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CASE REPORT

Suspected chyle leak during complex spine surgery A unique case of propofol infusion resulting in lipid emulsion pooling in the surgical field

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ABSTRACT

The authors report a case of propofol infusion being mistaken for chyle during a two stage thoracic spinal fusion. Propofol is commonly used during spine surgery to facilitate neuromonitoring and there are no reported cases of these observations in the spine literature. We describe the positioning, timing, and treatment in a patient that required prolonged care to rule out a chylothorax. Chyle and the pharmacologic and physiologic effects of propofol are discussed. This review outlines our reasoning and steps used to rule out a chyle leak in the setting of propofol-based anesthesia.

Key words: chest tube, chylothorax, motor evoked potential monitoring, neuromonitoring, propofol infusion syndrome, PRIS, thoracic duct, thoracotomy, total intravenous anesthesia, TIVA

Introduction

Intravenous propofol infusion is often used to provide anesthesia for patients undergoing surgical procedures requiring motor evoked potential (MEP) monitoring. We present a unique case in which high - dose propofol - given over a prolonged period of time - resulted in lipid emulsion pooling in the operative field during elective bilateral extracavitary excision of T7 with posterior instrumentation.

Case presentation

A 22 year old, 170 cm, 85 kg female presented with thoracic myelopathy due to a T7 hemivertebrae. Following a history, physical exam, and imaging she was scheduled for a bilateral extracavitary excision of T7 with posterior instrumentation, requiring prone positioning for several hours. When placed in the prone position, the patient's neuromonitoring status showed no motor signals in her legs and very faint signals in her arms. Without neuromonitoring, it was felt that the patient would be at increased risk for cord ischemia. The operative plan was therefore changed to a limited right posterolateral thoracotomy and excision of the anterior hemivertebrae.

Four days later, she underwent an uncomplicated right thoracotomy and excision of the anterior hemivertebrae with MEP monitoring. Anesthesia time for the first stage was 370 minutes, of which 240 minutes involved maintenance with a continuous propofol infusion (100-250 mcg/kg/min). Chest tube placement, to suction overnight, revealed minimal serosanguineous drainage. Two days later, a second stage posterior extracavitary excision of the hemivertebrae and stabilization with percutaneous pedicle screw instrumentation was performed with MEP monitoring. Anesthesia time for the second stage was 607 minutes, of which 547 minutes involved maintenance with a continuous propofol infusion (175-225 mcg/kg/min). While excising the vertebrae it was noted that, after the left pedicle and part of the vertebral body were removed, a white "milky" substance was beginning to pool at the bottom of the surgical cavity. Thoracic surgery was consulted intraoperatively and they believed that this was a potential chyle leak. The remainder of the operation was completed without complication. Chest tube and surgical drain (placed adjacent to the site of the suspected chyle leak) output was monitored for 5 days. Because of the suspected chyle

leak, parenteral nutrition with short and medium chain fatty acids was initiated immediately postoperatively. Postoperatively, no chyle was visible in the drain or chest tube. Pleural fluid analysis revealed a triglyceride concentration of 67 mg/dl, which is below the concentration (>110 mg/dl) indicative of a chylous effusion. Trials of whole milk and other liquids that contained long chain fatty acids did not result in increased chest tube and surgical drain output, or chylous appearance. The surgical drain and chest tube were discontinued on postoperative day (POD) #5 and POD #6, respectively.

