

ABSTRACT

CORRELATION BETWEEN TUMOR NECROSIS FACTOR- α (TNF- α) LEVELS AS A PREDICTOR AND LIVER ENZYMES AS PARAMETERS OF DRUG INDUCED LIVER INJURY (DILI) ON EPILEPTIC PATIENS TAKING PHENYTOIN MONOTHERAPY

**(Study Conducted at Neurology Outpatient Unit
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Background – The widely used phenytoin anti-epileptic drug may cause rare but fatal side effects such as drug induced liver injury (DILI). Phenytoin can cause dili through the mechanism of formation of phenytoin reactive metabolites followed by covalent bonds that can be associated with idiosyncratic reactions through activation of the immune response, including involving inflammatory cytokines such as TNF- α levels.

Objective – The aim of this study was to analyze the correlation between TNF- α levels as a predictor and ALP & ALT levels as parameter of DILI in patient using phenytoin monotherapy as anti epileptic drug.

Method – This observational study was approved by the Ethics Committee of Dr Soetomo Teaching Hospital. Blood samples were obtained from patients who visit Neurology Outpatient Unit from June to July 2018 and TNF- α , ALP, and ALT levels were assessed by using ELISA. The correlation between TNF- α , ALP, and ALT were analyzed using Spearman test as it was non parametric data.

Result – 39 patients were included in this study. There is no correlation between increase in level of TNF- α with increase in level of ALT, ALP, and ALT/ALP ratio, indicated by $p= 0.757, 0.933, \text{ dan } 0.829$, respectively. However, if it is differentiated based on length of use, the results showed that there was a significant correlation between increase in level of TNF- α with increase in level of ALP and ALT/ALP ratio tested by Spearman's non-parametric statistical test with $p=0.007$ and 0.036 . There is significant effect of phenytoin use on decrease of seizure intensity and duration before and after phenytoin monotherapy ($p=0.001$).

Conclusion – There was no significant correlation between TNF- α serum levels with serum levels of ALP, ALT, and ALT/ALP ratio. The use of phenytoin as antiepileptic drug is effective to reduce the seizure intensity and duration and there was no DILI incident recorded in epileptic patient using phenytoin in this research.

Keywords: *epilepsy, phenytoin, monotherapy, adverse effects, drug induced liver injury, TNF- α , ALP, ALT*