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Anesthesiology

CASE REPORT OF PSEUDOCHOLINESTERASE ENZYME DEFICIENCY

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ABSTRACT **Introduction:** Pseudocholinestersase enzyme is a plasma enzyme that is responsible for the degradation of the succinylcholine in the plasma. Its deficiency is either genetic or acquired. Deficiency of pseudocholinesterase is a rare condition where there is delayed emergence of the patient from the effect of succinylcholine due to its prolonged action. **Epidemiology:** It is a rare disorder with incidence in homozygotes of 1 in 2000-5000 people and heterozygotes of 1 in 500 people. **Case study:** A child was taken for emergency direct laryngoscopy for foreign body removal under general anaesthesia, after there no emergence from succinylcholine and the patient was shifted to icu for mechanical ventilation, after which patient was tested for pseudocholinesterase enzyme which was found to be deficit. **Physiology:** Succinlycholine is a depolarizing muscle relaxant which act on the acetylcholine receptors to cause the muscle relaxation. **Pathophysiology:** Pseudocholinesterase deficiency is either or acquired, due to which there is prolonged action of the succinylcholine and delayed emergence. **Diagnostic test:** Dibucaine number is the diagnostic test for pseudocholinesterase deficiency. **Treatment:** Only effective treatment is mechanical ventilation and family counselling to be cautious in future and not to use succinylcholine or mivacurium. **Conclusion:** Pseudocholinesterase deficiency remains undiagnosed until the patient undergoes succinylcholine exposure. Mechanical ventilation and family counselling are the mainstay for this condition.

KEYWORDS : Pseudocholinesterase Deficiency, Butyrylcholinesterase Deficiency, Residual Neuromuscular Blockade, Delayed Emergence, General Anesthesia

INTRODUCTION:

Pseudocholinesterase is a plasma enzyme produced in the liver that is responsible for the metabolism of common anesthetic drug like Succinylcholine and mivacurium, as well as ester local anaesthesia including cocaine. Individuals with a normally functioning version of the enzyme rapidly metabolize succinylcholine and mivacurium, (less than 10 minutes for succinylcholine). With an inherited deficiency, the defective form of the enzyme is unable to metabolize succinylcholine and mivacurium to same degree, leading to prolonged neuromuscular paralysis for those who inherited atypical pseudocholinesterase enzyme.

It may be either genetic(homozygous or heterozygous) or acquired. Pseudocholinesterase deficiency, sometimes called as butyry lcholinesterase deficiency, is a rare disorder in which the neuromuscular blocking drugs succinylcholine and mivacurium cannot be metabolized properly in the blood plasma. This article summaries the pharmacologic and physiologic data relevant to understanding the basic pathophysiology associated with pseudocholinesterase deficiency and illustrates a case study of a child suspected of having the disorder after a prolonged delay in emergence from general anaesthesia.

Etiology:

- It may be acquired of inherited.
- Inherited form of the enzyme transfers in an autosomal recessive manner secondary to mutations in the butyrylcholinesterase gene, located on chromosome 3 (3q26.1-26.20).
- It may be heterozygous with only one gene mutated, or homozygous with both gene for the acetycholinesterase mutated. Heterozygotes present with approximately 30% increase in duration of neuromuscular block. Homozygotes present with neuromuscular block of 2-3 hrs.

Epidemiology:

Rare condition which occurs in 1 in 2000-5000 people for homozygotes and in heterozygotes, incidence is 1 per 500. Male female ratio is 2:1. It is more prevelant in races like jewish, persian, Turkish, arya vysya indian native and alaskan people.

Case study:

A 6.5 years old male child of Dalwadi cast (weight 20 kg, height 128cm) presented with history of coin ingestion. The coin was at the level of T1-T2 vertebrae and so treatment to be done was direct laryngoscopy sos esophagoscopy for coin removal under general anaesthesia.

Procedure:

The patient was taken for operation in emergency condition, but was NPO for 6 hrs. A 22-gauge IV line secured in right dorsum and continuous iv drip of DNS was standard. Patient was taken into the OT and was given premedication of Inj. Ondansetron 1.6 g iv, Inj. Glycopyrrolate 80 mg iv , Inj. Midazolam 0.4 mg iv.Standard monitor were applied including pulse oximeter and 5 lead ECG.

Induction:

The patient was preoxygenated with face mask with 100% oxygen for 5 minutes. Induction done with Inj. Ketamine 20 mg iv and sevoflurane as inhalational agent followed by succinylcholine 40 mg. Atraumatic intubation with oral ported cuffed endotracheal tube number 5 mm was done. Bilateral air entry checked, found to be equal. Tube fixed properly.

Maintenance was done with O_2 and N_2O of 50:50% ratio, with sevoflurane as inhalational agent.

Direct laryngoscopy was done and the coin was removed smoothly. After the removal, the patient was given 100% oxygen and inhalational agent was stopped. The patient was not breathing spontaneously and was still completely unresponsive to painful stimuli. Confirmation was made that all anaesthetics, both IV inhalational had been appropriately discontinued. The patient was not responsive for more than 1.5 hrs. throughout that time, patient was maintaining SPO2 (98-100%), pulse (110-120 / min) and was vitallt stable.

After 1.5 hrs, the patient was shifted to PICU for mechanical ventilation and until the patient gains spontaneous respiration and adequate muscle tone. After about 2.5 hours, the patient had spontaneous respiration and also spontaneous muscle tone but not enough to be extubated.

