Pseudocholinesterase Deficiency in an Indian Community

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ABSTRACT

Background: India, the seventh largest country, 3rd largest standing army and one of the oldest civilizations in the world, with a literacy rate of 74.04%. Indian population was a mixture of 46,73,034 categories of different castes and sub-caste each related to a specific occupation. Arya Vysya is a Hindu Indian caste with a total population of 22,952,000. Methods: Pseudocholinesterase is a glycoprotein enzyme with complex molecular structure synthesized in the liver and specifically hydrolyzes certain exogenous cholinesters. Pseudocholinesterase deficiency is a genetic enzyme abnormality or acquired alteration in the metabolism of choline esters in this patient may experience a paralysis of the respiratory muscles, to overcome this, required more time mechanically-assisted breathing. The presence of the genetic defect is not realized until one is exposed to succinylcholine or mivacurium. Results: Arya Vysya community people of India having deficiency of pseudocholinesterase is the most affected people than any other with homozygous mutation incidence rate of 2-4%. Very recent studies in 2016 reveal that malnutrition-induced pseudocholinesterase deficiency is also a possible etiology. Conclusion: It was suggested that the Arya Vysya Community people with a history of pseudocholinesterase deficiency should tell his or her doctor if when they undergo anesthesia for surgery to avoid potentially serious unwanted adverse effects.

Key words: India, Arya Vysya, Pseudocholinestase, Pseudocholinestrase deficiency, Choline esters, Acholest test paper.

INTRODUCTION

India, the 7th largest country, 3rd largest standing army and one of the oldest civilizations in the world, with 29 states and 7 union territories. India has achieved all-round socio-economic progress during the last 70 years of its Independence with a literacy rate of 74.04%. As per March 2011 census reports, India’s population, stood at 1.2 billion (623.7 million males and 586.4 million females) and at present in 2016 it is 1.3 billion. Hinduism (79.8%) is the largest religion in India and a home to two major language families of Indo-Aryan (74%) and Dravidian (24%).[1-3] Socio Economic and Caste Census 2011 conducted by the Registrar General of India has reported that, Indian populations was a mixture of 46,73,034 categories of caste, sub-caste, synonyms, different surnames, gotras in the caste and clan names and each related to a specific occupation.[4,5]

Arya Vysya Community: Arya Vaishya (Arya Vysya) is an Indian caste belongs to the religion of Hinduism. Their population in India is 22,952,000[6] with Gavara and Kalinga...
Pseudocholinesterase: It was reported that, cholinesterase was of 2 types, one is acetylcholinesterase and another one is pseudocholinesterase. Acetylcholinesterases inactivates acetylcholine produced at the neuromuscular junction during neurotransmission whereas pseudocholinesterase, a glycoprotein enzyme having complex molecular structure synthesized in the liver and immediately released into the plasma with a half-life of 12 days also found in many tissues with the exception of red blood cells, and its function is unknown, it has been suggested that it may specifically hydrolyze certain exogenous cholinesters which inhibit acetylcholinesterase.

Pseudocholinesterase deficiency: It is a genetic enzyme abnormality or acquired alteration in the metabolism of choline esters such as succinylcholine, mivacurium, and ester-linked local anesthetics including procaine, chloroprocaine, and, to a lesser extent, cocaine in which the body’s production of butyrylcholinesterase (BuChE) also known as pseudocholinesterase, serum cholinesterase, plasmacholinesterase, and false cholinesterase was impaired.

Symptoms: Unless an affected person was given choline ester drugs and ester-linked local anesthetics, pseudocholinesterase deficiency does not produce any symptoms. Mostly, the patient may experience a paralysis of the respiratory muscles, to overcome this, required more time mechanically-assisted breathing.

Causes: Pseudocholinesterase deficiency can be inherited (genetic) or acquired. Genetic pseudocholinesterase deficiency is due to abnormal alleles that code for the synthesis of pseudocholinesterase and this known as faulty gene which results in abnormal or inadequate levels of plasma enzyme. This faulty gene known as BCHE gene, located on chromosome 3 (3q26.1-q26.2) and its region spans about 70 kb and has 4 exons and 3 introns. Acquired pseudocholinesterase deficiency due to having physiological conditions like chronic infections (tuberculosis), severe burn injuries, liver diseases, malignancy, malnutrition, organophosphate pesticide poisoning, uremia, pregnancy, cardiopulmonary bypass, leprosy and all these conditions may cause lower levels of plasma pseudocholinesterase.

Pathophysiology: In normal healthy persons, about 90% of i.v. administered succinylcholine was inactivated before it reaches to the neuromuscular junction. The left over 10% succinylcholine dose then acts as an acetylcholine receptor agonist and causes depolarization results in initiation of skeletal muscle twitching with in one minute and it was again normal within five minutes. In people with pseudocholinesterase deficiency having very high levels of succinylcholine results in too much and too long depolarization can be taken place and it will be continued may be upto eight hours.

