

citrate) as premedication for surgery procedures.⁴ They demonstrated that administration of oral transmucosal fentanyl citrate results in rapid increases in plasma fentanyl concentration, with accompanying dose-related sedation, analgesia, respiratory depression, and common opioid side effects (including pruritus, nausea, vomiting, and difficulty with micturition), but without changes in arterial blood pressure or pulse rate. Smaller doses (0.5–1 mg) of oral transmucosal fentanyl citrate produced analgesia for short periods and produced some sedation, with little respiratory depression, thereby deserving evaluation as premedication in patients. Higher doses of oral transmucosal fentanyl citrate (greater than 2 mg) produced respiratory depression and a higher incidence of side effects.⁴

Stanley *et al.* also reported that two volunteers swallowed an entire 5-mg lollipop; neither experienced sedation, but both experienced 15–20 min of sleepiness approximately 60–80 min after oral ingestion. These observations suggested that, as the lollipop dissolved, some penetrated through the mucosa of the mouth, pharynx, and esophagus, reaching the systemic circulation *via* the venous drainage and right atrium without passage through the liver. In contrast, virtually all venous drainage from the stomach and small intestine passes through the liver *via* the portal circulation. The high hepatic clearance may explain why oral administration of 5 mg fentanyl produced few opioid-related effects, whereas buccal liquefaction produced sedation, analgesia, and respiratory depression.⁴ The relative lack of opioid effects in these two volunteers was noted by our patient as well.

Little information is available about gastrointestinal absorption of fentanyl, although *The Extrapharmacopeia* states that absorption does occur from the gastrointestinal tract with rapid onset but short duration of action.⁵

In summary, this case demonstrates oral ingestion of fentanyl as well as the difficulty of detection of fentanyl with the usual comprehensive drug screens. Detection and quantification are now generally performed with gas chromatography/mass spectroscopy (although radioimmunoassays can be used).⁶ When fentanyl abuse is suspected, the laboratory should be requested to screen for it specifically. The treating physician should be particularly alert to the possibility of fentanyl abuse when working with anesthesia and operating room personnel.

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Isolated Masseter Muscle Spasm and Increased Creatine Kinase without Malignant Hyperthermia Susceptibility or Other Myopathies

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There is much controversy about the definition, significance, management, and family counseling of patients

who develop masseter muscle spasm (MMS) after succinylcholine.^{1–4} The clinician must consider whether MMS correlates with malignant hyperthermia susceptibility (MHS) and whether to recommend further investigation such as a muscle biopsy to evaluate the presence of myopathy and/or the halothane–caffeine contracture test to diagnose MHS. Measurement of creatine kinase (CK) within 24 h may show extreme elevations, which may be helpful in the diagnosis of MHS or a myopathy. A previous report⁵ documented that CK values of greater than 20,000 IU are highly suggestive of MHS as diagnosed by the halothane–caffeine contracture test. The only patient who did not have MHS had a myopathy that was dem-

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onstrated on histologic examination of a muscle biopsy specimen.

The purpose of this report is to describe a patient who developed MMS and CK values > 20,000 IU without muscle disease or MHS as evidenced by a normal muscle biopsy specimen and a normal halothane-caffeine contracture test, respectively.

CASE REPORT

A 5-yr-old child was scheduled for an inguinal hernia repair. The child had had two previous operations (one for strabismus repair) without anesthetic problems. Previous anesthetics had consisted of halothane/N₂O/O₂. Succinylcholine had not been used. The child had no signs or symptoms of muscle diseases, and there was no family history of muscle diseases or abnormal reactions to anesthesia. Physical examination was normal.

The child fasted for more than 8 h and was brought to the operating room after receiving an intramuscular injection of meperidine, hydroxyzine, and atropine. Anesthesia was induced with halothane and N₂O. He then was given 1.5 mg/kg succinylcholine and 0.01 mg/kg atropine. Upon attempts at intubation, the jaw muscles were noted to be rigid, and the mouth was opened only with considerable difficulty. No other muscle rigidity was noted. The heart rate was 120 beats/min, and the temperature was 37.5° C. End-tidal CO₂ was not measured. The procedure was cancelled because of the association of MMS with MHS. Arterial blood gas analysis showed a pH of 7.26, P_{O₂} of 143 mmHg, P_{CO₂} of 37 mmHg, and base excess of -10.0 mm. The child was treated with 1 mg/kg dantrolene and monitored in the intensive care unit. The initial postoperative CK value was 326 IU (normal 30-170 IU). CK values increased to a maximum of 40,000 IU within 12 h and 35,700 IU within 24 h and slowly decreased over 48 h. Myoglobinuria lasted less than 24 h and was treated with mannitol. The child made an uneventful recovery without manifesting other signs of malignant hyperthermia.

Nine years later, at the age of 14 yr, the child underwent extensive evaluation for neuromuscular disorders. A detailed neurologic examination performed by a neurologist did not show evidence of a myopathy. Electromyograph testing of the lower extremity and paraspinal muscles did not show abnormalities. Baseline CK values measured in both the child and the parents were normal. The halothane-caffeine contracture test to diagnose MHS as well as a routine muscle biopsy were performed at the University of South Florida.

