Lipid Emulsion Treatment for Post Spinal Anesthesia Myoclonus

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Abstract

Two case reports of myoclonus of legs post spinal anesthesia treated successfully by IV lipid emulsion are first described in the medical literature.

A review of cases of myoclonus post regional anesthesia (spinal or epidural) are discussed with the hypothesis that the Lipid Emulsion effects are on the mitochondria and the intracellular calcium.

Keywords: Myoclonus; Post spinal anesthesia myoclonus, Post epidural anesthesia myoclonus, Intralipid, Lipidem, Fat emulsion, Mitochondria, Intracellular calcium.

Case Report No 1

43-years-old, healthy female patient was scheduled for drainage of an abcess on the right buttock. In the past she had given 2 Spinal Anesthesia for Cesarian sections uneventfully. For surgery this time, Spinal Anesthesia performed at L3-4 with 6 mg bupivacaine 0.5% heavy and 20 mcg fentanyl uneventfully. Time of surgery was 30 min. Myoclonic movement of both legs occurred 60 min post-op. She remained fully conscious and had no other local neurological symptoms. Vital signs were stable. LAST was ruled out. She was under close monitoring, but myoclonus was not diminished in 2 hours. Lipid challenging therapy was considered. After an infusion of 250 ml Lipidem 20% over 30 min abnormal movement diminished gradually and disappeared in 60 min. No recurrent of myoclonus episode was noted thereafter.

The patient's myoclonus can be seen in the following video [23]:

Case Report No 2

A female 34 years-old, 39 weeks of pregnancy. Her precedent had two vaginal delivery (the second time with the assistance of Forceps). She was healthy and had expected a normal delivery but failed. The Cesarian section was performed under Spinal Anesthesia. The 27 Quincke Needle was introduced at L3-4 uneventfully. Dose of SA was 7.5 mg Bupivacaine heavy 0.5% (Aguettant)+25 mcg Fentanyl. The operation lasted 45 min without any medication added. Approximately 100 min postop, patient had myoclonus on the left leg as in the following Video [24].

The movement of the right leg was normal. The sensory feeling of both legs returned nearly normal. Other systems were with no particular problems. No LAST, hemodynamic was stable, she was totally conscious, no shivering, no other neurological signs.

Since the anesthesiologist (TTD) learned from anesthesiologist (TAN) his case through discussions in the group on Facebook, he used LIPIDEM 20% (B. Braun) right away, not wasted time as in anesthesiologist (TAN) case (case no.1). After 5 min of IV Lipid emulsion infusion the myoclonus decreased significantly (see the video after Lipidem infusion) [25]. and gone away in 30 min of the IV lipid emulsion infusion.

Discussion

Lipidem

Lipidem is an intralipid like lipid emulsion (using Soybean oil and Egg yolk) with the following composition:

Lipoplus®/ Lipidem® Composition 1000 ml of emulsion contains: Medium-chain triglycerides: 100.0 g Soybean oil, refined: 80.0 g Omega-3-acid triglycerides: 20.0 g Essential fatty acid content per liter: Linoleic acid (omega-6): 48.0-58.0 g Alpha-linolenic acid (omega-3): 5.0-11.0 g Eicosa-pentaenoic acid and docosahexaenoic acid: 8.6-17.2 g Caloric content per liter: 7,900 kJ ≈ 1,910 kcal. Osmolality: approx. 410 mOsm/kg. Titration acidity or alkalinity (to pH 7.4): less than 0.5 mmol/l NaOH or HCl pH: 6.5-8.5. The other ingredients are glycerol, egg lecithin, all-rac-α-Tocopherol, ascorbyl palmitate, sodium oleate, sodium hydroxide (for pH adjustment) and water for injections. B. Braun Melsungen AG Carl-Braun-Straße 134212 Melsungen, Germany.

Myoclonus

Myoclonus creates significant disability for patients. This symptom or sign can have many different etiologies, presentations, and pathophysiological mechanisms. A thorough evaluation for the myoclonus etiology is critical for developing a treatment strategy. The best etiological classification scheme is a modified version from that proposed by Marsden et al. in 1982. Clinical neurophysiology, as assessed by electromyography and electroencephalography, can be used to classify the pathophysiology of the myoclonus using a neurophysiology classification scheme. If the etiology of the myoclonus cannot be reversed or treated, then symptomatic treatment of the myoclonus itself may be warranted. Unfortunately, there are few controlled studies for myoclonus treatments.

