



Intralipid for the treatment of local anaesthetic cardiotoxicity

VCCAMM recently received notification of a patient who received 20ml 0.75% ropivacaine as an inadvertent intravascular injection and suffered a cardiac arrest. The patient required protracted cardiac resuscitation and management that included the administration of intravenous Intralipid 20%. The outcome was excellent with the patient making a complete recovery. We take this opportunity to provide a brief review of the role of Intralipid 20% for treatment of local anaesthetic induced cardiotoxicity.

In a 2008 review in *Anesthesia and Analgesia*, John Rowlingson reviewed the history and status of intralipid rescue (1).” *Weinberg et al.*(2) investigated the possible metabolic connection of toxicity from only 22 mg of bupivacaine in a patient who was subsequently found to have carnitine deficiency. In their experimental model, it was demonstrated that inducing cardiotoxicity was profoundly more difficult in rats that had been pre-treated with lipid.(3) This led to intentional studies in rats, and then dogs, which established that animals given pre- or follow-up treatment with lipids for bupivacaine overdose recovered remarkably well (2.,3). These data, originally from 1998 (4) suggested that lipid infusion had the potential to be a "... novel treatment of bupivacaine-induced cardiotoxicity," set the scene for a trial of such therapy in actual patient management. *Rosenblatt et al.*(5) reported the first clinical application of such therapy in 2006, and another report from *Litz et al.* (6) soon followed.

Indeed, another interesting observation culled from a short list of case reports is that the time to lipid emulsion administration is getting shorter (5,7,8,9). *Rosenblatt et al.*(5) reported on a patient who had been in resuscitation for approximately 30 min before Intralipid was administered. *Warren et al.*(8) and *Litz et al.*(6) started treatment within 10 min of CPR initiation, whereas *Litz et al.*(7) started lipid therapy within minutes of making the diagnosis of local anesthetic toxicity, as did *Ludot et al.*(9) This trend is a marked redirection of the initial recommendations made in learned commentaries by Groban, Butterworth and Weinberg (and before any human application), which advocated routine CPR measures and then a trial of lipid emulsion before giving up the resuscitative effort”.(10,11)

This content of this and other work has been considered to be of sufficient validity that it has resulted in “the Association of Anaesthetists of Great Britain and Ireland recommending in August 2007 that lipid emulsion be immediately available to all patients given potentially cardiotoxic doses of local anaesthetic drugs” (12).

There still remains no experimentally derived dosing regimen. However a review conducted by Weinberg and published on his website seems reasonable and suggests that despite lack of definitive evidence, “20% Intralipid: 1.5 mL/kg as an initial bolus, followed by 0.25 mL/kg/min for 30-60 minutes. Bolus could be repeated 1-2 times for persistent asystole. Infusion rate could be increased if the BP declines”(13). This regime is consistent with the doses used successfully in the above case reports.

Serving as a reminder that this is an area of treatment that is still being explored, there is a case report from South Africa in 2009 in which there was recurrence of cardiotoxicity at 40 minutes after treatment with a bolus of Intralipid.

“Accidental intravascular administration of bupivacaine during performance of a brachial block precipitated convulsions followed by asystole. The patient was rapidly resuscitated using cardiopulmonary resuscitation, supplemented by 150 mL of 20% lipid emulsion. Nonetheless,

cardiac toxicity reappeared 40 min after completion of the lipid emulsion. In the absence of further lipid emulsion, amiodarone and inotropic support were used to treat cardiotoxicity. This case suggests that local anesthetic systemic toxicity may recur after initial lipid rescue. Since recurrence of toxicity may necessitate administration of additional doses of lipid emulsion, a sufficient quantity of lipid emulsion should be available when regional anesthesia is performed”(14).

Of note in this case is that after successful resuscitation the patient developed elevated serum amylase levels which is indicative of the need to monitor pancreatic function in these patients post treatment. This may prove to be a limiting factor in the dosage of Intralipid but further studies are required in this area.

In summary it has been recommended by several authors and in Journal editorials that Intralipid 20% should be available whenever cardiotoxic doses of local anaesthetics are administered, and it should be used early during resuscitation for cardiotoxicity. Of interest a recent paper has demonstrated the possible harmful effects of Intralipid administered to rabbits who had suffered a cardiac arrest with hypoxia in the absence of local anaesthetic toxicity (15). The ramifications of this and possible explanations are covered in an accompanying editorial by Weinberg that highlights the need to avoid hypoxia in resuscitation (16). Finally a paper by Mazolt indicates that a fall in pH such as can occur in hypoxia reduces the affinity of lipid binding of both ropivacaine and bupivacaine that is the putative mechanism of action of Intralipid 20%. Therefore Intralipid 20% is only recommended for resuscitation of patients with cardiotoxicity due to local anaesthetic, and is contra-indicated in all other resuscitation settings (17).

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