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Interaction of Pancuronium and Corticosteroids

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Pancuronium bromide is a bis-quaternary ammonium compound with a steroid nucleus. It produces a competitive, nondepolarizing neuromuscular blockade characterized by fade on tetanic stimulation and posttetanic facilitation.[1] An apparent reversal of pancuronium-induced neuromuscular blockade by the intravenous administration of hydrocortisone has been reported recently.[2] A case that may represent a rapid termination of pancuronium-induced paralysis in a patient receiving massive doses of steroids is presented.

Report of a Case

A 21-year-old, 75-kg, white man was admitted for evaluation and treatment of idiopathic thrombocytopenic purpura. The platelet count on admission was 4,000/mm^3, and treatment with prednisone, 100 mg per day, orally, was begun. Following failure of the platelet count to rise above 30,000/mm^3, the prednisone dose was increased to 250 mg per day. This resulted in a cushingoid appearance without increase in circulating thrombocytes. The patient was, therefore, scheduled for splenectomy.

Preoperative evaluation elicited an unremarkable past history. Physical examination disclosed no abnormality except the cushingoid appearance and resolving ecchymoses. Results of laboratory studies, other than the platelet count of 65,000/mm^3, were normal. The patient was premedicated with Innovar, 1.5 ml, and atropine, 0.4 mg, im, 45 minutes before anesthesia. Induction was accomplished with Innovar, 7 ml in increments, and nitrous oxide (67 per cent) and oxygen (33 per cent) via semiclosed circle absorber system. Pancuronium bromide, 8 mg (0.1 mg/kg), was given iv, respiration was supported, and after 3 minutes the larynx was easily exposed and an 8.0 mm cuffed endotracheal tube inserted. Relaxation at the time of intubation was excellent and the cords were flaccid.

Sixty minutes after intubation an additional 2 mg of pancuronium was given during section of the left rectus muscle. However, 15 minutes later the surgeon reported inadequate relaxation and exposure. At that time a peripheral nerve stimulator was attached to subcutaneous needles placed in the medial volar surface of the forearm. Stimulation produced good twitch responses, no fade on tetanic stimulation and no discernible posttetanic facilitation. Three additional 2-mg doses of pancuronium, iv, over the next 60 minutes failed to cause any fade of tetanic contraction, but posttetanic facilitation was seen. The surgical procedure was completed uneventfully despite no improvement in abdominal relaxation. At the end of the procedure, neostigmine, 2.5 mg, and atropine, 1.0 mg, were administered iv for reversal and the trachea was extubated without difficulty.

Discussion

Pancuronium may be used to provide relaxation for intubation, with recommended doses ranging from 0.06[3] to 0.1 mg/kg.[1,4] Conditions suitable for intubation are present in 2 to 5 minutes, depending on the dose used. Our patient received 0.1 mg/kg pancuronium, which provided relaxation for easy laryngoscopy. We feel that adequate relaxation at laryngoscopy is evidence of profound neuromuscular blockade at that time. We postulate that an unusually rapid termination of action was responsible for the inadequate intraoperative relaxation in this case. In this young patient the only unusual factors were his thrombocytopenia and massive doses of prednisone. The recent report by Meyers of partial reversal of pancuronium-induced blockade by hydrocortisone points out the potential interaction of the two compounds.[2] We believe that an interaction between the pancuronium used for muscle relaxation and the corticosteroids our patient received may have

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caused an unusually rapid termination of action. The exact nature of this interaction is unclear, but may revolve around the similarities of their steroid nuclei. The interactions may include competition at the myoneural junction, altered protein binding, or induction of hepatic biotransformation. Lack of potency of the drug lot is an additional possibility. However, the pancuronium administered came from two ampules of the same batch. No problem from the drug was encountered in other patients.

We have presented a case that may exemplify a rapid termination of pancuronium-induced neuromuscular blockade. We believe an interaction between the steroid-based pancuronium nucleus and administered corticosteroids caused this abnormality. We recommend careful monitoring of neuromuscular transmission in patients receiving large doses of steroids when pancuronium is used for muscle relaxation.

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Bupivacaine-induced Seizure after Accidental Intravenous Injection, A Complication of Epidural Anesthesia

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The case of a patient who had generalized convulsions after accidental intravenous injection of bupivacaine is presented.

Report of a Case

A 40-year-old woman who had cervical cancer was scheduled for hysterectomy. She was 148 cm tall and weighed 56 kg. There was no past history of epileptic seizure. She did not receive preanesthetic medication. An epidural catheter was placed into the second lumbar intervertebral space. After aspiration, 75 mg of 0.5 per cent bupivacaine were administered. Upon injection of the drug, the patient became unresponsive and her eyelids started blinking. This was followed by a generalized convulsion. The patient was given oxygen by mask immediately, but two more seizures occurred. Diazepam, 5 mg, iv, terminated the seizure activity. Venous blood was withdrawn just after the diazepam injection, within 2 to 3 minutes after the first convulsion. The operation was completed using narcotic anesthesia (pentazocine, diazepam, and N_2O/O_2). There was no evidence of postoperative complications. Blood pressure was 120/60 torr before the seizures and 140/70 torr just after them. Pulse rate was 100/min before the seizures and 130/min just after them. The venous plasma level of bupivacaine was 3.0 μg/ml.

Discussion

The seizure threshold of bupivacaine has been reported to be 4 μg/ml in the dog.[1] Munson *et al.*[2] found that the threshold level was 2.5 to 5.7 μg/ml (mean 4.5 μg/ml) in the rhesus monkey. However, Moore *et al.*[3] reported that a venous blood concentration of 1.2 to 3.4 μg/ml did not induce seizure during epidural block in man. This report is difficult to be assessed because some patients received diazepam for premedication. Also, epidural block is associated with a slower increase in plasma levels of local anesthetics than direct iv injection. In our case the venous plasma level of bupivacaine was 3.0 μg/ml. Ryan[4] reported that the plasma level of bupivacaine during a convulsion was 2.3 μg/ml. These levels are lower than previously reported seizure thresholds in man.

The arterial plasma and cerebrospinal fluid levels were higher than venous plasma levels.[3,5] Drug elimination in blood after iv injection is rapid, especially in the initial few minutes. These are the reasons the venous level of bupivacaine during convulsions in this case was lower than seizure thresholds previously reported. An iv dose of 5 mg diazepam was able to stop the seizure. That is the dose reported to be effective by Munson *et al.*[2] Routine use of diazepam for premedication of the patient who may receive epidural or local anesthesia is advisable.[6]

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