The halothane-caffeine contracture test was performed and interpreted in accordance to standards set by the North American Malignant Hyperthermia Group.⁶ A portion of the vastus lateralis muscle was used for testing. Less than 4 h elapsed from excision of the muscle to completion of the test. Anesthesia consisted of sedation with midazolam and fentanyl and a lateral femoral cutaneous and femoral nerve block performed with 1% mepivacaine. Six strips were analyzed for their response to incremental doses of caffeine. Five strips were analyzed for their response to 3% halothane. The contracture response to 3% halothane varied from 0.0 g to 0.35 g; a normal response is ≤ 0.7 g contracture. All 6 strips tested with caffeine showed normal responses (*i.e.*, caffeine-specific concentration < 4 mM; response to 2 mM caffeine ≤ 0.2 g; 7% of maximum contracture occurred at greater than 2 mM caffeine concentration). The results of the halothane-caffeine contracture test were therefore interpreted as normal. The muscle was sent to the Armed Forces Institute of Pathology for detailed examination. Histologic (hematoxylin and eosin, Gomori's trichrome, Masson's trichrome, periodic acid Schiff) examination did not reveal signs of a myopathy (*i.e.*, there was no fiber atrophy or inflammation). Detailed histochemical examination (myofibrillar adenosine triphospha-

tase, reduced nicotinamide adenine dinucleotide dehydrogenase, non-specific esterase, myoadenylate deaminase) showed a normal distribution of Type I and Type II fibers, a lack of ragged red fibers, a lack of central cores, and no evidence of a myopathy. Biochemical assay of enzyme activity for carnitine palmitoyl transferase deficiency was performed because patients with this myopathy frequently have normal histology. Enzyme activity was normal.

The child and family members have continued to do well without signs or symptoms of a myopathy. The child has not received other anesthetics.

DISCUSSION

There have been few children with masseter muscle rigidity and extremely elevated CK values who have undergone muscle biopsy testing for MHS. This is the first case documented of a child who had MMS followed by CK values greater than 20,000 IU but who did not show evidence of a myopathy by physical examination, electromyography, or detailed histologic examination or evidence of MHS by the halothane-caffeine contracture test. Rosenberg and Fletcher⁵ examined 77 patients who developed MMS after receiving succinylcholine. In 7 patients, CK values were greater than 20,000 IU. Six of these patients had an abnormal halothane-caffeine contracture test, and MHS was therefore diagnosed. The remaining patient, who had a normal contracture test, had Becker's muscular dystrophy demonstrated on histologic examination. The correlation of MHS as diagnosed by muscle biopsy to CK values > 20,000 IU was statistically significant at *P* < 0.05 by the test of significance between two proportions. Indeed, a CK value > 20,000 IU was the only predictor of MHS in the study. Dysrhythmias, postoperative fevers, arterial blood gases, myoglobinuria, and histologic examination of the muscle did not correlate with a positive contracture test. The authors concluded that "a CPK of > 20,000 IU in the perioperative period is indicative of either MH susceptibility or an underlying myopathy."

There are many possible reasons for the discrepancy between the results in our case and those reported previously.⁵ One reason might be that our patient did not meet criteria for inclusion in the previous study. We doubt this, however, because our patient was referred to our muscle biopsy center by a practicing anesthesiologist who clearly documented "jaw muscle rigidity" after succinylcholine administration. This is the same inclusion criteria used in the previous study. Another possible reason is that the muscle biopsy itself was performed differently in our laboratory and could have led to a false negative result. However, the halothane-caffeine contracture test was performed using standardized techniques,⁶ and criteria for normal *versus* abnormal results in our laboratory and in Rosenberg and Fletcher's⁵ laboratory are similar. More importantly, there has never been a documented false negative halothane contracture muscle test result in any

biopsy center in North America using recommended standards.⁶ It is therefore unlikely that in our case the MHS negative result was incorrect. The incidence of false positive results (specificity) has recently been shown to vary greatly among different biopsy centers.⁷ It is therefore possible that one of the six previously reported⁵ patients with a positive contracture result may not be malignant hyperthermia-susceptible and therefore may be similar to our patient. It is also possible that our patient has an underlying myopathy that was not diagnosed by our investigation. This is unlikely, however, because family history, physical examination, baseline CK value, electromyography, and exhaustive histologic examination all were normal.

The most probable cause of the apparent discrepancy may be statistical. A *P* value of < 0.05 shows only that the two groups are different 95% of the time. Therefore, one might expect, as more patients are tested, to find a normal patient like ours. Indeed, Rosenberg has recently examined a child with MMS and with CK values > 50,000 IU within 24 h who had a normal contracture test and normal histologic examination.‡

We are left to assume that a child for whom MHS is not diagnosed by biopsy and for whom no myopathy is found by histologic examination can have greatly increased CK values after halothane and succinylcholine. In Littleford *et al.*'s study⁴ on continuing the triggering anesthetic after MMS, some patients' CK values increased to as high as 138,240 IU. Although Littleford *et al.*'s study is controversial, none of those patients developed fulminant malignant hyperthermia. The results of muscle histology or the halothane-caffeine contracture test were

not reported.⁴ Increases of CK to as great as 180,000 IU have been reported in healthy patients after 20 min of leg exercises.⁸

In conclusion, we describe a patient who developed isolated MMS and CK values of > 20,000 IU with normal muscle by extensive histologic examination and a normal halothane-caffeine contracture test response. The likelihood of MHS or a myopathy in patients who develop MHS after succinylcholine and who have CK values of > 20,000 IU is great but not absolute. Patients should be counseled appropriately. Although the contracture test may have false positive results, it should be recommended to such patients, as should neurologic evaluation and muscle biopsy for myopathies.

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Tight Mask Fit Could Have Prevented "Airway" Obstruction

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Recent investigations by March and Crowley¹ demonstrate the potential inadequacies of anesthesia apparatus

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checkout procedures despite the use of a Food and Drug Administration (FDA)-recommended checklist.‡ Our institution uses an adaptation of this checklist, which is printed on the back of each anesthetic record, and requires a signature by the anesthesiologist (fig. 1). Our

‡ United States Food and Drug Administration: Anesthesia Apparatus Checkout Recommendations. Rockville, MD, Federal Register, February 1987.