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Short Commentary

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Reversal of spinal anaesthesia and prevention of post operative complications using intralipid emulsion

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Abstract

Intravenous lipid emulsion has been gaining ground as a real antidote to bupivacaine adverse reactions and toxicity. Spinal bupivacaine works through reversible binding at sodium channels. Cardiovascular collapse is one of the evidences of bupivacaine toxicity, and this can most of the time be resistant to relevant resuscitation. Various animal studies have been published investigating the use of intravenous lipid in local and non local anesthetic toxicity. Twenty six human cases who had complications with spinal or epidural anaesthesia in the past were enrolled for this study. Intravenous lipid emulsion was given to each of these patients after surgery. It is found that Intravenous lipid emulsion can be used to reverse both the normal actions and abnormal actions following spinal anaesthesia. It is capable of mitigating the drug related adverse effect in the post operative period. Hence, the need to make the drug available in our hospitals.

Keywords: Bupivacaine; Intralipid; Post operative complications; Spinal anaesthesia.

Introduction

Lipid emulsion administration has been effective in the treatment of cardiovascular collapse and central nervous system symptoms caused by local anesthetic toxicity, including that of bupivacaine, levobupivacaine, ropivacaine, lidocaine and mepivacaine [1]. Some authors [1-4] have tried lipid emulsion in the treatment of complications following toxicity of other drugs. They found that lipid emulsion may be effective in alleviating intractable cardiovascular collapse induced by toxic doses of these non-local anesthetic drugs. Toxicity of drugs that were treated with intravenous lipid emulsion include calcium channel blockers (verapamil), tricyclic antidepressants (amitriptyline) and beta-blockers. These are documented in reports of successful lipid emulsion treatment for the toxicity caused by non-local anesthetic drugs [2-4]. Complications following intrathecal administration of bupivacaine has been successfully managed with intravenous administration of lipid emulsion [3,4]. Owing to some post complications following bupivacaine spinal and epidural anaesthesia, we hypothesise that intravenous lipid emulsion is capable of reversing actions of bupivacaine and by extension attenuate post operative complications following bupivacaine use. Hence, the need to carry out this prospective and observational case study.

Materials and methods

This is a prospective observational study of reversal of spinal anaesthesia among patients who previously had post operative complications following spinal anaesthesia in the past. This study was carried out between January 2016 and December 2020. This study was approved by the institution Ethics

and Review Committee. Informed consent was obtained from all the participants. Twenty six patients, who had drug-related complications in the past following administration of spinal or epidural bupivacaine, were recruited into this study. Six of them were women who had previous emergency caesearean delivery under subarachnoid block. Five of the patients were recruited from urological unit. Another five patients had been exposed to epidural anaesthesia in orthpaedic unit in the past. Ten patients, who had exposure to spinal bupivacaine in the gynaecological unit, were among the patients recruited for this study. Patients received ranitidine 50 mg and 10 mg metoclopramide intravenously prior to surgery. For each of the patients, one 16G intravenous cannulae were put in place for the purpose of this study. Routine monitoring such as non-invasive monitoring was commenced and documented including Non-Invasive Blood pressure (NIBP), Oxygen Saturation (SPO_2), Pulse Rate (PR), Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP). Each patient had a total fluid of 1 litre for preloading. Induction of spinal anaesthesia was achieved with patients in sitting position. Their legs were hanging from the edge of the operating table with the support of a stool under their feet. They were asked to bend the neck forward and arch out their back maximally. Under aseptic condition, the spinal needle was introduced into the subarachnoid space. After withdrawing the stylet from the spinal needle, appearance of the free flow of cerebrospinal fluid in the hub of the needle indicated a successful placement. All patients received 3 ml of 0.5% hyperbaric bupivacaine over 15s intrathecally in the L3-4 or L2-3 intervertebral space. The patients were immediately put in supine position with a 15° left lateral tilt using wedge under the right hip for obstetric patients. Sensory bock height was assessed using loss of sensation to gentle pin prick test. A sensory block height of T6 was the minimum desired level of block for the commencement of the surgery. The following parameters: pulse rate, systolic blood pressure, diastolic blood pressure, and oxygen saturation were recorded every three minute for the first fifteen minutes, every 5 min for the next 15 minutes and every ten minutes thereafter till the end of surgery. At the end of surgery, each patient was given 100 ml of 20% intravenous lipid emulsion. Incidence of post operative complication was monitored in the patients for the next 24 hours. Time to first analgesia is the period between when intralipid is administered to the time patients will make their first request for pain relief.

Primary outcome measure was the reversal of bupivacaine spinal anaesthesia and prevention of incidence of post operative complications using intralipid.

Results and discussion

The original purpose for the constitution of Lipid emulsion was aimed at providing parenteral nutrition to patients, especially those critical ones in Intensive Care Units and other wards for critical patients [2]. However, further researches made it clear that lipid emulsion could be used to treat local anesthetic-induced and non-local anaesthetic induced systemic toxicity [3-6]. Both human and animal studies have proved that intralipid emulsion can reverse the action of bupivacaine and attenuate bupivacaine-induced cardiac toxicity [5-11]. According to Table 1 in this study, twenty six patients who had complications following spinal anaesthesia or epidural anaesthesia in the past were studied. Six out of these patients were obstetric, five were from urology unit, ten were from gynaecological unit and five were from orthopaedic unit. Table 2 shows nature of the previous drug related complications in the patients. Nine people had leg paralysis, urinary retention were found in seven patients, five persons had post dural puncture headache and bradycardia was found in five of them. Clinical variable assessment following intralipid shows that there was no drug-related post operative complications in the patients studied. Majority of the patients had reversal of their anaesthesia within two hours post operatively as documented in Table 3.

