Plasma cholinesterase deficiency in a neonate

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We report a two-day-old infant who had a period of apnoea lasting six hours following the intravenous administration of succinylcholine (Sch). The results of her plasma cholinesterase level and dibucaine number indicate a congenital absence of plasma cholinesterase (PChE) enzyme, although both parents and siblings had normal cholinesterase levels and dibucaine numbers. This is believed to be the youngest reported case of prolonged apnoea after the administration of succinylcholine.

Nous rapportons le cas d'un bébé de deux jours qui présente une période d'apnée de six heures après l'administration intraveineuse de succinylcholine. Les résultats du dosage de la cholinestérase plasmatique et de l'épreuve à la dibucaine montrent une absence congénitale de cholinestérase plasmatique (PChE), malgré des dosage normaux chez les parents et la fratrie. Nous croyons qu'il s'agit là du plus jeune cas d'apnée prolongée après administration de succinylcholine.

Prolonged apnoea after succinylcholine occurs most commonly due to a genetic variant of cholinesterase. Several case reports have documented succinylcholine-induced prolonged apnoea in infants with the youngest reported case being a three-week-old infant.¹⁻³ We report a case of prolonged neuromuscular blockade after succinylcholine administration to a two-day-old infant.

Case report

A two-day-old, 3.5 kg neonate presented for awake nasal fiberoptic laryngoscopy and rigid bronchoscopy under anaesthesia for the evaluation of inspiratory stridor. She was the full term product of an uncomplicated pregnancy

born by normal spontaneous vaginal delivery to a gravida 2 para 1 healthy 32-yr-old female. The child was otherwise healthy and the family history is unremarkable. The SpO₂ measured with a probe placed on the left thumb, ranged from 80 to 95% in air. After administration of atropine and oxygen, the patient underwent awake fiberoptic nasal pharyngoscopy. Following the diagnosis of vocal cord paralysis, succinylcholine, 2.0 mg · kg⁻¹, was given iv to facilitate diagnostic rigid bronchoscopy. Maintenance of anaesthesia was provided with an inhaled gas mixture of 1% halothane in oxygen. At the completion of the 15 min procedure, halothane was discontinued.

When no movement or ventilatory effort occurred in 10 minutes, peripheral nerve stimulation revealed absence of response to single twitch and tetanic stimuli. Presuming a diagnosis of cholinesterase deficiency, we sedated the child with midazolam 0.1 mg · kg⁻¹ and fentanyl 2 µg · kg⁻¹. Endotracheal intubation was maintained and mechanical ventilation was instituted. Two hours later, spontaneous eye opening and movement appeared. Six hours following succinylcholine, when train-of-four stimulation demonstrated four twitches and sustained tetanus, the trachea was extubated. Cholinesterase activity measured at three days of age was 0.2 U · ml⁻¹ (normal: 3.4–6.5 U · ml⁻¹) and the dibucaine number was <5% (normal: 73–90%).* Because of the suspicion of plasma cholinesterase deficiency, serum values of plasma cholinesterase and dibucaine numbers were sent on both parents and an older sibling at the same time. Her mother's cholinesterase activity was 3.8 U · ml⁻¹ and dibucaine number 87%. Her father's cholinesterase was 3.8 U · ml⁻¹ and dibucaine number was 84%. Her sister had a cholinesterase activity of 4.2 U · ml⁻¹ and a dibucaine number of 88%.

Discussion

Prolonged apnoea after neuromuscular blockade can be attributed to a wide variety of contributing factors, especially in the neonate. Our initial differential diagnosis

Key words

ANAESTHESIA: paediatric;

ENZYMES: cholinesterase;

NEUROMUSCULAR RELAXANTS: succinylcholine.

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*The plasma cholinesterase level was measured by the Boehringer Mannheim cholinesterase method at the SmithKline Beecham Clinical Laboratories, Van Nuys, California. This method utilizes acetylthiocholine as the substrate. Fluoride and chloride numbers were not determined.

included hypothermia, hypoglycaemia, hypocalcaemia, acidosis, hypoxaemia, medication error, and catastrophic neurologic event.⁴ Although each of these was considered and ruled out, the deciding factor was the absence of neuromuscular transmission as determined by the peripheral nerve stimulator.

Pseudocholinesterase is found in most tissues including plasma. The plasma enzyme is synthesized in the liver. The molecular weight of the major isoenzyme of PChE is approximately 360,000, but there are many minor components that have a lower molecular weight.⁵ PChE has a half-life in serum of 14 days.⁶ There is negligible enzyme activity of plasma cholinesterase in human colostrum and breast milk for at least the first 22 postpartum days.⁷

Healthy pregnant women, compared with non-pregnant women, have a reduction of PChE activity during late pregnancy through the early postpartum period ranging from 15 to 33% below baseline levels. Low cholinesterase values were found in 10% of patients in late pregnancy and during labour, in 20% of patients one day postpartum, and in 60% of patients two days later. These values return to pre-pregnancy levels at approximately six weeks postpartum. In most cases, however, there are no clinical differences in SCh activity and duration of neuromuscular blockade.⁸

The infant less than six months of age has about one half of the PChE activity of an older child or adult. The low level of PChE does not seem to prolong the duration of action of a single dose of SCh in infants.^{9,10}

The presence of a genetically determined atypical PChE is often considered only after an otherwise healthy patient experiences prolonged neuromuscular blockade, following a conventional dose of SCh. Approximately 90% of the population is homozygous for the usual allele of serum PChE and have a normal response to SCh. Approximately 1 in 200–480 patients have a heterozygous expression of atypical pseudocholinesterase activity.^{5,11} These patients manifest a modestly prolonged duration of neuromuscular blockade following a single dose of SCh, and dibucaine inhibits 40–60% of the enzyme activity.¹¹

One in 2800–3200 patients^{5,11} is homozygous for atypical PChE. This type of patient has a greatly prolonged neuromuscular block following SCh. Dibucaine inhibits only 20% of the enzyme activity. The dibucaine number which reflects the quality of the PChE and not the quantity of the enzyme that is in the circulating plasma is normally 73–90% in all age groups.

In addition to those patients who are homozygous for an abnormal gene of PChE, there are patients who are homozygous for a silent gene for cholinesterase. These patients are a heterogeneous group: some patients possess 2% of normal activity while others have zero level of

PChE activity. Patients who are heterozygotes for the silent gene have serum PChE levels between 28% and 114% of normal.⁵

Our patient demonstrated markedly prolonged paralysis from a single dose of SCh. The results of her PChE level and dibucaine number indicate a congenital absence of plasma cholinesterase enzyme.

Some paediatric anaesthetists may allow newborns, during bronchoscopy, to maintain spontaneous ventilation throughout the procedure. However, the use of a muscle relaxant allows the delivery of a lower halothane concentration and prevents coughing and laryngospasm.¹²

This appears to be the youngest documented case of prolonged apnoea after succinylcholine. The fact that both parents and her sibling displayed normal PChE enzyme activity and normal dibucaine numbers, points to the fact that our patient was homozygous for the silent gene and that both of her parents may have been heterozygous for the normal and the silent gene. Although the use of succinylcholine in children has decreased markedly in present clinical practice, the same problem can occur with mivacurium, a new relaxant also metabolized by pseudocholinesterase.^{13,14} Patients with pseudocholinesterase deficiencies demonstrate prolonged neuromuscular block after the *iv* administration of mivacurium.¹³

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