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Cardiovascular and core temperature responses to acute organophosphate intoxication in rats

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Abstract

Introduction

Organophosphates (OP) are cholinesterase inhibitors that are used as pesticides in agriculture and as nerve agents in chemical warfare. Surprisingly, we have limited information on the time course of cardiovascular responses to acute OP intoxication at doses that cause cholinergic crisis in humans. OP-induced QT prolongation has been shown to lead to fatal ventricular arrhythmia and delayed death, however, not all cardiac failures are associated with QT prolongation.

Methods

Rats were implanted with a BP/ECG telemetry device and 14 d later, acutely intoxicated with the OP diisopropylfluorophosphate (DFP, 4 mg/kg, sc) followed 1 min later by atropine sulfate (2 mg/kg, im) and pralidoxime (25 mg/kg, im) to block peripheral cholinergic toxicity. BP/ECG data were grouped based on the rat's survival time: <15 min (n=11, group A), >15 min and <17 hours (n=9, group B), and >17 hours (n=4, group C).

Results

In conscious, freely moving rats, DFP injection significantly increased BP (+87±10 mmHg), HR (+177±32 bpm), core temperature (+4.0±0.7 °C), and occurrences of premature ventricular complexes (PVC). These increases were similar in all three groups. Around the peak pressor response, group A had abrupt drops in BP and HR (cardiovascular collapse) that was triggered by supra-ventricular events (sinus bradycardia and/or AV blocks). A similar pattern of cardiovascular collapse was observed in group B, hours after DFP injections. Furthermore, after the initial pressor response, half of the rats in group B had significant lower pulse pressure and BP despite a maintained HR.

Conclusion

Our data suggest that DFP-induced cardiovascular collapse may be centrally mediated and that compromised cardiac function may also contribute to the cardiovascular collapse in delayed death.