Discussion

Anesthesia and During Motor Evoked Potential Monitoring

For decades, somatosensory evoked potentials (SSEP) were considered the gold standard monitoring tool for assessing the integrity of neuronal pathways in patients undergoing spine (or plexus) surgery during general anesthesia. (1) However, numerous case reports emerged during this time describing motor pathway injury despite normal intraoperative SSEP monitoring. (1) As a result, MEP monitoring was developed to assess anterior descending motor pathways. (1,2) Unfortunately, previous animal- and human-based studies reported dramatic deterioration of traditional analog MEPs with even scant amounts of inhaled (e.g., isoflurane) or many intravenous (e.g., propofol) anesthetics thereby precluding intelligible data acquisition during general anesthesia using these options. (3) During the early stages of MEP development, the anesthesia armamentarium typically consisted of one or more of the following intravenous medications: opioid, benzodiazepine, ketamine, and muscle relaxant (when appropriate). However, these anesthetics were often cumbersome to administer and raised concerns about intraoperative awareness and prolonged emergence. (3)

The next generation of MEP monitors, incorporating digital processing, demonstrated less erroneous interpretation due to the pharmacophysiologic effects of intravenous propofol and low-dose isoflurane. This has simplified anesthetic management of these types of cases and lessened the concerns of intraoperative awareness and delayed emergence. Currently at our institution, we typically provide total intravenous anesthesia with combined propofol and opioid infusions during acquisition of baseline signals. Subsequently, inhaled volatile anesthesia may be titrated in as tolerated by the MEP signal response. It is imperative to avoid dramatic changes in the level of anesthesia (intravenous or inhaled) during the critical period(s) of surgery (e.g., spine distraction) so as to avoid falsely positive signal changes.

Propofol Anesthesia

Propofol is a hypnotic agent that is commonly used for induction and maintenance of anesthesia. Propofol (2,6-diisopropofol) is the most frequently used intravenous anesthetic in current use. (4) The current formulation consists of 1% (wt/vol) propofol, 10% soybean oil, 2.25% glycerol, and 1.2% purified egg phosphatide. (5) The oil portion is 10% or 100 mg/mL of fat. This is much higher than the normal triglyceride level which is 1.5 mg/mL or 150 mg/dL. Serum triglyceride levels of more than 10 mg/mL or 1000 mg/dL have been know to cause pancreatitis and lead to propofol infusion syndrome (PRIS). The hypnotic action of propofol is mostly mediated by enhancing γ-aminobutyric acid (GABA)–induced chloride current through its binding to the β-subunit of the $GABA_A$ receptor. Sites on the β_1-subunit (M 286), β_2-subunit (M 286), and β_3-subunit (N265) of the transmembrane domains are crucial for the hypnotic action of propofol. (5) The α-subunit and γ_2-subunit subtypes also seem to contribute to modulating the effects of propofol on the GABA receptor. Propofol, through its action on $GABA_A$ receptors in the hippocampus, inhibits acetylcholine release in the hippocampus and prefrontal cortex. (5) The α_2-adrenoreceptor system also seems to play an indirect role in the sedative effects of propofol. (4) Propofol results in widespread inhibition of the N-methyl-D-aspartate (NMDA) subtype of glutamate receptor through modulation of sodium channel gating, an action that also may contribute to the drug's central nervous system (CNS) effects. Studies have shown that propofol has a direct depressant effect on neurons of the spinal cord. (5) In regard to neuromonitoring, the motor pathways and MEPs are susceptible to anesthetic agents at three sites along the neuraxis: motor cortex, anterior horn cells, and the neuromuscular junction. (2)

In the clinical setting, several infusion schemes have been used to achieve adequate plasma concentrations of propofol. (5) Maintenance dose infusion rates necessary to achieve surgical anesthesia typically range from 100 to 200 μg/kg/min. (5)

Patients (frequently pediatric, rarely adults) receiving high-dose long-term (exceeding 48 hours) propofol infusions, may demonstrate a rare constellation of symptoms referred to as the PRIS. (6,7) PRIS is defined as the occurrence of bradycardia recalcitrant to therapy and progressing to asystole, lipemic plasma, fatty liver enlargement, metabolic acidosis with base deficits exceeding 10 mmol/l, rhabdomyolysis or myoglobinuria. (7) The lipemia is likely due to failure of hepatic lipid regulation, possibly related to poor oxygenation or low glucose plasma concentrations. Lipemia could lead to sequestration of propofol into the lipid phase thereby decreasing free propofol levels (i.e., the pharmacologically active form of the drug) and apparent insensitivity to propofol. (6,7) Fat overload associated with propofol infusions may also contribute to increased free fatty acids. (6,7) Fat metabolism analysis of patients with PRIS resemble those found in patients with mitochondrial cytopathies, acquired acyl-carnitine metabolism deficiencies, hereditary mitochondrial fatty acid metabolism impairment resembling medium-chain acyl-CoA dehydrogenase deficiency, or low carbohydrate supply (because energy demand is satisfied by lipolysis if car-

