Pseudocholinesterase deficiency and organophosphorous insecticide use

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Fortunately, the incidence of anesthetic-related complications is rare, but all anesthetists should be aware of premonitory signs and symptoms in order to maintain the patient's safety under anesthesia. The authors present a case study of a patient with pseudocholinesterase deficiency that was not preoperatively identified, and a review of the literature.

Pseudocholinesterase is a glycoprotein that is synthesized by the liver and is found in the plasma but not in the red blood cell. It can be found in other body tissues such as the brain, kidney, intestine and pancreas. Physiologically, the function of this enzyme is unknown; however it hydrolyzes a number of esters such as choline, but is less specific than true acetylcholinesterase. Persons possessing the abnormal enzyme are perfectly normal until exposed to succinylcholine or local anesthetics which are esters of benzoic acid derivatives, such as procaine, chloroprocaine, and tetracaine. The result is prolonged apnea from succinylcholine, or a prolonged block from the ester local anesthetics.

Plasma cholinesterase activity may be abnormal due to genetic defects, or due to acquired defects. In 1958, Kalow and Davies described two types of genetically determined pseudocholinesterase, one normal and the other abnormal. It was estimated that 96% of the population is homozygous for the normal genes, while 3 to 4% is heterozygous for the atypical genes. One in 2,800 people is homozygous for the autosomal-recessive genes for the atypical enzyme. The atypical enzyme is less effective than the normal enzyme in hydrolyzing acetylcholine, and is unable to hydrolyze succinylcholine in therapeutic concentrations at the normal rate.

This atypical gene is also more resistant to cholinesterase inhibitors such as dibucaine, a local anesthetic. Dibucaine inhibits the activity of normal pseudocholinesterase to a greater degree than the atypical enzyme. The "dibucaine number" represents the percentage of inhibition of pseudocholinesterase by dibucaine under standard conditions. This number allows the practitioner to determine two things. First, the dibucaine number distinguishes between an acquired and a genetic defect in the ability of pseudocholinesterase to hydrolyze succinylcholine. Second, the dibucaine number helps determine the genotype. The dibucaine number of the normal population, which is homozygous for the normal gene, is 80%, which means that 80% of the enzyme is inhibited by dibucaine. The population which is homozygous for the atypical gene has a dibucaine number of 20%. Heterozygote individuals having a normal and an abnormal enzyme have a dibucaine number between 50 and 65%.

Plasma cholinesterase activity also may be abnormal due to an acquired defect. That is, an individual who is homozygous for the normal gene
may demonstrate a reduced ability to hydrolyze succinylcholine due to alterations in enzyme synthesis. Since pseudocholinesterase is synthesized in the liver, reduced levels of the enzyme can be found in patients with liver disease such as acute hepatitis and hepatic metastasis. Pregnant patients have a lower pseudocholinesterase level during the last trimester and early postpartum period. A lowered pseudocholinesterase level may be found in burned patients and in patients suffering from diseases such as carcinoma, collagen disease, chronic debilitating disease, chronic anemia, uremia, myxedema, and malnutrition.

Certain drugs have been found to reduce pseudocholinesterase activity; these drugs include neostigmine, echothiope eye drops, monoamine oxidase inhibitors, antineoplastic drugs, oral contraceptives, propanidid, chlorpromazine, and pancuronium. Accidental organophosphate poisoning inhibits pseudocholinesterase activity by binding totally and irreversibly to the enzyme, thus prolonging the neuromuscular blockade with succinylcholine. The duration of the block depends on the time it takes for the liver to synthesize more normal enzyme, a process that can take from a few days to months. However, prolonged apnea after succinylcholine administration has been successfully terminated by the infusion of the Behringwerke solution of human serum cholinesterase. This solution is not available in the United States, however. It has also been reported by Epstein and his co-workers that 87% of pseudocholinesterase is retained in banked blood after being stored for 21 days at 4° Centigrade. He also found that 100% of pseudocholinesterase activity is present in fresh frozen plasma kept for seven weeks at -70° Centigrade.

Case study

A 61-year-old Caucasian female was scheduled for a breast biopsy to rule out or verify a metastatic process from a previous breast carcinoma. Less than a year before, the patient had undergone a left modified radical mastectomy under general anesthesia without any complications from the surgery or anesthesia. Appropriate-for-weight doses of sodium thiopental, succinylcholine, and curare had been used to induce and intubate the patient. Anesthesia had been maintained with nitrous oxide, fentanyl, and enflurane. The patient had met extubation criteria quickly and had an uneventful recovery.

The same nurse anesthetist performed the anesthesia for the second breast biopsy. The patient was interviewed preoperatively and assigned an ASA 2 status for general endotracheal anesthesia based solely on her mild obesity (5 foot, 3 inches, and 82 kg), and the metastatic process. All preoperative laboratory test results were within normal limits. After her baseline vital signs were obtained on the operating table, preoxygenation and precuurarization were completed; the patient experienced no untoward reaction. The anesthesia was again a sodium thiopental induction; succinylcholine facilitated intubation (after the patient’s airway had been assured); and maintenance was with nitrous oxide, oxygen, fentanyl, and enflurane, using controlled ventilation of 750 cc tidal volume at 8 breaths per minute. No additional muscle relaxants were used, and there were no problems or complications throughout the surgery. During the procedure, a sample of the breast mass was sent to pathology as a frozen section, and the tentative results were reported malignant.

