

Use of Lipid Emulsion to Reverse the Effects of Regional Anesthesia: A Novel Indication

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Abstract

A reported novel use of intravenous lipid emulsion (ILE) therapy is to reverse the local anesthetic effects on nerves with peripheral regional and neuraxial anesthesia. This is not well-established, therefore a review of the literature was undertaken.

Medline and Embase databases were searched, as well as Google for grey literature. Indexed and non-indexed literature discussing ILE administration for regional and neuraxial anesthetic blocks were identified. Cases of Local Anesthetic Systemic Toxicity (LAST) were included, provided they also described reversal of peripheral or neuraxial blockade.

Our search revealed fifteen patient case reports, but no clinical trials or review articles. Two indexed reports originating from the USA demonstrated rapid reversal of peripheral nerve blockade following administration of ILE therapy for LAST. A further two indexed USA cases of inadvertent total spinal anesthesia showed prompt resolution of hemodynamic compromise and progressive recovery of motor and sensory function after ILE infusion. Unindexed reports originating from Vietnam elucidated seven cases of spinal/epidural anesthesia and four cases of peripheral regional anesthesia in which motor and sensory neurological deficit attributable to the local anesthetic appeared to be reversed by ILE administration.

These reports explore several novel uses for ILE outside its established role in the treatment of LAST. ILE may have applications in (1) The treatment of high or total spinal anesthesia, (2) The treatment of unintended or prolonged peripheral nerve blockade, and (3) Hastening recovery of sensory and/or motor function following uncomplicated neuraxial or peripheral regional anesthesia. However, these reports are only hypothesis generating. Further research is required to assess a causal relationship.

Keywords

Intravenous lipid emulsion, Intralipid, Regional anesthesia, Spinal anesthesia, Local anesthetic systemic toxicity, Day surgery

Introduction

Intravenous lipid emulsion (ILE) therapy is commonly used to treat local anesthetic systemic toxicity (LAST) and has demonstrated some efficacy in treating other drug toxicities, particularly cardiotoxicity from lipophilic drugs [1]. While the precise mechanism by which ILE

exerts its effect remains unknown, the leading theory is that it acts as a 'lipid sink' to extract lipophilic drug molecules from target receptors, thus reducing concentrations in the heart, brain and other body tissues. Alternative theories include reduced binding of local anesthetics to sodium transport channels, direct promotion of sodium channel function recovery, and replenishing ATP stores from increased uptake of fatty acids by mitochondria [1,2].

A less well-established technique is the use of ILE to antagonize the primary nervous system effects of regional anesthesia - such as total spinal anesthesia or prolonged neural blockade. Although there are few published reports on the effectiveness of ILE in this capacity, there are anecdotal reports of successful use in multiple cases. In our own department, ILE has been used to successfully reverse a high spinal block, and to reverse a phrenic nerve palsy secondary to a brachial plexus block. We conducted a literature review to identify cases in which ILE was administered to reverse the effects of regional anesthesia, in order to better understand the potential utility of this practice.

Methods

As the practice lacks a standardized approach and terminology, conducting a systematic review was deemed difficult. A scoping review was thus undertaken. Web of Science, MEDLINE, Embase and Cochrane CENTRAL databases were searched using the terms 'lipid emulsion' or 'Intralipid' in combination with any of: 'regional', 'block', 'spinal', 'anesthesia', or 'reversal'. A Google search was also undertaken using the same parameters to identify 'grey' and unindexed literature.

No language or publication date restrictions (up to August 2022) were applied, and human studies and case reports were included. The references of relevant articles were also reviewed. Cases involving treatment of LAST were included provided they also reported the reversal of peripheral or neuraxial blockade.

Results

This search revealed fifteen relevant case reports but no clinical trials or review articles. Likely due to the inconsistent terminology and paucity of reports, several of these articles claim to be the first report of this phenomenon - indicating the need for a review of the literature. Only four case reports have been published in indexed journals, summarized as follows.

