Case study of a pseudocholanisterase deficiency

Summary

This paper comments a case of recovery delay after general anesthesia due to a pseudocholanisterase deficiency. The author presents the case and how it was handled, give a brief overview of the different possible sources of delayed recovery after general anesthesia, and propose a literature-based approach to assess and manage recovery delay. The paper concludes with the four key aspects related to pseudocholanisterase deficiency, namely mechanical ventilation until complete elimination of succinylcholine, determination of pseudocholanisterase levels, avoidance of exposure to succinylcholine, and notifications for subsequent treatments.

Key Words

DELAY RECOVERY, PSEUDOCHOLANISTERASE DEFICIENCY, SUCCINYLCHOLINE

Introduction

The enzyme pseudocholinesterase is produced by the liver and released into the plasma. It is involved in the metabolism of muscle relaxants such as succinylcholine and mivacurium. Pseudocholinesterase deficiency, arising from inherited, acquired, and iatrogenic causes, produces prolonged neuromuscular blockade after succinylcholine administration. Here, we report a delayed recovery from paralysis by succinylcholine in A 67 years old female with a genetically inherited pseudocholinesterase deficiency that hadn't been diagnosed preoperatively.

Observation

A 67 years old female weighing 52 kg presented with right femoral neck fracture due to an accidental fall from a chair. Physical evaluation was normal.

Her past medical history was notable for chronic obstructive pulmonary disease (COPD), chronic high blood pressure, epilepsy, osteoporosis, and depressive syndrome. Her surgical history listed appendectomy, resection of an ovarian cyst, and left femoral neck fracture. Her ongoing medications included valproic acid 500 mg, paracetamol-codeine, tilidine-naloxone, alendronic acid, calcium carbonate-colecalciférol, and lorazepam. The patient denied allergies.

The preoperative lab results showed a hemogram and electrolytes within normal ranges apart from a slight anaemia (HB: 11.6 g/dL), and a slight lowering of platelet count (137000/mm^3). She had a normal baseline coagulation, renal function and ions.

The total body scanner didn't show any other acute injury. The patient was scheduled for emergency surgery.

For the anesthetic procedure, routine monitoring of non-invasive blood pressure, electrocardiogram, and peripheral oxygen saturation were applied. Before induction, blood pressure was measured at 160/80 mmHg, and heart rate was 75/min. Anesthesia was induced using 70 mg of propofol 1%, 5 µg of sufentanil,20 mg of lidocaine 2 %, 25 mg of ketamine, and 2 g of cefazoline. Neuromuscular blockade was provided with succinylcholine at a dose of 1 mg/kg. Nasotracheal intubation was accomplished using a size 7.0 cuffed tube and the tube was fixed after ascertaining its correct placement. Anesthesia was maintained using 50 % oxygen, 50 % nitrous oxide and sevoflurane 1.5 %. During surgery, intravenous fluids were used to sustain a mean arterial pressure of 115 mmHg. Surgery and anesthesia were uneventful. The case lasted for 1 hour. Although no additional doses of neuromuscular blocking agent were administered, and although sevoflurane was switched off and replaced with 100 % oxygen at the time of skin closure, the patient showed no signs of arousal or spontaneous ventilation, even after 15 minutes.

TOF stimulation with 60 Hz was applied. The patient had 4 twitches without fading but with very low amplitude. The patient body temperature was 37.3℃. Arterial blood gas analysis showed mild respiratory acidosis (pH: 7.26, the rest of was normal). Therefore hypoglycemia, dyselectrolytemia, and hypothermia could be excluded. In order to compensate for the mild respiratory acidosis, mechanical ventilation was intensified.

Comment [BV1]: 60 mA?

Afterwards, the patient began to respond to external stimuli. However, low tidal volume and increased end-tidal CO2 were observed. For this reason, a decision was to perform a brain CT scan was made. No acute cerebral injury was objectified after comparison with the pre-operative body scan. Therefore, our patient was transferred to the recovery room, where the mechanical ventilation was continued. The patient was ventilated using

a tidal volume of 400 mL, a respiratory rate of 12/min using a BiPAP mode, 40 % inspired fraction of oxygen, and 5 mmHg of positive end-expiratory pressure. Active external heating was applied. Three hour after her admission to the recovery room, the patient was responding well, was stable, and her trachea was extubated. Blood samples were collected for plasma cholinesterase measurement. Lab results showed 1.8 UI of plasma cholinesterase, while the normal values for females are between 4.4 and 13.5. Dibucaine number was 43 %, while the normal values are between 68-78 %. These results confirmed our hypothesis for the reason of delayed recovery.

Comment [BV2]: /L? /dL?

Discussion

Delayed emergence from anesthesia can be due to physiological causes (hypoglycemia, hyperglycemia, dyselectrolytemia, hypothermia), or pharmacological causes (opioid/benzodiazepine over dosage, residual neuromuscular blockade).

Metabolic causes

Hypoglycemia

Neuroglycopenia manifests as confusion, abnormal behavior, seizures, and coma. In the elderly population, lateralizing neurological signs are commonly seen. Postoperative hypoglycemia most often results from poorly controlled diabetes, starvation, and alcohol consumption. Alcohol impairs gluconeogenesis, and exacerbates hypoglycemia in starved patients, or those with minimal energy reserves.

Hyperglycemia

Severe hyperglycemia can prolong unconsciousness after anesthesia. A venous blood glucose > 14 mmol/L causes osmotic diuresis and dehydration in the untreated patient. The effects of dehydration range from drowsiness to acidosis.