The treatment strategy for the myoclonus is best derived from the neurophysiology classification scheme categories:

1) cortical,

2) cortical-subcortical,

3) subcortical-nonsegmental,

4) segmental, and

5) peripheral.

A cortical physiology classification is most common. Levetiracetam is suggested as first-line treatment for cortical myoclonus, but valproic acid and clonazepam are commonly used. Cortical-subcortical myoclonus is the physiology demonstrated by myoclonic seizures, such as in primary epileptic myoclonus (e.g., juvenile myoclonic epilepsy). Valproic acid has demonstrated efficacy in such epileptic syndromes with other medications providing an adjunctive role. Clonazepam is used for subcortical-nonsegmental myoclonus, but other treatments, depending on the syndrome, have been used for this physiological type of myoclonus. Segmental myoclonus is difficult to treat, but clonazepam and botulinum toxin are used. Botulinum toxin is used for focal examples of peripheral myoclonus. Myoclonus treatment is commonly not effective and/or limited by side effects [1].

Myoclonus remains a challenging movement phenotype to characterize, evaluate, and treat. A systematic assessment of the temporal sequence, phenomenology, and distribution of movements can assist in the rational approach to diagnosis and management.

Cortical forms of myoclonus are increasingly recognized as primarily cerebellar disorders. A syndrome of orthostatic myoclonus has been recognized by electrophysiology in patients with neurodegenerative disorders, mainly in Alzheimer disease, accounting for impairments in gait and balance previously mischaracterized as normal pressure hydrocephalus or orthostatic tremor. Tyrosine hydroxylase deficiency and Silver-Russell syndrome (uniparental disomy of chromosome 6) have been established as two novel causes of the myoclonus-dystonia syndrome. Mutations in the glycine receptor (GlyR) α1-subunit gene (GLRA1) explain the major expression of hyper ekplexia, an inherited excessive startle disorder, but newly identified mutations in GlyR β-subunit (GLRB) and glycine transporter 2 (GlyT2) genes (SLC6A5) account for "minor" forms of this disorder manifested as excessive startle and hypnic jerks. The entity previously known as palatal myoclonus has been reclassified as palatal tremor in recognition of its clinical and electromyographic features and no longer enters the differential diagnosis of myoclonic disorders. Increasing documentation of psychogenic features in patients previously characterized as having propriospinal myoclonus has cast doubts on the existence of this distinctive disorder.

Myoclonus can be a prominent manifestation of a wide range of disorders. Electrophysiologic testing aids in distinguishing myoclonus from other mimics and classifying them according to cortical, subcortical, or spinal origin, which assists the choice of treatment. Despite the lack of randomized clinical trials, levetiracetam appears most effective in patients with cortical myoclonus, whereas clonazepam remains the only first-line therapeutic option in subcortical and spinal myoclonus [2].

Post spinal/epidural anesthesia myoclonus

Perioperative spinal myoclonus is extremely rare. Many anaesthetists and perioperative practitioners may not diagnose or manage this complication appropriately when it occurs. This case report of unusual acute spinal myoclonus following regional anaesthesia highlights certain aspects of this rare complication that have not previously been published [3].

A series of four consecutive patients who developed acute lower-limb myoclonus following spinal or epidural anaesthesia are described. The case series occurred at three different hospitals and involved four anaesthetists over a 3-year period. Two Caucasian men, aged 90-years-old and 67-years-old, manifested unilateral myoclonus. Two Caucasian women, aged 64-years-old and 53-years-old, developed bilateral myoclonus. Myoclonus was self-limiting in one patient, treated with further regional anaesthesia in one patient and treated with intravenous midazolam in two patients. The overall outcome was good in all patients, with no recurrence or sequelae in any of the patients.

This case series emphasizes that spinal myoclonus following regional anaesthesia is rare, has diverse pathophysiology and can have diverse presentations. The treatment of perioperative spinal myoclonus should be directed at the aetiology. Anaesthetists and perioperative practitioners who are unfamiliar with this rare complication should be reassured that it may be treated successfully with midazolam [3].