At the completion of the surgical procedure, eduction was anticipated by turning off the enflurane 15 minutes before the dressing was applied. The nitrous oxide was turned off at the last suture, and oxygen was turned to 6 L/minute. There was no response to verbal or tactile stimulation during emergence, nor was there a response after reversing the narcotic with 0.4 mg of intravenous naloxone. There was no residual smell of enflurane in the reservoir bag, and 100% oxygen was continued. There was no response to peripheral nerve stimulation before or after the intravenous administration of 0.5 mg glycopyrrolate and 2.5 mg neostigmine. The arterial blood gas was normal for the degree of ventilation, and the pupils were equal in size and not pinpoint.

Consultation with another nurse anesthetist verified the principal anesthetist’s suspicion of pseudocholinesterase deficiency, probably secondary to the metastatic disease process, and appropriate recovery room equipment was requested. Verbal contact was initiated with the patient, explaining what was happening, that the anesthetist knew she could hear, that the situation was in control, and what was going to be done.

The patient was transferred to the recovery room while still intubated. Ventilation was controlled with 100% oxygen via a Mapleson “D” breathing apparatus. Ventilation was continued in the recovery room with a portable ventilator with 40% oxygen and appropriate tidal volume and rate. It was noted that the patient’s blood pressure was slightly elevated to 150/90, and this was thought to be due to subjective discomfort after naloxone administration. Nalbuphine 10 mg IV
was given to relieve pain since it does not contribute to respiratory depression.

A Foley catheter was inserted in order to prevent discomfort from a full bladder, and to initiate intake and output recording for hydration status. Several venous blood tests were drawn and sent to the laboratory. These tests included a pseudocholinesterase enzyme activity, dibucaine inhibition, electrolytes, glucose, and blood urea nitrogen (BUN). The electrolytes, glucose, and BUN were normal preoperatively, but were drawn for comparison. Continuous verbal contact was maintained throughout every procedure and laboratory test. The recovery room staff was made aware of the apparent complication; and the need for constant verbal and tactile reassurance, comfort measures such as warm blankets, and consistency in her care were stressed. Her waiting family members were told of the need for continued ventilation, and the probable cause of the complication. They were also frequently reassured of her well-being while she was in the recovery room.

Several small intravenous doses of nalbuphine were administered at intervals throughout the patient's recovery in order to reduce the discomfort of the biopsy site, and to attempt to reduce her anxiety about the unexpected paralysis. Every 30 minutes, the peripheral nerve stimulator was used to assess the return of muscular tone. After 30 minutes in the recovery room, and exactly two hours after the intravenous injection of succinylcholine for intubation, the patient was able to slowly and partially open her eyes in response to questions, but there was no other muscular activity or response to peripheral nerve stimulation.

Over the next two hours, the patient's muscle tone gradually returned to normal. Exactly four hours after the intubating dose of succinylcholine was first administered, the patient was appropriately responsive, had full muscle strength in all extremities, and met extubation criteria easily. After suctioning, the patient was extubated with protective clothing. Also on the package was a note to physician and veterinarian:

**Paramite** is a cholinesterase inhibitor. Do not use the product on animals simultaneously or within a few days before or after treatment with or exposure to cholinesterase inhibiting drugs, pesticides, or chemicals... Do not get in eyes, on skin or clothing. Do not breathe spray mist. Use only in well ventilated areas. Wear rubber gloves, goggles and protective clothing.

Also on the package was a note to physician and veterinarian:

**Paramite** is an organophosphorous insecticide. Atropine is antidotal. Usual symptoms of organophosphorous poisoning in man include: headache, blurred vision, weakness, nausea, discomfort in the chest, vomiting, abdominal cramps, diarrhea, salivation, sweating, and pin-point pupils.

This information was relayed to the patient and her husband. Because of the husband's exposure to the insecticide, he agreed to have a serum pseudocholinesterase level submitted. The results were normal. The patient's postoperative course was excellent without any surgical complications and no further anesthetic complications. The pseudocholinesterase level was taken several times.
Finally, the anesthetist must consider the possibility of a neurologic response to anesthesia and surgery, the anesthetist must count the patient's preoperative health history and esthetics must be considered. Taking into account the patient's preoperative health history and response to anesthesia and surgery, the anesthetist must consider the possibility of a neurologic event. If any non-depolarizing muscle relaxants were used, they should be reversed with a reversible anticholinesterase such as neostigmine. If there are signs of excess narcotic effect, such as respiratory depression or pin-point pupils, narcotic reversal should be considered. The possibility of an agonist effect of muscle relaxants and inhalation anesthetics must be considered. If any non-depolarizing muscle relaxants were used, they should be reversed with a reversible anticholinesterase such as neostigmine. If there are signs of excess narcotic effect, such as respiratory depression or pin-point pupils, narcotic reversal should be considered. The possibility of an agonist effect of muscle relaxants and inhalation anesthetics must be considered.
ACKNOWLEDGEMENT

The authors wish to thank the laboratory service of the Naval Hospital, Camp Lejeune, North Carolina, for their help, and specifically Mr. John Mullen of the Serology Department. They wish also to thank the recovery room staff for their prompt response to an unusual complication.

The opinions expressed are the authors' alone, and do not reflect the opinions of the U.S. Department of Defense, the U.S. Navy, or the Naval Hospital, Camp Lejeune, North Carolina.

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