Turner, et al. report a case of total spinal anesthesia with respiratory arrest following an interscalene block (30 mL 0.25% bupivacaine) [3]. The patient was intubated and administered 20% ILE (reported as 85 mg, though likely intended as 85 mL), with progressive recovery of motor and sensory functions over four hours. They were discharged the following day with no neurological abnormalities. The authors note that it was “difficult to ascertain” whether the lipid emulsion affected recovery, given the variable half-life of bupivacaine and that spontaneous recovery may occur in a similar timeframe.

Kamel, et al. describe a case of LAST with a dense sensory and motor block in the left lower limb following local anesthetic infiltration (80 mL 0.5% bupivacaine) into the surgical site for a posterior colpoperineorrhaphy and transobturator sling insertion [4]. The peripheral signs were thought to represent inadvertent blockade of the left femoral and obturator nerves. The patient was given 20% ILE (100 mL) over one minute, followed by a further 400 mL over 20 minutes. The initial bolus was followed by rapid resolution of LAST symptoms. Sensation and motor power gradually returned during the infusion, with only residual paraesthesias in the left lower limb once the infusion was complete, which were no longer present the following day. The authors suggested that the temporal association between ILE administration and resolution of the peripheral sensory and motor changes may represent a causal relationship.

Torrie, et al. report a case of LAST and dense right upper limb sensory and motor blockade following ultrasound-guided placement of an interscalene brachial plexus catheter, with a local anesthetic bolus (15 mL 2% lidocaine) in addition to subcutaneous infiltration (3 mL 1% lidocaine) [5]. The patient was administered 20% ILE (1.5 mL/kg = 86 mL), followed by 0.25 mL/kg/min for 30 minutes (total dose 414 mL), with prompt resolution of LAST symptoms. This was accompanied by almost complete reversal of the upper limb sensory and motor block within five minutes.

Gupta, et al. describe a case of total spinal anesthesia following an interscalene block with “10 mL of bupivacaine and 30 mL of ropivacaine, of unknown concentrations” [6]. The patient was intubated, administered two liters of crystalloid, and commenced on a dopamine infusion for bradycardia and hypotension. After approximately 90 minutes, 20% ILE was administered (1.5 mL/kg = 125 mL) over one minute, followed by 0.013 mL/kg/

min for two hours (total dose 250 mL). Hemodynamic parameters normalized over the first 30 minutes from the initial dose of ILE, after which neurological function began to recover. Two hours later, extubation was performed successfully. Full neurological recovery occurred with discharge 30 hours after presentation.

Eleven further cases have been reported across five separate publications by Joseph Eldor and co-authors from Vietnam. These are published in Volume 1 Issue 1 of the *Journal of Health Science and Development* - which doesn't appear to be indexed by any major indexation service and lists Eldor as Editor-in-Chief. The cases described in these papers include one case of ILE to reverse sensory and motor blockade with epidural anesthesia postoperatively [7]; three cases of ILE to treat high spinal anesthesia [8]; three cases of ILE to hasten neurological recovery following spinal anesthesia for day case procedures [9]; and four cases of ILE to reverse brachial plexus nerve blocks [10,11]. These articles incorporate long confusingly-worded discussion sections that shed little light on this interesting and novel topic, and none describe ethics approval or informed consent. Interestingly, in each of the cases of high spinal anesthesia [8] the surgical procedure was continued during or after resuscitative efforts without any indication that the ILE treatment led to an inadequate surgical block.

Discussion

Altogether, these cases present several different potential uses for ILE beyond its established role in the treatment of LAST. It may have a role in (1) The treatment of high or total spinal anesthesia (in addition to supportive care), (2) Treatment of unintended or prolonged peripheral nerve blockade, and (3) Hastening recovery of sensory and/or motor function following uncomplicated neuraxial or peripheral regional anesthesia.

The quality of evidence to support these practices remains poor, with only a limited number of case reports and no clinical trials. Particularly given the variability in local anesthetic metabolism and duration of neural blockade in clinical practice, these reports are only hypothesis generating, suggesting a potential avenue for further research. Other cases in which ILE has been used to antagonize the primary nervous system effects of regional anesthesia may have been unreported in the literature and it is unclear how widespread this practice may be. The reported cases likely exhibit publication bias as a report of unsuccessfully using a drug for a novel indication would not be expected to be published. A clinical trial under controlled conditions is feasible and would be of great interest in helping to either bring an effective treatment into more mainstream practice, or to discourage an ineffective practice.