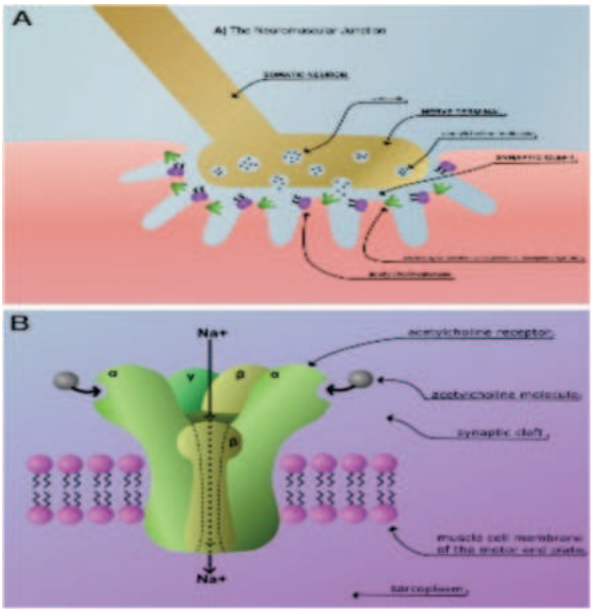
Around 3 hours later, the patient was extubated smoothly with all muscle tone adequately achieved. The post operative period, investigation done for pseudocholinesterase. Enzyme which was found to be deficit.

Value:

Pseudocholinesterase enzyme: 0.142 u/ml (5.32 - 12.92 u/ml)

Family history:
The patient has no family history of any such incidence or no exposure of the patient to any anaesthetic drugs in the past.

Physiology of neuromuscular junction:
The neuromuscular junction is the synapse or site of interaction, between a somatic neuron and skeletal muscle that is composed of the nerve terminal, motor end plate of the muscle and the synaptic cleft.



When a somatic neuron depolarizes, it releases approximately 60,000 to 100,000 acetylcholine (ACh) molecules from the neuron into the synaptic cleft to attach to the muscle-type / nicotinic type-1 ACh receptors (N1AChRs) located on the motor end plate. When 2 ACh molecules attach on the N1AChR, a conformational change occurs of the receptor protein which causes the opening of Na+ ion channel within the structure of receptor, resulting in influx of Na+ ions inside the sarcoplasm of the skeletal muscle cell. This causes the increase in the transmembrane potential, and initiating the muscle cell depolarization. This causes contraction of action of the actin-myosin complexes in myofibrils, causing muscle contraction.

The sodium channels get inactivated until the resting membrane potential of the cell is reestablished. Reactivation of channel occurs (within 15 minute). Acetylcholine molecules in the synaptic cleft are metabolized by acetylcholinesterase enzyme located in synpatic cleft. Acetylchloline molecules that manage to diffuse away from synaptic cleft, is metabolized by butyrylcholinesterase in blood plasma, also known as pseudocholinesterase.

Pathophysiology:
Sch is structurally 2 conjoined Ach molecules, so Sch engages with the N1AchR just like acetylcholine molecules. Sch is metabolised by PchE in the plasma and the extracellular fluid.

Normal Pseudocholinesterase is a glycoprotein composed of 4 identical subunits and is encoded by the gene E_1^u found on chromosome 3. Amino acid substitution in the E_1^u gene causes pseudocholinesterase to have a decreased affinity for Sch, prolonging the normal metabolism of the depolarizing neuromuscular block. Same is with mivacurium.

As the pseudocholinesterase is formed in the liver, acquired cause of PChE includes conditions like malnutrition, pregnancy, post partum periods, burns, liver disease, kidney disease, hemodialysis, MI, CHF, malignancy, chronic infection. Certain other medicines and chemicals such as organophosphate, insecticides, NAD inhibitors, and anticholinesterase drugs can inhibit the activity of the enzyme.

When Sch is injected into the blood stream, normally 90% of the drug is metabolized within 1 minute by pseudocholinesterase, leaving 10% free to perform its action within the neuromuscular junction. Individuals who have structurally ineffective or insufficient quantities of PChE will have higher amounts of active SCh circulating for longer amounts of time.

Chromosome 3q26 is the location of all mutations of the PChE gene. 5 alleles have been identified that code for PChE, usual, atypical, flouride resistant, K-variant and silent.

Diagnostic test:
Dibucaine is a local anesthetic that inhibits ~80% of PChE activity in normal individuals. Heterozygotes (individuals carrying 1 variant allele) will have PChE enzyme activity inhibited by approximately 40–60%.

Homozygotes (with 2 variant alleles) will have their enzyme activity inhibited by ~20%. The percentage of inhibition of referred as **dibucaine number**. The lower the dibucaine number, the longer residual neuromuscular blockade is present.

Treatment / Management :
Mainstay of the treatment involves respiratory support with mechanical ventilation will the spontaneous resolution of neuromuscular blockade.

Patients should also remain sedated during this period. Conservative, supportive treatment with sedation and mechanical ventilation until recovery. This treatment has more risk than reversal with transfusion of plasma or use of other medications, which is less reliable.

Patient and Family Education:
Individuals diagnosed with Pseudocholinesterase deficiency should inform their doctor about their condition before any surgery. Future anesthetics should avoid administration of Sch and mivacurium to avoid prolonged neuromuscular blockade.

Family members of patients with Pseudocholinesterase deficiency are encouraged to have laboratory testing for Pseudocholinesterase.

CONCLUSION:
Pseudocholinesterase deficiency is a rare cause of prolonged paralysis, regarding which any doctor using neuromuscular blockade should be educated.

When suspecting the diagnosis, supportive care should be given to ensure patient safety, a PChE level and DN should be obtained and genetic testing should be offered if indicated.

Genetic counselling should be offered to patients and family members.

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