We report a case of spinal myoclonus induced by the tip of an intrathecal catheter in a 35-year-old patient with severe, adult-onset, generalized dystonia of unknown cause, treated for 2 years using intrathecal baclofen [3]. One month after a falling episode, the patient developed focal myoclonus of the right proximal leg whenever she stood up from a seated position. The electrophysiologic recordings were compatible with spinal segmental myoclonus, originating at a focus corresponding to the L2-S2 segments. At this site, the tip of the intrathecal catheter was demonstrated by myelography to be in close proximity to the nerve roots and conus medullaris. The myoclonus resolved promptly once the catheter tip was withdrawn. This report represents an unusual complication of intrathecal catheter systems that, if recognized, can lead to prompt therapeutic intervention [4].

A nulliparous woman presented with pre-eclampsia at 39 weeks' gestation. A combined spinal-epidural anaesthesia was employed for Caesarean section, but the spinal component produced no discernible block, so the epidural was topped up with 20 ml ropivacaine 0.75% without problem and surgery was uneventful. A week after delivery she developed twitching of her legs and opisthotonus, that was initially thought to be eclampsia but was subsequently diagnosed as spinal myoclonus. She was treated with oral carbamazepine and diazepam, with improvement over the next 4 days, and discharged home a week later taking oral carbidopa and levodopa. Her symptoms resolved completely 6 months after the initial event [5].

We report a patient who developed paraplegia following percutaneous nephrolithotresis of the left kidney under epidural anaesthesia [6]. The cause of the paraplegia was unknown, but occlusion of the anterior spinal artery or central arteries and arachnoiditis, possibly due to the epidural anaesthesia, may have taken part in the onset and progression of the paralysis. The patient had spinal myoclonus corresponding to the spinal levels where myelomalacia was found by magnetic resonance (MR) imaging [6]. Spinal myoclonus following neuraxial anesthesia is rare. This report describes a case of myoclonus-like involuntary movement that occurred during the recovery from epidural anesthesia for a cesarean delivery. The patient's symptom improved with the administration of benzodiazepine, and the patient recovered with no neurological sequelae. In conclusion, epidural anesthesia can cause spinal myoclonus, which can be treated with a benzodiazepine [7].

Involuntary movement during and after neuraxial anesthesia, such as spinal and epidural anesthesia, is rarely observed. In this report, we describe a case of myoclonus-like involuntary movement of the upper extremities in a patient undergoing a planned repeat cesarean section under spinal anesthesia with bupivacaine that completely subsided after administration of 2 mg of midazolam [8]. The myoclonus-like movement did not recur or cause any apparent neurological side effects [8].

It is presented in this case report a very rare complication after spinal anesthesia to provide subsidies to the management and therapeutic conduct [9]. This is a 63-year old African-Brazilian patient, ASA I, scheduled for transurethral resection of the prostate (TURP). He underwent subarachnoid anesthesia with bupivacaine (15 mg) without adrenaline. Intercurrences were not observed during puncture, and the patient was positioned for surgery. Soon after positioning the patient, he complained of severe pain in the perineum region followed by involuntary tonic-clonic movements of the lower limbs. The patient was treated with a benzodiazepine to control the myoclonus without response. This episode was followed by significant agitation and the patient was intubated. He was maintained in controlled ventilation and transferred to the Intensive Care Unit. Despite all biochemical and imaging tests performed, an apparent cause was not detected. The medication was not changed and the same batch of anesthetic had been used in other patients that same day without intercurrences.

After ruling out all possible causes, the diagnosis of spinal myoclonus after spinal anesthesia with bupivacaine was made by exclusion [9]. Spinal myoclonus is an unusual, self-limiting, adverse event that may occur during spinal anesthesia. The exact cause and underlying biochemical mechanism of spinal myoclonus remain unclear. A few cases of spinal myoclonus have been reported after administration of intrathecal bupivacaine. We report a case in which spinal myoclonus recurred after two episodes of spinal anesthesia with bupivacaine at a 1-year interval in a 35-year-old woman [10]. The myoclonus was acute and transient. The patient recovered completely, with no neurologic sequelae [10].

