tion and thus interfere with vasodilation. SNP is metabolized to form five free CN ions. A portion of the CN may combine with methemoglobin to form cyanmethemoglobin, or be converted by a hepatic and renal enzyme system, rhodanese, to thiocyanate (TCN), which is excreted in the feces, saliva and urine. The rate of CN elimination decreases when enzyme systems that convert CN to TCN become saturated. Excess CN can bind tissue cytochrome oxidase, interfere with electron transport, and produce tissue hypoxia. To minimize this likelihood, some investigators have recommended that the maximum total dose of SNP acutely administered not exceed 1.0 mg/kg. In situations in which hypotension is clinically needed, especially when the need extends over several hours or more, it may not be possible to adhere to this recommendation, especially if tachyphylaxis occurs.

To prevent tachyphylaxis and the possibility of CN intoxication, maneuvers to lower blood CN should be instituted. Infusion of sodium thiosulfate (150 mg/kg) will decrease CN by facilitating the conversion of CN to TCN. The nitrates will bind CN to the ferric ion of methemoglobin, decreasing blood CN. This method has been used to treat industrial CN poisoning, but may be dangerous during anesthesia because cardiovascular instability may occur and because methemoglobin cannot bind oxygen. Intravenous administration of hydrogenocobalamin has been shown to decrease blood CN in guinea pigs and appears to be equally effective in man. When these methods to decrease blood CN are not available, and when SNP dose requirements are greater than 1 mg/kg (acutely administered), SNP should be discontinued and other hypotensive agents or techniques initiated.

The total doses of SNP infused in the cases reported here were 79.2 mg (1.10 mg/kg), 87.04 mg (1.28 mg/kg), and 97.3 mg (1.39 mg/kg). High blood CN levels resulted in each case. Metabolic acidosis was not seen at the time tachyphylaxis occurred, confirming in vitro findings that tachyphylaxis resulted from high blood CN levels at physiologic pH.

References

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Prolonged Response to Succinylcholine Following Physostigmine

Aaron F. Kopman, M.D.,* Gregory Strachovsky, M.D.,† Lee Lichtenstein, D.M.D.‡

Prolonged neuromuscular blockade may follow the administration of succinylcholine (SCh) when an anticholinesterase has been given beforehand. Pyridostigmine, neostigmine, hexafluorenium, etrophonium, and echotoephate iodoside have all been shown to potentiate the action of an initial dose of SCh, presumably due to their ability to reduce serum cholinesterase activity.

We recently encountered a case in which adminis-
tation of physostigmine, another anticholinesterase, was associated with marked prolongation of the effect of a subsequent dose of SCh.

**Report of a Case**

A 25-year-old woman weighing 70 kg was scheduled for emergency cesarean section. The patient had no significant antecedent medical history. Operative delivery had been decided upon after a prolonged first stage of labor did not progress to full cervical dilatation.

Preanesthetic medication consisted of meperidine, 50 mg, Promazine, 50 mg, and scopolamine, 0.65 mg, iv, 11:00 a.m. At noon, the patient received the same drugs iv again in half these dosages.

Upon arrival in the operating room, the patient was delirious and totally uncontrolled. At 1:45 p.m., 2 mg physostigmine were given iv, but because there was some question as to whether the iv route was intact, an additional 2 mg physostigmine were administered im. Within 5 min the patient had quieted down enough to be transferred to the operating table.

At 2:00 p.m. general anesthesia was induced with 250 mg thiopental sodium and endotracheal intubation was performed following a dose of 100 mg SCh. Until delivery of the infant at 2:05 p.m. anesthesia was maintained with nitrous oxide, 6 l/min, and oxygen, 4 l/min in a semiclosed circle system. Following clamping of the umbilical cord, 20 mg alphaprodine were given to supplement the anesthetic technique. No other drug was administered except 20 units of oxytocin, added to the iv infusion.

At 2:20 p.m. it was noticed that no spontaneous respiratory efforts were present, and an attempt to elicit an evoked muscle response by stimulation of the patient's left ulnar nerve at the wrist was unsuccessful. Using supramaximal stimulation, there was no evidence of twitch, tetanus, or posttetanic facilitation until 2:45 p.m. Over the next 25 min, neuromuscular function gradually returned to normal. During the recovery period, the patient showed poorly sustained tetanus in response to 50-Hz stimulation and prominent posttetanic facilitation. The trachea was extubated at 3:45 p.m. The postoperative course was uneventful. A sample of the patient's blood was drawn on the fifth postoperative day and examined for plasma cholinesterase activity. The sample had a dibucaine number of 64.6 (normal range 74–85) and a benzoylcholine rate of 0.02 pmol/min at 30 C (normal range 18–138). These results indicate that the patient was heterozygous for atypical plasma cholinesterase.

**Discussion**

A dose of less than 1.6 mg/kg SCh in this patient produced total paralysis lasting 45 min and significant weakness for an additional 20–25 min, as evidenced by evoked responses to peripheral nerve stimulation. Paralysis of this duration following this dose of SCh is definitely an abnormal response. Katz et al. found that following 1.0 mg/kg SCh, 10 per cent recovery occurred in about 10 min (range 4–15 min), and that even following 2.0 mg/kg, recovery was essentially complete in about 18.0 min (range 12–24 min).

Kalow and Gunn stated that heterozygotes for atypical plasma cholinesterase do not have greatly prolonged responses to SCh. They estimated that a dose of SCh that would produce apnea lasting 5 min in a normal individual would induce 7 min of total paralysis in heterozygotes and about an hour of apnea in abnormal homozygotes. Since the incidence of the gene for atypical cholinesterase in the general population is about one in about 25, it is likely that many of the reports of "normal" human responses to SCh in reality also included heterozygous individuals. We believe, therefore, that the prolonged apnea this patient experienced was the result of physostigmine inactivation of plasma cholinesterase and was not primarily genetically determined. In view of the increasing usage of physostigmine in anesthetic practice, we feel that this predictable but not yet widely appreciated drug interaction should be reported.

**References**

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