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Lipid peroxidation and reactive neuroinflammation during the acute phase of methanol poisoning

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Objective: During the Czech Republic methanol mass poisoning outbreak, we measured the acute concentrations of lipid oxidative damage markers and leukotrienes in blood serum of the patients with confirmed methanol poisoning.

Methods: The acute concentrations of 4-hydroxy-trans-2-hexenal (HHE), 4-hydroxynonenal (HNE), malondialdehyde (MDA), and leukotrienes LTB4, LTC4, LTD4, LTE4 were measured by liquid chromatography-electrospray ionization-tandem mass spectrometry in blood serum of 28 patients admitted with acute methanol poisoning and in 36 survivors two years after discharge.

Results: The maximum acute serum concentrations of all three measured markers of lipid oxidative damage were significantly higher than the follow-up serum concentrations measured two years after discharge: HHE 40.1±6.7ng/ml versus 17.7±4.1ng/ml; $p<0.001$; HNE 71.7±8.0ng/ml versus 35.4±2.3ng/ml; $p<0.001$; MDA 80.0±7.2ng/ml versus 40.9±1.9ng/ml; $p<0.001$. The peaks of acute concentrations of HHE, HNE, MDA were registered on the days 3-4 after admission. In the survivors without visual and CNS sequelae of methanol poisoning, acute serum concentrations of lipid oxidative damage markers were higher than in the patients who survived with health sequelae of poisoning: HHE 44.6±7.6ng/ml versus 31.0±12.0ng/ml; HNE 78.6±9.9ng/ml versus 60.0± 13.0ng/ml; MDA 88.6±9.1ng/ml versus 69.0± 13.0ng/ml; all $p<0.05$. There was a correlation between the concentrations of markers of lipid oxidation damage and the concentrations of the measured leukotrienes: HHE correlated with LTC4 (r=0.713), LTD4 (r=0.676), LTE4 (r=0.819), LTB4 (r=0.746). HNE correlated with LTC4 (r=0.663), LTD4 (r=0.608), LTE4 (r=0.771), LTB4 (r=0.717), MDA correlated with LTC4 (r=0.785), LTD4 (r=0.735), LTE4 (r=0.814), LTB4 (r=0.674); all $p\leq0.001$. Lipid peroxidation markers correlated with anion gap (r=-0.388, -0.428, -0.334; p=0.045, 0.026, 0.080 for HHE, HNE, MDA, correspondingly). The follow-up serum concentrations of lipid oxidation markers in the survivors with and without visual/CNS sequelae of poisoning measured two years after discharge did not differ. We did not register persisting elevation of serum concentrations of measured biomarkers in the group of survivors of acute methanol poisoning two years after discharge.

Conclusion: The results of our research demonstrate that lipid oxidative damage plays a significant role in the mechanisms of toxic brain damage in acute methanol poisoning. The concentrations of all three measured biomarkers were elevated comparing to the follow-up concentrations in the survivors two years after discharge. Neuronal membranes lipid oxidation with leukotriene-mediated neuroinflammation in acute methanol poisoning appears to be a part of the neuroprotective mechanisms preventing the damage caused by direct cytotoxic effect of formic acid. The elevation of lipid oxidation markers was moderate, adaptive, and transient. No cases of persistent elevation have been registered in the survivors two years after discharge.