Hyponatremia

Serum sodium concentration < 110 mmol/L causes seizures, coma, and increased mortality. The causes of a hyponatraemia pertinent to anesthesia are the conditions that may develop during operation.

Hypothermia

Neurological and respiratory changes occur with decreasing temperature, e.g. confusion (< 35°C), unconsciousness (< 30°C), apnea (< 24°C), absent cerebral activity (< 18°C). The direct hypothermic effects on the brain tissue are associated with cardiovascular and respiratory disturbances that occur at higher temperatures.

Hypercapnia

Hypercapnia, detected by central chemoreceptors, initially stimulates ventilation but thereafter depresses the regulatory respiratory centers of the brain causing hypoventilation and apnea. Respiratory acidosis results from hypoventilation, rendering the patient acidemic

Neurological causes

The common mechanism is ischemic brain destruction. Periods of hypoxemia or ischemia may occur during surgery; these are often the result of inadequate cerebral perfusion secondary to low mean arterial pressure (MAP). Cerebral auto-regulation in the normal brain occurs between 60 and 160 mmHg of mean arterial pressure. Intracranial hemorrhage, thrombosis, or infarction can occur in association with intraoperative arrhythmias, hypo- or hypertension, or in patients with abnormal cerebral vasculature.

Pharmacological causes

The residual effects of a drug are influenced by a number of factors. This renders the choice of an ideal dose for a given patient difficult, insofar as the same dose can have a very different effect on apparently similar patients.

Benzodiazepines

Benzodiazepines combined with high-dose opioids can have a pronounced effect on respiratory depression, producing hypercapnia and coma.

Opioids

There are two major mechanisms resulting in opioid-induced coma: respiratory depression and direct sedation through opioid receptor activation. The sensitivity of the brainstem chemoreceptors to carbon dioxide is reduced by opioids, with subsequent dose-dependent respiratory depression and hypercapnia.

Hypnotic anesthetic agents

Propofol has a large volume of distribution at steady-state and a relatively long elimination half-life. Therefore, the effect of propofol after total intravenous anesthesia (TIVA) can be prolonged, particularly after long lasting surgeries.

Residual neuromuscular blockade: Cholinesterase deficiency

Neuromuscular blockade duration after succinylcholine is primarily determined by plasma cholinesterase hydrolysis. Succinylcholine is the only available depolarizing neuromuscular blocking agent for clinical use. When succinylcholine is not metabolized by cholinesterase, prolonged activation of the acetylcholine receptors occurs.

Depolarization neuromuscular block is also called Phase I or accommodation block. It often follows muscle fasciculation. Prolonged exposure of the neuromuscular junction to

succinylcholine can result in a desensitization block or Phase II block. In patients with atypical plasma cholinesterase, Phase II block can develop after a single dose of the drug. The block is characterized by fade of the train-of-four (TOF) twitch response, tetanic fade and post-tetanic potentiation, which are all features of competitive block. After the initial depolarization, the membrane potential gradually returns towards the resting state, even though the neuromuscular junction is still exposed to the drug. Neurotransmission remains blocked throughout.

In patients with pseudocholinesterase variations, biochemical investigations such as the dibucaine number (DN) determination, and pseudocholinesterase (PChE) concentration measurement can help identifying individuals at risk for prolonged paralysis following the administration of succinylcholine. DN is the percent of pseudocholinesterase (PChE) enzyme activity that is inhibited by dibucaine. Decreased PChE enzyme activity in conjunction with a DN less than 30 suggests high risk for prolonged paralysis.

Reasons for plasma cholinesterase activity variation may be physiological, acquired or inherited. Among the physiological changes, the first trimester of gestation sees a 20% decrease in PChE activity. Neonates also display decreased PChE activity.

Several diseases are associated with a decrease in plasma cholinesterase activity, such as liver diseases, cancer with distant metastasis, malnutrition and extensive burns.

Plasmaferesis, oral contraceptives, and noncompetitive cholinesterase inhibitors (cyclosphamide) are also responsible for some pseudocholinesterase activity decreases. Inherited disorders of pseudocholinesterase activity are not frequent. Atypical homozygosis is estimated to occur in 1/3000 to 1/10000 patients, which are sensitive to succinylcholine. Heterozygosis occur in 1/25.

Management of patients with prolonged apnea after succinylcholine primarily involves controlled ventilation and sedation, which should be maintained until muscle strength fully recovers. Subsequent patient and relatives counselling is important, and the need for extensive investigation should be stressed, in order to identify the variant carried by the patient.

Approach to assess and manage delay in recovery

A stepwise approach to assessing and managing the unconscious patient is outlined in Figure 1 in the appendix. Clearly, it is important to assess each case individually.

Conclusion

In conclusion, if pseudocholinesterase deficiency is the suspected cause of unexpected prolonged apnea after succinylcholine administration, the following measures are very important: 1) controlled mechanical ventilation with adequate sedation until succinylcholine is completely metabolized; 2) determination of pseudocholinesterase levels in the patient and all family members; 3) avoidance of further exposure to succinylcholine, mivacurium, and administer local anaesthetics; and 4) adequate notification of pseudocholinesterase deficiency to care givers during any subsequent hospitalization.

Comment [BV3]: What does this mean?

References

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Appendix

Fig1. Approach to assess and manage delay in recovery