Abnormal sensitivity to sevoflurane in children with mitochondrial defects.

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Introduction. As diagnosis and care for children with mitochondrial diseases improves, it has become increasingly common for them to undergo surgery; often a muscle biopsy is required for diagnosis. Surgical procedures usually involve a general anesthetic for these patients, which are typically young children. While many different anesthetic techniques have been used successfully for patients with mitochondrial disease, there are reports of serious, unexpected complications occurring during and following anesthetic exposure.

Previously, we reviewed charts from 35 children who have come to the operating room for diagnosis or treatment of putative mitochondrial disease. We induced these children very slowly with a single volatile anesthetic, sevoflurane. Seven of these children were very hypersensitive to sevoflurane and had defects consistent with decreased function of mitochondrial complex I. We are now performing a prospective study of sensitivity to sevoflurane in children presenting for workup of a possible mitochondrial defect.

Methods. Each of the patients presented for muscle biopsy to assay abnormalities in oxidative phosphorylation and electron transport. To limit the anesthetic dose for patients with mitochondrial disease, we used a Bispectral Index (BIS, Aspect) to compare sensitivities in the patients. The children presented with a common constellation of symptoms that included hypotonia, developmental delay, failure to thrive, and lactic acidosis. All patients were anesthetized with sevoflurane only, titrating the dose to that which kept the BIS at 50-60 prior to surgical incision. The rest of the case was maintained, usually on sevoflurane, with other agents added as needed.

Results. We have studied 12 patients who have presented for muscle biopsy. Our results thus far are summarized in the Table. Two patients with mitochondrial defects had periods of respiratory depression postoperatively. One patient had seizures on induction with sevoflurane, which spontaneously resolved without further treatment. The final complication was a patient with prolonged nausea and vomiting requiring overnight stay in the hospital. Three patients had unusual sensitivities to sevoflurane; two had an increased sensitivity and one was resistant.

Discussion. All of the general anesthetic agents are known to directly inhibit mitochondrial function and may add to preoperative problems. However, reports have been published demonstrating that each of the above anesthetics has been used successfully in a few patients with mitochondrial disease. Again, it must be recalled that the specific genetic cause of the mitochondrial disease is almost never known with the mitochondrial patients. It may be that as the different types of mitochondrial disease are better defined, preferences for an anesthetic in certain cases may become clear. However, such a recommendation cannot be made at the present time.

Table

Patient #	Mitochondrial Defect	Sevoflurane Sensitivity	Hemodynamic Response	Complications
1.	None measured	Normal (2.5%)	Normal	None
2.	Complex IV	Normal	Normal	Respiratory depression post-op
3.	None measured	Normal	Normal	None
4.	Complex III	Resistant	Normal	Seizures after induction
5.	None measured	Normal	Normal	None
6.	Fatty acid acyltransferase	Increased	Normal	Post-op nausea/vomiting
7.	None measured	Normal	Normal	Respiratory depression post-op
8.	Fatty acid acyltransferase	Increased	Normal	None
9.	None measured	Normal	Normal	None
10.	Complex IV	Normal	Normal	None
11.	None measured	Normal	Normal	None
12.	None measured	Normal	Normal	None