Table 1: Patients with known complications of bupivacaine.

Unit	Number of patients	Percentage
Obstetrics	6	23.1
Urology	5	19.2
Gynaecology	10	38.5
Orthopaedics	5	19.2

Table 2: Previous drug-related post operative complications in the patients.

Types of complication	Number of patients	Percentage
Leg paralysis	9	34.6
Urinary retension	7	27.0
Post dural headache	5	19.2
Bradycardia	5	19.2

Table 3: Clinical variables following the use of intralipid emulsion.

Variables	Number of patients	Percentage
Post operative complications	Nil	Nil
Time to first analgesia		
Within 2 hours	21	80.8
Within >2 hours-4 hours	05	19.2

It has been suggested that Intralipid emulsion, when administered to animal and patients who have toxicity following bupivacaine, has a high capacity to bind bupivacaine [12-14] Moreover, intralipid improved the survival and hemodynamics of bupivacaine-induced cardiac toxicity in dogs [15]. Different animal studies have demonstrated the usefulness of intralipid emulsion in reversing the adverse effect of bupivacaine [12-16]. Rosenblatt et al. [17] reported the first clinical case of lipid emulsion for treating bupivacaine toxicity in 2006. They treated a 58-year-old male with lipid emulsion having had seizure and asystole (cardiac arrest) due to toxicity from bupivacaine and mepivacaine used in an interscalene brachial plexus block. A 100 ml of 20% intralipid (for Baxter Pharmaceuticals by Fresenius Kabi, Uppsala, Sweden) was given through the peripheral intravenous cannula. Cardiac compressions continued, and a defibrillation shock at 360 J was given. Within seconds, a single sinus beat appeared on the electrocardiogram, and 1 mg atropine and 1 mg epinephrine were administered. Within 15 s, while external chest compressions were continued, the cardiac rhythm returned to sinus at a rate of 90 beats/min. The blood pressure and pulse became detectable. An infusion of

lipid emulsion was started and continued at 0.5 ml kg. 1-min−1 over the following 2 h and then discontinued. The patient remained in sinus rhythm. He was weaned from mechanical ventilation, and his trachea was extubated [17]. This is in support of the present study that intravenous lipid emulsion can reverse normal and abnormal activities of local anaesthetic and non local anaesthetic agents, for example bupivacaine. One of the earliest cases describes the accidental injection of 40 ml of 1% ropivicaine for an axillary plexus block in an 84-year-old woman [18]. Shortly after the block was placed, the patient developed generalized tonic-clonic seizures followed by asystole. Standard resuscitation measures were unsuccessful and after 10 min of cardiovascular collapse, lipid emulsion was given by a bolus followed by an infusion. Normal cardiac rhythm returned, and blood pressure was restored to normal. The patient was discharged home in four days with near complete recovery. The reversal of the toxicity of ropivacaine was based on binding of lipid emulsion to the local anaesthetic agent, which also reversed further action of the drug [18]. This corroborates the findings in this study that lipid emulsion can at anytime stop the action of local anaesthetic agent and improve upon any mild, moderate or severe adverse reactions to the drugs. Eldor et al. [19] reported a case of a 71 year old woman who had combined spinal and epidural anaesthesia. She complained of loss of sensation on the non-operative leg after eight hours post operative period. After four hours of unsuccessful palliative treatment, her experienced was not improved. They decided to use lipid emulsion as a challenging therapy. A dose of 250 ml of lipidem 20% was infused over 30 minutes. Dramatically, and after completion of the lipid therapy, the sensory and movement of the non-operative leg returned to normal within 60 minutes. They advised that it would be proper to make the drug readily available while administering bupivacaine. The first clinical report of intravenous lipid emulsion resuscitation of a patient with toxicity induced by a non-local anesthetic drug was reported in 2008 by Sirianni et al. [20]. Administration of Intralipid infusion led to the dramatic recovery of a 17-year-old female patient with severe cardiovascular depression and seizure due to toxic doses of bupropion and lamotrigine [19]. According to reviews of many clinical case reports and laboratory studies, lipid emulsion can effectively treat cardiovascular collapse caused by a toxic dose of local anesthetics and non local anaesthetics casting hope in the management of adverse effects, toxicities and even chemical poisoning [3-6]. Based on our report and the reports of other authors, toxicity and other adverse reactions of bupivacaine can be successful managed by lipid emulsion treatment [4,5]. More studies with larger population size are still needed to determine the optimal dosing regimen, as well as to determine the potential adverse effects of lipid emulsion when used in the management local anaesthetic post operative complications.

Conclusion

Intravenous lipid emulsion can be used to reverse both the normal actions (anaesthesia) and abnormal actions (toxicity and post operative complications) of bupivacaine following spinal anaesthesia. This reversal is capable of mitigating the drug related adverse effects in both intraoperative and post operative period. Hence the need to make the drug available in our wards, theatre suites, Intensive Care Units and Accident and Emergency units of hospitals.

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