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Malignant Hyperthermia after Oral and Intravenous Pretreatment with Dantrolene in a Patient Susceptible to Malignant Hyperthermia

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We report the occurrence of malignant hyperthermia (MH) in a 7-year-old boy after both oral and intravenous (iv) dantrolene pretreatment and the administration of a "nontriggering" anesthetic. This report, in addition to the recent report of an episode of MH in a patient who had received oral dantrolene pretreatment alone,[1] substantiates that patients can have a malignant hyperthermic reaction, despite what was felt to be adequate pretreatment.

REPORT OF A CASE

This 7-year-old previously healthy boy, with no previous anesthetics and no family history of anesthetic difficulties, was scheduled for bilateral myringotomy and tube placement, tonsillectomy, and adenoidectomy. His preoperative physical examination was entirely normal. After induction of anesthesia with halothane and succinylcholine, ventricular dysrythmias, tachycardia, prolonged muscle rigidity, and masseter spasm rapidly occurred. The surgery was cancelled, and the patient was transferred to the recovery room awake and in stable condition. The creatinine phosphokinase (CPK) level postoperatively was 466 IU on the first day and declined to 191 IU over the next 2 days (normal up to 115 IU). There were no abnormalities in serum potassium or calcium levels and no myoglobinuria was present. A muscle biopsy was positive for susceptibility to malignant hyperthermia. The postoperative course was uneventful, and his surgery was rescheduled.

Eight months later, the patient was admitted to our hospital. A preoperative physical examination was entirely normal, as were all routine preoperative laboratory studies except for an alkaline phosphatase level that was 306 IU (normal 30–100) and a CPK level of 121 IU (normal level is up to 115 IU). The patient was pretreated with dantrolene, 4 $mg \cdot kg^{-1}$ orally for 24 h and then iv dantrolene 1 $mg \cdot kg^{-1}$ prior to induction of anesthesia. We used an anesthetic machine that had never been exposed to an inhaled anesthetic. After administration of oxygen, 5 $mg \cdot kg^{-1}$ of thiopental was given iv, followed by 6 $\mu g \cdot kg^{-1}$ of fentanyl, 0.15 $mg \cdot kg^{-1}$ of pancuronium, nitrous oxide, and oxygen after intubation of the trachea. Approximately 10 min after induction of anesthesia and the beginning of surgery, an arterial line was inserted, after which darkened blood was withdrawn. The $F_{I_{O_2}}$ was increased to 1.0, and hyperventilation was initiated. Analysis of arterial blood gases revealed a marked respiratory acidosis and a mild metabolic acidosis as well as a low Pa_{O_2} (Table 1). The heart rate, which was 110 beats/min at the start of the case, had increased gradually to 150 beats/min at the time the initial analysis of arterial blood gases was performed. At this time, additional dantrolene 2 $mg \cdot kg^{-1}$ was given iv and surgery was stopped. Following 10–15 minutes of hyperventilation with peak inspiratory pressures of 60 cmH_2O, the heart rate had decreased from a maximum of 160 beats/min to 130 beats/min and analysis of arterial blood gases were satisfactory (table 1). The muscle relaxants were reversed and the patient sent to the recovery room, awake, with a blood pressure of 150/100 mmHg and a heart rate of 113 beats/min. At no time was the rectal temperature greater than 37° C. Because analysis of arterial blood gases obtained in the recovery room revealed a recurrence of a mixed respiratory and metabolic acidosis (table 1), an additional dose of dantrolene, 1 $mg \cdot kg^{-1}$ was given iv. The pulmonary compliance, which was felt to be entirely normal at the start of this anesthetic, had decreased intraoperatively but was felt to be normal prior to extubation of the trachea. Copious clear pulmonary secretions were evident during the anesthetic, which had diminished markedly by the time the patient arrived in the recovery room. After a total dose of dantrolene 4 $mg \cdot kg^{-1}$ was given iv, analysis of arterial blood gases were satisfactory in the recovery room (table 1; 1010). The patient was admitted to the intensive care unit for overnight observation, and oral dantrolene 1 $mg \cdot kg^{-1}$ every 6 h was continued for the next 2 days. No sodium bicarbonate was administered during the perioperative course, and the patient had an uneventful recovery. The CPK level that was elevated preoperatively was well within the normal range postoperatively, and there was no myoglobinuria noted at any time.

DISCUSSION

A variety of prophylactic regimens have been described for patients known or highly suspected to have malignant hyperthermia. Our patient had what was felt to be adequate dantrolene pretreatment and a nontriggering anesthetic. Despite these measures, a life-threatening reaction to general anesthesia occurred. Adequate pretreatment is based on the study of Flewellen *et al.*,[2] who found that 2.4 $mg \cdot kg^{-1}$ of dantrolene iv will give predictable blood levels that will provide what currently is felt to be adequate MH prophylaxis.

Almost all anesthetic agents have been linked to MH, including nitrous oxide[3] and pancuronium,[4] two of the agents used in this case. Despite these case reports, most anesthesiologists have considered a N_2O-narcotic-relaxant anesthetic with such drugs to be nontriggering especially when used with "adequate" prophylactic pretreatment with dantrolene. There have been no reports of malignant hyperthermia linked to the administration of fentanyl.

Stress has been suggested as a cause of MH in many susceptible patients, especially when MH is found in un-

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TABLE 1. Blood–Gas Data

Time	Event	pH_a	Pa_{CO_2} (mmHg)	Pa_{O_2} (mmHg)	Base Excess (mEq/L)	FI_{O_2}	Therapy
0800	Preinduction	—	—	—	—	—	1 mg/kg iv dantrolene
0820	Induction	—	—	—	—	—	—
0845	Desaturated ABG	7.18	69	54	−5	0.3	↑ V_A, FI_{O_2}
0900		7.10	59	112	−4	1.0	↑ V_A, new machine, surgery stopped, 2 mg/kg iv dantrolene
0905	Anesth. stopped	7.40	36	275	−1	1.0	
0940	PAR	7.25	51	85	−5	0.21	1 mg/kg iv dantrolene
1010	PAR	7.34	43	212	−3		5 l/min by nasal prongs
1110	ICU	7.36	41	94	−2	0.21	

anesthetized patients.[5] Although our patient was not premedicated, he was not overly anxious, but there is no way of eliminating this as a trigger to this episode of MH.

The initial sign of an MH episode is extremely variable. Along with tachycardia and a mixed respiratory and metabolic acidosis, our patient had a gradual but pronounced deterioration of pulmonary compliance. Although body temperature did not increase, these findings are consistent with the diagnosis of malignant hyperthermia. The patient also produced copious amounts of clear pulmonary secretions that may have been a result of acute pulmonary edema, although there are other possible sources of this fluid. Acute pulmonary edema has not been reported to be a prominent sign in many case reports.

In summary, we present a case report of a young boy with known susceptibility to MH who, despite both iv and oral pretreatment with dantrolene, has a life-threatening malignant hyperthermic reaction.

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