INHIBITION OF CHOLINESTERASES FOLLOWING PERCUTANEOUS INTOXICATION WITH V AGENTS IN RATS

*Jiri Bajgar 1,2, Kamil Kuca 1,2,3, Jiri Kassa 3

1 Department of Chemistry, Faculty of Science, University of Hradec Kralove, Hradec Kralove, Czech Republic
2 Biomedical Research Center, University Hospital Hradec Kralove, Hradec Kralove, Czech Republic
3 Department of Toxicology and Military Pharmacy, Faculty of Military Health Sciences, University of Defence, Hradec Kralove, Czech Republic

Female Wistar rats were percutaneously (p.c.) intoxicated (1×LD₅₀) with VX and its two derivatives differing in their substitution on nitrogen (diethyl- and dibutyl- derivatives). Blood cholinesterase activity was continuously monitored; 100 min after the intoxication (or after death), acetylcholinesterase (AChE) activity was determined in diaphragm and brain parts (pontomedullar area - PM, frontal cortex - FC and basal ganglia – BG). Blood ChE activity remains unchanged at very short interval (5 min) after VX administration; this interval was prolonged for diethyl- and dibutyl derivatives. AChE activity was decreased to 20-30% of control values in diaphragm, then in FC (60-70%) and PM (54-74%). AChE activity in BG was relatively resistant (cca 80%). When the AChE activity was compared for all three agents in relationship to survival (11 animals) or death (7 animals), significant differences between the activities in survived (32%) and died (13%) rats were demonstrated in diaphragm but not in the blood. This tendency (higher AChE activity in survived animals) was also observed in PM and FC, however, not statistically significant. It is concluded that substitution on nitrogen atom probably influences penetration through the skin; the rest of agent molecule (phosphorus head) probably influences AChE inhibition. As hypothesis, AChE activity in diaphragm could be important for survival or death in case of p.c. intoxication with these types of V agents.

Keywords: VX; derivatives; blood; rat; diaphragm; brain parts; acetylcholinesterase; percutaneous intoxication