We report a case of spinal myoclonus following cesarean section [11]. The patient was a 34-year-old woman without history of neurologic disorders. In the operating room, after placement of an epidural catheter at T12-L1, bupivacaine 2.4 ml was administered intrathecally via a 25 G needle at L2-3. Epidural administration of ropivacaine (0.13%, 4 ml x hr(-1)) was started 72 min after spinal anesthesia. The intra- and postoperative courses were otherwise uneventful. The patient complained of involuntary jerky movements of her lower legs 195 min after the start of the spinal anesthesia. The sensory level was T12 and she could move her legs on command but could not stop her involuntary movements. The myoclonic movements ceased 150 min later without medication and did not reappear, despite restarting the epidural anesthesia with ropivacaine [11].

Propriospinal myoclonus is a rare disorder characterized by sudden, shock-like, involuntary jerks that arise from the axial muscles and spread both rostrally and caudally to other myotomes through slow polysynaptic pathways. It can be idiopathic or secondary to intrinsic and extrinsic spinal cord lesions; additionally, it can develop as an adverse effect to the administration of several drugs, including neuraxial local anesthetics. This article describes a case of transient propriospinal myoclonus in a 77-year-old woman undergoing surgery for hip replacement who received 12 mg of 0.5% normobaric bupivacaine administered by a 25-G spinal needle [12]. On postoperative day 1, the patient presented with spinal myoclonus, defined by clinical and electrophysiologic studies. Valproate and clonazepam controlled the symptoms, and on day 4 the myoclonus completely disappeared. Few cases of myoclonus induced by intrathecal bupivacaine administration have been

reported in the literature, but systematic reviews written to clarify the global incidence and the physiopathology of this complication are still lacking [12].

Focal myoclonus of peripheral origin, i.e., peripheral myoclonus (PM), is a rare disorder. Although PM always accompanies a lesion in the peripheral nerve, supplying the affected muscles, its mechanism remains unclear. Here we present a patient with focal myoclonus of the thigh muscles following a traumatic lesion in the femoral nerve [13]. Lumbar spinal anesthesia, as well as local anesthetic block of the femoral nerve, completely abolished the patient's myoclonus temporarily. This movement was remarkably diminished after a surgical exploration of the wound with the removal of fibrous tissue beneath the scar and liberation of the femoral nerve. This case suggests the contribution of a spinal relay mechanism in the development of PM, in addition to the contribution of a nerve lesion [13].

We report a patient who developed a rare neurological complication of spinal myoclonus possibly caused by an epidural catheter [14]. A 24-yr-old female received laparoscopy and intrauterine curettage under general combined with epidural anesthesia. Spinal myoclonus started about 4 hours after the last epidural drug injection and disappeared 2 hours following removal of the epidural catheter. The patient was discharged without any untoward neurological sequelae [14].

We herein report a case of spinal myoclonus following the administration of epidural anesthesia [15]. A 25-year-old woman underwent lumbar epidural anesthesia because of lumbago and cramps in her left lower limb. She immediately felt a lancinating pain in her left limb during anesthesia at the level of L 4/5 and soon developed myoclonus in her left thigh. The neurological examination revealed rhythmic myoclonus in the left quadriceps and adductor thigh muscles. The myoclonus disappeared after performing a blockade of the left L4 spinal root by using 1.5 ml of 1% lidocaine. An injury to the left L4 nerve root during the epidural anesthesia possibly caused an abnormal transmission of the impulses or ectopic hyperexcitability in the nerve root, which might lead to the disturbance of the spinal inhibitory interneurons and hyperexcitability of the anterior horn cells causing myoclonus. Since she did not demonstrate any muscular weakness, nor sensory loss during the lidocaine block, the 1% lidocaine appeared to block the sympathetic nerves or to suppress the ectopic hyperexcitability. The sympathetic nerves may be involved in the development of her spinal myoclonus [15].

