

## Letter to Editor

# Role of Toll Like Receptor Antagonist in Prevention of AKI Induced Neuro-Inflammation

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Ischemic acute kidney injury (AKI) has many consequences that affect the development of chronic kidney disease, following ischemia kidney; tissues are exposed to a reperfusion phase, where damage is caused by inflammatory mediators released following resolution of the ischemia. Accentuation of innate immunity during ischemia reperfusion injury (IRI) seem to be affected by toll like receptors, especially TLR-2 and TLR4 (white et al)

It has been demonstrated that AKI induced effects extends beyond kidneys and affects many systems including the brain where it has been associated with encephalopathy (white et al). Animal experiments have shown that AKI leads to inflammatory within the hippocampal region (Davenport et al) which was confirmed by (liu et al) who observed an increased number of activated microglia in the hippocampus of rats with AKI, which may account for a state of uremic encephalopathy.

In a previous study at Medical experimental research center (MERC). mohamedsalama et al found that TLR-4 was up regulated in AKI group compared to the sham group as evident by increase the density of TLR-4 in the hippocampus and striatum in parallel to increase in microglia in the same regions as previously reported by liu et al. The findings confirm the triggering effect of TLR-4 on AKI induced neuro-inflammation that possibly lead to AKI induced encephalopathy.

Eritoran is a second generation structural of a lipid A portion of LPS. In vivo and in vitro models, eritoran has been shown to be a potent antagonist of the biochemical and physiological effects of LPS

by blocking the translocation of TNF-B which results in decrease the expression of inflammatory cytokines Mullarkey M et al. It has been shown to be safe in humans wong YN et al. currently undergoing clinical development as a possible therapeutic agent for treatment of sepsis and for myocardial protection during coronary artery by bypass grafting.

We are trying to study the effect of TLR-4 blocking in preven on of AKI induced brain inflamma on in ischemic rat. by using 50 µL of eritoran (5mg/kg dissolved in vehicle) or vehicle intravenously alone 10 minutes before undergoing surgery to rats. Which are 20 and will be assigned to 2 groups 1- sham control (SH) with vehicle 2- AKI module where experimental (IRI) will be induced plus Eritoran. Then all rats will be scored by blinded investigator to evaluate the behavioral performance using open field activity, horizontal grid tests.

After scarification, the brain will be removed, dissected longitudinally and the right side will be xed in formalin prior to the following studies: 1- pyknotic neural cell counts H&E under light microscope for Hippocampus, SVZ and olfactory bulb 2- Microglial cell count after immunostainig for an iba 1 an bodies (represent ng microglial cells). The three previous areas will be counted using Image J analyzer. 3-TLR-4 immunostaining of the previous three sites and photomicrographs will be counted then analyzed regarding density of TLR-4 stained areas.

Descriptive statistics will be used to summarize variables for descriptive purposes and data will be tabulated and exposed to suitable statistical analysis tests.

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