While the evidence supporting this practice is limited,

it is worth considering if the benefits are likely to exceed the risks. The safety profile of ILE is relatively favorable, with severe complications only reported in rare cases [12,13]. It would thus be particularly attractive as a treatment option in life-threatening situations, such as total spinal anesthesia.

If ILE is indeed effective at hastening neurological recovery after neuraxial or peripheral regional anesthesia, this would present several important clinical opportunities. Firstly, it could facilitate regional anesthesia for more day case procedures and avert delayed hospital discharges due to persistent effects of regional anesthesia. Secondly, it may facilitate neurological examination in the early postoperative period, potentially allowing earlier diagnosis of nerve injuries or allowing regional anesthesia to be used for cases in which it may be otherwise contraindicated. Thirdly, it could be used in the treatment of adverse effects from regional anesthesia, such as high neuraxial blocks or phrenic nerve blockade with brachial plexus blocks.

Conclusion

The use of ILE to antagonize the primary nervous system effects of regional anesthesia is a novel concept with substantial potential clinical applications. Further research is required to assess its effectiveness.

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References

- Muller SH, Diaz JH, Kaye AD. Clinical applications of intravenous lipid emulsion therapy. *J Anesth.* 2015;29:920-6.
- Hoshino R, Kamiya Y, Fujii Y, Tsubokawa T. Lipid emulsion injection-induced reversal of cardiac toxicity and acceleration of emergence from general anesthesia after scalp infiltration of a local anesthetic: A case report. *JA Clin Rep.* 2017;3:9.
- Turner FN, Shih RD, Fishman I, Calello DP, Solano JJ. Total spinal anesthesia following an interscalene block treated with intravenous lipid emulsion. *Cureus.* 2019;11:e4491.
- Kamel I, Trehan G, Barnette R. Intralipid therapy for inadvertent peripheral nervous system blockade resulting from local anesthetic overdose. *Case Rep Anesthesiol.* 2015;2015:486543.
- Torrie AM, Dunitz J, Brookman JC. Apparent reversal of a successful peripheral neural blockade with intravenous lipid emulsion after treatment for local anesthetic systemic toxicity: A case report. *A A Pract.* 2020;14:e01336.
- Gupta A, Procopio GL, Charles PH, Hernandez M, Patel R. Inadvertent intrathecal administration of local anesthetics leading to spinal paralysis with lipid emulsion rescue. *Clin Pract Cases Emerg Med.* 2017;1:81-3.
- Eldor J, Nguyen TA. Lipid emulsion for Local Anesthesia Reversal (LAR) after prolonged spinal/epidural anesthesia. *J Health Sci Dev.* 2018;1:43-7.
- Eldor J, Pham V, Tran TP, Nguyen XL, Kien NT. Local Anesthesia Reversal (LAR) of Total Spinal Anesthesia (TSA) by Lipofundin (Lipid Emulsion). *J Health Sci Dev.* 2018;1:67-72.
- Eldor J, Kien NT. Local Anesthesia Reversal (LAR) of spinal anesthesia by lipid emulsion (Lipofundin 20%) for day case surgery. *J Health Sci Dev.* 2018;1:79-85.
- Eldor J, Hien VV, Kien NT. The first case report of Local Anesthesia Reversal (LAR) of the upper arm brachial plexus block by lipid emulsion. *J Health Sci Dev.* 2018;1:61-6.
- Kien NT, Hien VV, Khanh DT, Eldor J. Upper Arm Local Anesthesia Reversal (LAR) using lipofundin (3 case reports). *J Health Sci Dev.* 2018;1:73-8.
- Cave G, Harvey M, Graudins A. Intravenous lipid emulsion as antidote: A summary of published human experience. *Emerg Med Australas.* 2011;23:123-41.
- Tampakis K, Vogiatzakis N, Kontogiannis C, Spartalis M, Ntalianis A, Spartalis E, et al. Intravenous lipid emulsion as an antidote in clinical toxicology: A systematic review. *Eur Rev Med Pharmacol Sci.* 2020;24:7138-48.

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