The use of intrathecal diamorphine via an implanted portal system is described for pain control in a patient suffering from vertebral metastatic disease. The complication of myoclonic spasms affecting the lower half of the body occurred after 14 days, when increasing the bolus dose to 40 mg. The spasms lasted for 3 hr and then gradually subsided. Diamorphine was subsequently restarted at a lower dose of 15 mg twice daily. On increasing the dose to 20 mg diamorphine 10 days later, severe distressing myoclonic spasms recurred 20 min post injection. Myoclonus could only be controlled by instituting a local anesthetic intrathecal block. The patient was finally managed with 20 mg diamorphine per day by intrathecal infusion, and the pain was reasonably well controlled for the following 10 weeks without any recurrence of myoclonic spasms [16].

We report a case of periodic leg movements (PLM) observed in an 86-year-old man during either midthoracic epidural anesthesia or spinal anesthesia [17]. The PLM observed were stereotyped (extension of the big toe in combination with partial flexion of the ankle, knee, and hip lasting 3-5s) and repetitive (inter event intervals between jerks were 20-40s) for about 120 and 30 min respectively. The patient was awake but unaware of the PLM unless reminded. The present case was quite similar to sleep-related (noctural) myoclonus (SRM) in every respect except for its occurrence during wakefulness. SRM is more prevalent in the elderly population but its mechanism remains to be elucidated. Previously, we had reported a case of PLM observed in an elderly man with SRM [18]. In our two cases, PLM were seen only while the local anesthetic was acting on the spinal cord; therefore, these anesthesia-related PLM (ARPLM) may suggest that the spinal cord is involved. In particular, we consider that physiological changes seen commonly during non-rapid-eye-movement sleep and a certain phase of anesthesia, such as suppression of the descending inhibitory pathway, and pyramidal tract dysfunction are relevant to ARPLM. In addition, the concomitant alteration of the blood flow in the leg and changes due to aging of the spinal cord may also be involved [17].

Lipid emulsion effects on mitochondria and intracellular calcium

Local anesthetic toxicity is thought to be mediated partly by inhibition of cardiac mitochondrial function. Intravenous (i.v.) lipid emulsion may overcome this energy depletion, but doses larger than currently recommended may be needed for rescue effect. In this randomized study with anesthetized pigs, we compared the effect of a large dose, 4 mL/kg, of i.v. 20% Intralipid® (n=7) with Ringer's acetate (n=6) on cardiovascular recovery after a cardiotoxic dose of bupivacaine [18]. We also examined mitochondrial respiratory function in myocardial cell homogenates analyzed promptly after needle biopsies from the animals. Bupivacaine plasma concentrations were quantified from plasma samples. Arterial blood pressure recovered faster, and systemic vascular resistance rose more rapidly after Intralipid than Ringer's acetate administration (p<0.0001), but Intralipid did not increase cardiac index or left ventricular ejection fraction. The lipid-based mitochondrial respiration was stimulated by approximately 30% after Intralipid (p<0.05) but unaffected by Ringer's acetate. The mean (standard deviation) area under the concentration-time curve (AUC) of total bupivacaine was greater after Intralipid (105.2(13.6) mg·min/L) than after Ringer's acetate (88.1(7.1) mg·min/L) (p=0.019). After Intralipid, the AUC of the lipid-un-entrapped bupivacaine portion (97.0(14.5) mg·min/L) was 8% lower than that of total bupivacaine (p<0.0001). To conclude, 4 mL/kg of Intralipid expedited cardiovascular recovery from bupivacaine cardiotoxicity mainly by increasing systemic vascular resistance. The increased myocardial mitochondrial respiration and bupivacaine entrapment after Intralipid did not improve cardiac function [18].

Lipid emulsions have been used to treat various drug toxicities and for total parenteral nutrition therapy. Their usefulness has also been confirmed in patients with local anesthetic-induced cardiac toxicity. The purpose of this study was to measure the hemodynamic and composition effects of lipid emulsions and to elucidate the mechanism

associated with changes in intracellular calcium levels in myocardiocytes.

We measured hemodynamic effects using a digital analysis system after Intralipid® and Lipofundin® MCT/LCT were infused into hearts hanging in a Langendorff perfusion system [19,20]. We measured the effects of the lipid emulsions on intracellular calcium levels in H9c2 cells by confocal microscopy.

