

Controversies in paraquat poisoning

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Paraquat is just one of many poisons whose toxicity is due largely to production of free radicals or oxidative stress. It is notorious due to the frequency with which it is taken around the world and its high lethality ($\approx 70\%$) after oral ingestion. Tens of thousand of patients die each year and it is the leading single cause of suicide in a number of countries. There have been many animal studies on the mechanism of toxicity and methods to ameliorate the toxicity. Many animal studies are of unclear relevance to the treatment of humans (due to interspecies metabolic differences, or the timing or doses of poison or antidote). Largely this evidence has not been replicated in humans, leading to much of the approach being based on strongly held opinions rather than hard evidence. If there was more evidence, there would be less controversies.

The key area where there is clinical disagreement is the merits of treatments such as haemoperfusion/dialysis, immunosuppressants, and anti-oxidants. This is compounded by some weakness in the data on biomarkers and kinetics, and the limited extent to which these have been used to support small underpowered studies looking at clinical endpoints. Often these small studies show implausibly large benefits with poor or no documentation of exposure and no clinical evidence of a mechanism by which such impressive effects might be obtained. For example, in the typical clinical setting of acute paraquat poisoning occurring 3 to 4 hours previously, evidence is largely lacking that haemoperfusion leads to a significant enhancement of elimination, or that antioxidants substantially decrease free radical production or that immunosuppressants dramatically reduce inflammation.

Finally there is much controversy (political more than scientific) about the extent to which regulatory and formulation changes could and should be used to reduce lethal poisoning. Unfortunately, there is also insufficient research in this field to inform the debate.

A combination of strategies will be required to have a substantial decline in the deaths from paraquat poisoning. This will need to include strategies that reduce all self-poisonings, reducing access to paraquat except when required (safe storage), reducing the strength of paraquat, reformulation to reduce oral absorption, better assessment of risk and greatly improved treatment.