Epidemiology: Pseudocholinesterase deficiency is most common in Arya Vysya community people of India and Persian Jews. Complications: People who have pseudocholinesterase deficiency may be sensitive to certain anesthetic drugs and muscle relaxants. The majorly reported consequences of pseudocholinesterase deficiency are respiratory failure, prolonged paralysis and apnea after administration of succinylcholine or mivacurium. The presence of the genetic defect is not realized until one is exposed to succinylcholine or mivacurium.

Case Reports of Affected Hindu Arya Vysya Community

Arya Vysya community people of India having deficiency of pseudocholinesterase is the most affected groups than any other people with homozygous mutation incidence rate of 2-4%. A study was performed on 22 men and women of Arya Vysya community belonging to Coimbatore, Tamil Nadu state of India showed that 9 of them had pseudocholinesterase deficiency. The gene mutations responsible for absence of pseudocholinesterase activity were identified and it was associated with 58 different mutations, including frame shift mutations, deletions, substitutions, insertions of alu repeats, and mutations affecting intron/exon splicing. The silent phenotype of human pseudocholinesterase has a frequency of 1 in 100,000 in European and American populations, but an extremely high frequency of 1 in 24 in the Vysya community of India. Literature review revealed a total of 40 pseudocholinesterase deficiency cases were being reported in USA from 1956 to 2011. A very recent studies in 2016 reveals that malnutrition-induced pseudocholinesterase deficiency is also a possible etiology. A 36-year-old correctional officer with pseudocholinesterase deficiency when exposed...
to organophosphate toxicity he immediately developed abdominal cramps, diarrhea, sweating, excessive salivation, frequent urination, and increased bronchial secretions. A 19 year old girl underwent her first experience of general anesthesia for 30 minute dentoalveolar procedure and unexpectedly met extubation requirement for 5 hours due to pseudocholinesterase deficiency. The four patients in the Mostas Private Health Hospital, Turkey was identified with positive pseudocholinesterase deficiency. In all four of the patients, the prolonged blocks are deteriorated due to mivacurium use. A 72-year-old male underwent neck dissection and parotidectomy with facial nerve preservation. Endotracheal intubation was facilitated with succinylcholine. Prolonged muscle paralysis which was first detected after failure to stimulate the facial nerve with electrocautery, lasted five hours and it is due to pseudocholinesterase deficiency.

Prognosis: Administration of succinylcholine along with proper medical support particularly respiratory support measures like mechanical ventilation. In nonmedical condition in which subjects with pseudocholinesterase deficiency are exposed to cocaine, sudden cardiac death can occur.

Patient Education: Administration of pseudocholinesterase itself to the deficient people is one of the possible options. Behringwerke, a German pharmaceutical company, created a purified, injectable form of human pseudocholinesterase. Another, USA-based pharma company PharmAthene has begun using genetically modified goats to create pseudocholinesterase in large quantities. Treatment or management involves the avoidance of following class of drugs like drugs containing succinylcholine: quelicin, anectine; drugs containing mivacurium: mivacron; drugs containing pilocarpine: salagen; drugs containing butryrylcholine; drugs containing huperzine A and donepezil; drugs containing pilocarpine: salagen; drugs containing mivacurium: mivacron; drugs containing succinylcholine: quelicin, mivacurium, procaine, and cocaine. Indian Hindu Arya Vysya Community people with a history of pseudocholinesterase deficiency should tell his or her doctor if when they undergo anesthesia for surgery to avoid potentially serious unwanted adverse effects. Because pseudocholinesterase deficiency is rare, it is not tested for prior to surgery. This means that most patients are not diagnosed until they have an adverse reaction to medication during surgery, or unless they have a family history of the disorder.

Diagnosis: Polymerase chain reaction (PCR) was used to identify the mutations or variants exist on a particular piece of DNA. Testing for pseudocholinesterase deficiency before surgery was also useful for diagnosis. “Normal” is described as 3,200 to 6,600 IU/L. A plasma assay of pseudocholinesterase enzyme activity was used for diagnosis of pseudocholinesterase deficiency. Apart from that, pseudocholinesterase enzyme activity can be determined by using “Acholest Test Paper”. When a drop of the patient’s plasma was applied to the substrate-impregnated test paper, a colorimetric reaction occurs. The time taken by the exposed Acholest Test Paper to turn from green to yellow is inversely proportional to the pseudocholinesterase enzyme activity in the plasma sample.

CONCLUSION

Pseudocholinesterase deficiency results in delayed metabolism of only a few compounds of clinical significance like succinylcholine, mivacurium, procaine, and cocaine. Indian Hindu Arya Vysya Community people with a history of pseudocholinesterase deficiency should tell his or her doctor if when they undergo anesthesia for surgery to avoid potentially serious unwanted adverse effects. Because pseudocholinesterase deficiency is rare, it is not tested for prior to surgery. This means that most patients are not diagnosed until they have an adverse reaction to medication during surgery, or unless they have a family history of the disorder.

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REFERENCE