Infusion of Lipofundin® MCT/LCT 20% (1 ml/kg) resulted in a significant increase in left ventricular systolic pressure compared to that after infusing modified Krebs-Henseleit solution (1 ml/kg) (P=0.003, 95% confidence interval [CI], 2.4-12.5). Lipofundin® MCT/LCT 20% had a more positive inotropic effect than that of Intralipid® 20% (P=0.009, 95% CI, 1.4-11.6). Both lipid emulsion treatments increased intracellular calcium levels. Lipofundin® MCT/LCT (0.01%) increased intracellular calcium level more than that of 0.01% Intralipid® (P<0.05, 95% CI, 0.0-1.9).

These two lipid emulsions had different inotropic effects depending on their triglyceride component. The inotropic effect of lipid emulsions could be related with intracellular calcium level [19].

Accidental intravascular or high-dose injection of local anesthetics (LA) can result in serious, potentially life-threatening complications. Indeed, adequate supportive measures and the administration of lipid emulsions are required in such complications.

The study's objectives were threefold:

(i) evaluate the myocardial toxicity of levobupivacaine when administered intravenously;

(ii) investigate levobupivacaine toxicity on cardiomyocytes mitochondrial functions and cellular structure; (iii) assess the protective effects of a lipid emulsion in the presence or absence of myocardial ischemia. Domestic pigs randomized into two groups of 24 animals each, with either preserved coronary circulation or experimental myocardial ischemia.

Six animals from each group received either:

(i) single IV injection of saline,

(ii) lipid emulsion (Intralipid (®)),

(iii) levobupivacaine,

(iv) combination levobupivacaine-Intralipid (®).

Serially measured endpoints included: heart rate, duration of the monophasic action potentials (dMAP), mean arterial pressure, and peak of the time derivative of left ventricular pressure (LV dP/dtmax). In addition, the following cardiomyocytes mitochondrial functions were measured: reactive oxygen species (ROS) production, oxidative phosphorylation, and calcium retention capacity (CRC) as well as the consequences of ROS production on lipids, proteins, and DNA. IV injection of levobupivacaine induced sinus bradycardia and reduced dMAP and LV dP/dtmax. At the mitochondrial level, oxygen consumption and CRC were decreased. In contrast, ROS production was increased leading to enhanced lipid peroxidation and structural alterations of proteins and DNA. Myocardial ischemia was associated with global worsening of all changes. Intralipid (®) quickly improved haemodynamics.

However, beneficial effects of Intralipid (®) were less clear after myocardial ischemia [20].

Cocaine intoxication leads to over 500,000 emergency department visits annually in the United States and ethanol cointoxication occurs in 34% of those cases. Cardiotoxicity is an ominous complication of cocaine and cocaethylene overdose for which no specific antidote exists. Because infusion of lipid emulsion (Intralipid) can treat lipophilic local anesthetic toxicity and cocaine is an amphipathic local anesthetic, the authors tested whether lipid emulsion could attenuate cocaine cardiotoxicity *in vivo* [21]. The effects of lipid emulsion were compared with the metabolically inert sulfobutylether-β-cyclodextrin (SBE-β-CD; Captisol) in an isolated heart model of cocaine and cocaethylene toxicity to determine if capture alone could exert similar benefit as lipid emulsion, which exhibits multimodal effects. The authors then tested if cocaine and cocaethylene, like bupivacaine, inhibit lipid-based metabolism in isolated cardiac mitochondria.

For whole animal experiments, Sprague-Dawley rats were anesthetized, instrumented, and pre-treated with lipid emulsion followed by a continuous infusion of cocaine to assess time of onset of cocaine toxicity. For ex vivo experiments, rat hearts were placed onto a nonrecirculating Langendorff system perfused with Krebs-Henseleit solution. Heart rate, left ventricle maximum developed pressure (LVdevP), left ventricle diastolic pressure, maximum rate of contraction (+dP/dtmax), maximum rate of relaxation (-dP/dtmax), rate-pressure product (RPP=heart rate×LVdevP), and line pressure were monitored continuously during the experiment. A dose response to cocaine (10, 30, 50, and 100 µmol/L) and cocaethylene (10, 30, and 50 µmol/L) was generated in the absence or presence of either 0.25% lipid emulsion or SBE-β-CD. Substrate-specific rates of oxygen consumption were measured in interfibrillar cardiac mitochondria in the presence of cocaine, cocaethylene, ecgonine, and benzoylecgonine.

