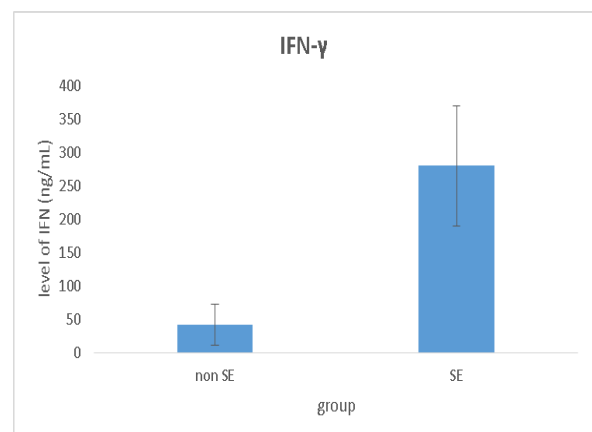

Figure 2. There are significant correlations between status epilepticus with levels of IFN-γ

DISCUSSION

The study involved 30 study sample consisted of 15 samples of the studies included in the group of children with seizure with SE sample with children seizure without SE. This research was observational analytic with cross sectional study design with sampling consecutive sampling. On the characteristics of the study, sample obtained characteristic differences between the two groups, namely the Hb level. Consistent with previous studies, seizures in children with mild anemia obtained with average levels hb: 10.[9, 10]

Gender respondents in this study included 16 girls and 20 boys. This is in contrast to some previous research, including a study by Fita et al in the group of SE survey respondents mostly women, as much as 9/15 of research subjects. While the non SE group of male respondents earned more than women that is 8/15 of respondents. [11]

The average age of patients with status epilepticus is ((2 years 10 months). From the literature show that cases, primarily affects children aged <3 years, with a peak incidence at the age of 6-18 months. This is similar to a previous study by Fita et al that showed an average of 28.65 months. Seizures are said to be more common in the age of 17-34 months. Various studies have also shown that the incidence of seizures occurred at an early age compared to older age. At the early age of life when brain development is still in the developmental window, if there is a traumatic insult to the brain may have a higher risk for seizures caused by their complications. [5,11]It is similar to studies in children conducted by Choi, and he mentioned increased serum IFN-γ levels in children seizure with SE (p = 0.00) . [5]In the mean difference test between the levels of IL-10 were also significant differences (p< 0.00). This is similar to Choi research that says that IL-10 serum levels in pediatric patients with SE were not significantly different than control (Choi et al., 2011). However, it is different with the results of Sinha. The researchers said the relationship between serum levels of IL-10 and SE incidence in adult epilepsy patients (Sinha et al., 2008). As a result, a high value in the group without SE seizures is caused by the same cause. Although the results of this study are similar to the results of research only in children with SE, still need further research to determine the role of IL-10 in children in experimental animals many of which suggested a

link between the two.Evaluation of the number of leukocytes in the blood of study subjects showed higher results in the group of patients with SE (13 622 uL) compared with the group of patients with non SE (9318 / uL). This is similar to research by Fita the number of leukocytes 13 784 / ul, while in seizure with SE 13 551 / ul.[11]The calculation of the levels of IFN-γ in the group of patients with status epilepticus showed higher results than the group nonSE. The results showed IFN-γ was higher in seizure with SE (280.18 ng / mL) compared with seizure nonSE group (42.01 ng / mL), this result was statistically significant with p = 0.000, actually in both study groups.

CONCLUSSION

There was significant correlation the levels of IL-10 and IFN-γ in children with status epilepticus. Necessary better research methods, especially in the control of confounding factors through the inclusion criteria of exclusion, or statistical matching techniques. Further research is needed that connects SE with other cytokines to prove the role of inflammation in the pathophysiology of SE in children. Researching other cytokines that affect the status epilepticus which may be a confounding factor.

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