Reversal of Bupivacaine-Induced Cardiotoxicity in Daphnia magna With Intralipid

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Local anesthetics are used to temporarily block nerves from transmitting pain signals during invasive medical procedures. Complications can arise when large doses are inadvertently administered intravenously causing local anesthetic systemic toxicity (LAST). LAST can cause seizures and cardiovascular collapse. Intralipids have been used to counter the effects of LAST in humans, however optimal timing is unknown. Intralipid is a fat emulsion composed of soybean oil and phospholipids. This project investigates the pharmacodynamics of bupivacaine on Daphnia magna. Daphnia are translucent organisms with an observable beating heart that can be counted under the microscope. Bupivacaine and Intralipid were titrated to study their effects on heart rate. Increasing concentrations of bupivacaine had an inverse dose-dependent effect; an EC50 of 0.045% at 10-minutes was calculated. There was no major difference in heart rate in Daphnia treated with Intralipid. In rescue trials, a 60:1 molar ratio of Intralipid to bupivacaine successfully reversed cardiotoxicity, supporting the proposed 'lipid sink' mechanism of Intralipids. Results demonstrated that 20% Intralipid was significantly more effective than 2% (p=0.0001) and its efficacy was time-dependent. When administered 5-minutes after bupivacaine exposure, heart rates recovered ~80% of baseline. However, treatment at 10-minutes post-exposure resulted in ~50% recovery. This novel identification of a window for Intralipid treatment emphasizes the importance of early intervention to maximize the effectiveness of Intralipid reversal of LAST. Future studies can refine optimal timing and test Intralipid treatment as an antidote for overdoses or administration of other lipophilic drugs.

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