SEIZURE DURATION AND BRAIN PATHOLOGY FOLLOWING EXPOSURE TO THE NERVE GAS-SARIN: THE EFFECT OF ANTI-INFLAMMATORY TREATMENTS

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Sarin, an organophosphate (OP) nerve agent inhibits acetylcholinesterase and causes upon exposure a cholinergic crisis that includes tremors, hyper-salivation, seizures, and if not treated promptly death. Cholinergic overstimulation, a well-established model for seizures, is commonly used to screen promising drugs. We have previously shown that seizures following sarin cause an inflammatory state in the brain characterized by prolonged elevation in the level of the inflammatory markers PGE_2, IL1-β, IL-6 and TNF-α followed by specific brain pathology. In the present study we measured the effect of various anti-inflammatory drugs on the duration of seizures, the level of inflammatory markers and brain pathology following sarin exposure. Rats were pretreated with the carbamate pyridostigmine and the oxime HI-6 to ensure survival and 20 minutes later were exposed to sarin followed by atropine sulfate 1 minute later. All animals developed acute seizures that lasted up to several hours. Anti-inflammatory drugs were screened as neuro-protectants in two paradigms: early 5-30 minutes and late, starting at 4 hours and administered twice daily for 48h. Ibuprofen, minocycline, dexamethasone and methylprednisolone enhanced the seizure intensity and the ensuing brain injury when administered immediately following sarin. Late anti-inflammatory treatments had no demonstrable beneficial effect on the extent of the brain damage some of the drugs had partial effect in reducing the levels of inflammatory markers. It is suggested that the elevation in the levels of inflammatory markers following seizures has a beneficial effect in the resolution of the seizures and the attenuation of the brain damage.