Treatment with lipid emulsion delayed onset of hypotension (140 seconds vs. 279 seconds; p = 0.008) and asystole (369 seconds vs. 607 seconds; p = 0.02) in whole animals. Cocaine and cocaethylene induced dose-dependent decreases in RPP, +dP/dtmax, and -dP/dtmax abs (p<0.0001) in Langendorff hearts; line pressure was increased by cocaine and cocaethylene infusion, but not altered by treatment. Lipid emulsion attenuated cocaine- and cocaethylene-induced cardiac depression. SBE-β-CD alone evoked a mild cardio depressant effect (p<0.0001) but attenuated further cocaine- and cocaethylene-induced decrements in cardiac contractility at high concentrations of drug (100 µmol/L; p<0.001). Finally, both cocaine and cocaethylene, but not ecgonine and benzoylecgonine, inhibited lipid-dependent mitochondrial respiration by blocking carnitine exchange (p<0.05).

A commercially available lipid emulsion was able to delay progression of cocaine cardiac toxicity *in vivo*. Further, it improved acute cocaine- and cocaethylene-induced cardiac toxicity in rat isolated heart while SBE-β-CD was effective only at the highest cocaine concentration. Further, both cocaine and cocaethylene inhibited lipid-dependent mitochondrial respiration. Collectively, this suggests that scavenging-independent effects of lipid emulsion may contribute to reversal of acute cocaine and cocaethylene cardiotoxicity, and the beneficial effects may involve mitochondrial lipid processing [21].

We hypothesized that acute lipid-induced insulin resistance would be attenuated in high-oxidative muscle of lean trained (LT) endurance athletes due to their enhanced metabolic flexibility and mitochondrial capacity [22]. Lean sedentary (LS), obese sedentary (OS), and LT participants completed two hyperinsulinemic euglycemic clamp studies with and without (glycerol control) the coinfusion of Intralipid. Metabolic flexibility was measured by indirect calorimetry as the oxidation of fatty acids and glucose during fasted and insulin-stimulated conditions, the latter with and without lipid oversupply. Muscle biopsies were obtained for mitochondrial and insulin-signaling studies. During hyperinsulinemia without lipid, glucose infusion rate (GIR) was lowest in OS due to lower rates of nonoxidative glucose disposal (NOGD), whereas state 4 respiration was increased in all groups. Lipid infusion reduced GIR similarly in all subjects and reduced state 4 respiration. However, in LT subjects, fat oxidation was higher with lipid oversupply, and although glucose oxidation was reduced, NOGD was better preserved compared with LS and OS subjects. Mitochondrial performance was positively associated with better NOGD and insulin sensitivity in both conditions. We conclude that enhanced mitochondrial performance with exercise is related to better metabolic flexibility and insulin sensitivity in response to lipid overload [22].

Conclusion

Two case reports of myoclonus of legs post spinal anesthesia treated successfully by IV lipid emulsion are first described in the medical literature.

A review of cases of myoclonus post regional anesthesia (spinal or epidural) are discussed with the hypothesis that the Lipid Emulsion effects are on the mitochondria and the intracellular calcium.

References

1. Caviness JN (2014) Treatment of myoclonus. Neurotherapeutics 11: 188-200.

2. Espay AJ, Chen R (2013) Myoclonus. Continuum (Minneap Minn) 19: 1264-1286.

3. Bamgbade OA, Alfa JA, Khalaf WM, Zuokumor AP (2009) Central neuraxial anaesthesia presenting with spinal myoclonus in the perioperative period: a case series. J Med Case Rep 3: 7293.

4. Ford B1, Pullman SL, Khandji A, Goodman R (1997) Spinal myoclonus induced by an intrathecal catheter. Mov Disord 12: 1042-1045.

5. Menezes FV, Venkat N (2006) Spinal myoclonus following combined spinal-epidural anaesthesia for Caesarean section. Anaesthesia 61: 597-600.

6. Hachisuka K, Ogata H, Kohshi K (1991) Post-operative paraplegia with spinal myoclonus possibly caused by epidural anaesthesia: case report. Paraplegia 29:131-136.

