Anticonvulsant Effectiveness of Scopolamine Against Soman-Induced Seizures in African Green Monkeys

John McDonough, U.S. Army Medical Research Institute of Chemical Defense
Joseph McMonagle, US Army Medical Research Institute of Chemical Defense
Benedict Capacio, US Army Medical Research Institute of Chemical Defense

Prolonged epileptic seizures are a hallmark feature of intoxication with highly toxic anticholinesterase nerve agents such as soman. Benzodiazepine drugs like diazepam or midazolam are typically used to control these seizures. However, studies in both rats and guinea pigs have shown that potent, centrally acting anticholinergic drugs such as scopolamine can also terminate such seizures. The present study was performed to determine if scopolamine could produce similar anticonvulsant effects in a nonhuman primate model of soman intoxication. Adult male African green monkeys, implanted with telemetry devices to record cortical electroencephalographic activity, were pretreated with pyridostigmine (0.02 mg/kg; IM) and 40 min later challenged with 15 ug/kg (IM) of the nerve agent soman. One min after soman exposure the animals were treated with atropine (0.4 mg/kg; IM) and the oxime 2-PAM (25.7 mg/kg; IM). One min after the start of seizure activity the animals were administered scopolamine (0.01 – 0.1 mg/kg; IM), using an up-down dosing design over successive animals. Scopolamine was highly effective in stopping soman-induced seizures under these conditions with an ED50 = 0.033 mg/kg (0.019 – 0.056 mg/kg = 95% confidence limits). Seizure control was rapid, with all epileptiform activity stopping on average 20.7 min after scopolamine treatment. A separate PK study showed that absorption of scopolamine peaked at approximately 10 min after IM administration and a dose of 0.032 mg/kg produced maximum plasma levels of 16.9 ng/ml. The results show that scopolamine exerts potent and rapid anticonvulsant action against soman-induced seizures and that it may serve as a valuable adjunct to current antidote treatments for nerve agent intoxication.