bohydrate supply is low). (6,7) In some cases, lipemia was the first indication of impending PRIS. (6,7)

There is really only one case reported in the literature of propofol mimicking a chyle leak. Vokes, in 2006, noticed a milky substance in a neck dissection for a recurrent cervical chordoma with multiple masses. (4) About 6 hours after anesthesia was begun they visualized a milky fluid and they had already tied off the thoracic duct and no leak was found in that area. They knew the patient had not eaten for several hours before surgery and doubted that chyle was leaking. They observed that the substance was coming from multiple bleeding areas and was separating itself from the blood. The propofol rate was 350 mcg/kg/min during surgery and they drew a syringe full of the substance and blood which layered out after 20 minutes. They also sent a sample for analysis and it had a triglyceride level of >100 mg/mL (or 10,000 mg/dL). They recommended aspirating a sample of suspected fluid, chyle or propofol, and having it sit to separate. They also sent samples for analysis to detect the triglyceride level.

Chyle

Chyle is lymph fluid which is usually a milky substance found in the thoracic duct and other lymph vessels draining the enteric system. It is produced after eating a fatty meal and contains chylomicrons from long chain triglycerides and lymphocytes in an electrolyte balance similar to plasma. The milky color clears after fasting and returns rapidly after eating fat containing meals. Leakage of chyle, usually iatrogenic in origin at the time of an intrathoracic procedure, can lead to an intrathoracic collection termed chylothorax. Left unrecognized, a chylothorax can lead to respiratory compromise, nutritional depletion and a relative immunocompromised state due to loss of immunoglobulins from the systemic circulation. Leaks are commonly treated with oral fasting and parenteral nutrition to allow the low pressure system to seal. In general, this can take approximately one week to resolve such that normal oral feeding can resume without reoccurrence of the chylothorax.

Propofol mimicking chyles leaks has not been reported in the spine literature. Due to the large volume of cases being performed using propofol and narcotics as the anesthetic, it is worth reviewing this situation to educate others of the potential misdiagnosis when one entity is mistaken for the other. Chyle can range from 400 mg to 6000 mg/dL of fat depending on the proximity to a high fat meal and is often considered in the differential diagnosis when high volume outputs are recorded persistently from intrathoracic drains. With continued fasting, lymph fluid from a chylothorax becomes more serous in nature as its high lipid content progressively decreases. Propofol has a concentration of 10,000 mg/dL of fat and can appear very similar to fat.

Putting it all together

After reviewing the situation and the literature, several points can be made to support our belief that the fluid was propofol. First, the initial stage of the operation was performed via a right sided thoracotomy. Although injury to the thoracic duct can occur with a right sided thoracotomy, it more commonly occurs after a left sided procedure. Second, we noticed the "milky substance" while posteriorly entering the left hemithorax during the second stage of her operation, after the patient was nil per os for 72 hours. In a fasting patient, the presence of "milky fluid" occurring in the opposite hemithorax of the initial operation, that could not be manifested radiographically, clinically or by quantitative drain output analysis by provocative postoperative lipid loading maneuvers, suggests that the "milky fluid" was likely propofol extravasation into the surgical cavity. In our case, our patient did not manifest the clinical aberrations typically associated with PRIS. However, due to the prolonged nature of her surgeries performed under anesthesia maintained with a high propofol infusion rate, hepatic and extrahepatic lipid regulation may have been impaired thereby leading to lipemia.

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