7. Kang HY, Lee SW, Hong EP, Sim YH, Lee SM, et al. (2016) Myoclonus-like involuntary movements following cesarean delivery epidural anesthesia. J Clin Anesth 34: 392-394.

8. Nakamoto T, Hirota K, Iwai T, Shingu K (2015) Complete resolution of myoclonus-like involuntary movements under subarachnoid block after midazolam administration in a patient undergoing cesarean section: a case report. Korean J Anesthesiol 68: 193-195.

9. Abrão J, Bianco Mde P, Roma W, Krippa JE, Hallak JE (2011) Spinal myoclonus after subarachnoid anesthesia with bupivacaine. Rev Bras Anestesiol 61: 619-623.

10. Lee JJ, Hwang SM, Lee JS, Jang JS, Lim SY, et al. (2010) Recurrent spinal myoclonus after two episodes of spinal anesthesia at a 1-year interval -A case report. Korean J Anesthesiol 59: S62-S64.

11. Hisano Y, Nakamura K, Kitamura R, Ogino Y, Hirata S, et al. (2010) Myoclonus following spinal and epidural anesthesia--a case report. Masui 59: 770-772.

12. Zamidei L, Bandini M, Michelagnoli G, Campostrini R, Consales G (2010) Propriospinal myoclonus following intrathecal bupivacaine in hip surgery: a case report. Minerva Anestesiol 76: 290-293.

13. Shin HW, Ye BS, Kim J, Kim SM, Sohn YH (2007) The contribution of a spinal mechanism in developing peripheral myoclonus: a case report. Mov Disord 22: 1350-1352.

14. Nakatani K, Nakafusa J, Katekawa Y, Chinen K (1999) Spinal myoclonus possibly caused by epidural anesthesia. Masui 48: 1248-1249.

15. Ogata K, Yamada T, Yoshimura T, Taniwaki T, Kira J (1999) A case of spinal myoclonus associated with epidural block for lumbago. Rinsho Shinkeigaku 39: 658-660.

16. Cartwright PD, Hesse C, Jackson AO (1993) Myoclonic spasms following intrathecal diamorphine. J Pain Symptom Manage 8: 492-495.

17. Watanabe S, Ono A, Naito H (1990) Periodic leg movements during either epidural or spinal anesthesia in an elderly man without sleep-related (nocturnal) myoclonus. Sleep 13: 262-266.

18. Heinonen JA, Schramko AA, Skrifvars MB, Litonius E, Backman JT, et al. (2017) The effects of intravenous lipid emulsion on hemodynamic recovery and myocardial cell mitochondrial function after bupivacaine toxicity in anesthetized pigs. Hum Exp Toxicol 36: 365-375.

19. Park J, Kim YA, Han JY, Jin S, Ok SH, et al. (2016) Lipofundin® MCT/LCT 20% increase left ventricular systolic pressure in an ex vivo rat heart model via increase of intracellular calcium level. Korean J Anesthesiol 69: 57-62.

20. Mamou Z, Descotes J, Chevalier P, Bui-Xuan B, Romestaing C, et al. (2015) Electrophysiological, haemodynamic, and mitochondrial alterations induced by levobupivacaine during myocardial ischemia in a pig model: protection by lipid emulsions? Fundam Clin Pharmacol 29: 439-449.

21. Fettiplace MR, Pichurko A, Ripper R, Lin B, Kowal K, et al. (2015) Cardiac depression induced by cocaine or cocaethylene is alleviated by lipid emulsion more effectively than by sulfobutylether-β-cyclodextrin. Acad Emerg Med 22: 508-517.

22. Dubé JJ, Coen PM, DiStefano G, Chacon AC, Helbling NL, et al. (2014) Effects of acute lipid overload on skeletal muscle insulin resistance, metabolic flexibility, and mitochondrial performance. Am J Physio 15: 307.

Supporting Links

23. https://www.youtube.com/watch?v=dXdJkvX-jlo&feature=youtu.be

24. https://www.youtube.com/watch?v=W9QbSiV3pxQ&app=desktop

25. https://www.youtube.com/watch?v=7DIu9gpkCuo&feature=youtu.be