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Is Oxidative Stress in Acute Organophosphorus Insecticide Poisoning Pathological?: A Systematic Review of the Evidence

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OBJECTIVES: To determine whether there is consistent human evidence of oxidative stress in acute organophosphorus insecticide self-poisoning; whether animal evidence suggests a causative role for oxidative stress; and whether there are human data showing benefit from antioxidant treatment.

METHODS: We conducted a systematic review using the PubMed, EMBASE and MEDLINE databases, and the Cochrane Database of Systematic reviews, based upon the following search terms: 'organophosphate poisoning', 'oxidative stress' and 'antioxidant'. Articles related to chronic organophosphorus poisoning, use of medicines without antioxidant benefits, or subjects other than oxidative stress were excluded. The search returned 256 results of which 18 studies were considered relevant.

RESULTS: Observational human studies: All eleven human studies reported the presence of oxidative damage to lipids and proteins. Eight of nine studies reported variable increases in a weak marker of lipid peroxidation, malondialdehyde.

ANTIOXIDANT INTERVENTION STUDIES IN ANIMALS: After treatment with an antioxidant, all five studies showed an improvement in either markers of oxidative damage or antioxidant activity. One high quality mouse study showed that administration of acetylcysteine 200mg/kg reduced malondialdehyde by 35% and increased survival rates by more than 60%.

ANTIOXIDANT INTERVENTION STUDIES IN HUMANS: Two small randomized controlled trials found that using acetylcysteine as an adjunct to standard treatment reduced atropine requirements by 77% and 55% but did not affect clinically relevant outcomes.

CONCLUSIONS: The two human clinical studies were too small to provide any clear evidence to support the use of acetylcysteine in organophosphorous poisoning. Acetylcysteine appeared to be beneficial in animal studies, but this could be mediated via increased synthesis of the endogenous detoxifying agent, glutathione, rather than through a direct antioxidant effect. Further research into mechanisms of oxidative stress in acute organophosphorus poisoning, combined with large unambiguous clinical trials of antioxidants, are required before they can be used routinely in treatment.