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Pre-Anesthetic Consultation Request for Patients with Mitochondrial Disease

Dear Anesthetist,

This patient, who has a confirmed diagnosis of mitochondrial disease, is being referred for pre-anesthetic consultation to allow you time to consider options for anesthesia. Many anesthetic medications have real or potential toxicity at the level of the mitochondria. However, for some medications, the risk of toxicity is more than with others. For example, propofol has been found to have an inhibitory effect on mitochondrial function which is greater than that for other anesthetics and mitochondrial myopathy is a risk factor for propofol infusion syndrome. While certainly there may be circumstances where the advantages of propofol outweigh the disadvantages of alternative agents (for example, in very short procedures or the use of propofol for induction only), a 2014 consensus statement from the Mitochondrial Medicine Society (reproduced below with permission) suggest that propofol not be used for maintenance of anesthesia in patients with confirmed mitochondrial disease. Alternatives like sevoflurane and remifentanil could be considered options.

In addition to the choice of anesthetic, there are some more general issues to address which will increase the likelihood of this patient having a safe surgical procedure with rapid recovery from anesthesia. As with any patient with myopathy, this patient may take longer than other patients to recover from neuromuscular blockade. Fasting times should be minimized and dextrose containing solutions can help provide an energy source while the patient is fasting. For these reasons, where possible, scheduling a patient with mitochondrial disease as the first procedure in the morning will increase the likelihood of same day discharge in situations where that is appropriate to the surgical procedure.

We have enclosed a brief summary of recommendations for mitochondrial disease and anesthesia for your review. If you have questions about the mitochondrial disease in this patient and would like to discuss this with one of the mitochondrial medicine physicians at the Adult Metabolic Diseases Clinic, please call the clinic at 6048755965 (open Mon-Fri 8:00-16:00) and one of our physicians would be happy to discuss the case with you. The risk/benefit balance of any particular anesthetic agent will need to be considered for each individual patient based not only on their diagnosis of mitochondrial disease but also on concomitant medical issues which will be reviewed by you at the consultation.

Thank you for assessing this patient.

Diagnosis and management of mitochondrial disease: a consensus statement from the Mitochondrial Medicine Society Parikh, Sumit *et al*,*Genetics in Medicine* (2014).

Anesthesia

Many patients with mitochondrial disease have generally tolerated anesthesia. More recent reports from studies of small populations of mitochondrial patients or limited outcome measures have suggested that anesthetics are generally safe.[117–120] There are also reports of serious and unexpected adverse events in these patients—both during and after an anesthetic exposure—including respiratory depression and white matter degeneration.[121–123] Thus, there remains a physician perception that these patients are vulnerable to a decompensation during these times. Anesthetics generally work on tissues with high-energy requirements and almost every general anesthetic studied has been shown to decrease mitochondrial function.[124–130] This occurs more so with the volatile anesthetics [124,126,128] and propofol.[131,132] Propofol and thiopental are typically tolerated when used in a limited fashion, such as during an infusion bolus. Susceptibility for propofol infusion syndrome has been suggested but not yet proven.[133–135]

Narcotics and muscle relaxants are also frequently used in the operating room. These drugs (with the possible exception of morphine) are generally tolerated because they do not seem to alter mitochondrial function.[136,137] However, they can create respiratory depression, and caution must be used in mitochondrial patients who may already have hypotonia, myopathy, or an altered respiratory drive. The risk of malignant hyperthermia does not seem to be increased in mitochondrial patients. Finally, mitochondrial patients are often vulnerable to metabolic decompensation during any catabolic state. Catabolism is often initiated in these patients because of anesthesia-related fasting, hypoglycemia, vomiting, hypothermia, acidosis, and hypovolemia. Therefore, limiting preoperative fasting, providing a source of continuous energy via IV dextrose, and closely monitoring basic chemistries are important.

Consensus recommendations for anesthesia

1. Patients with mitochondrial diseases are at an increased risk of anesthesia-related complications.

2. Preoperative preparation of patients with mitochondrial disease is crucial to their perioperative outcome. Patients should minimize preoperative fasting and have glucose added to their perioperative IV fluids, unless they are on a ketogenic diet or have been demonstrated to have adverse reaction to higher glucose intake.

3. Caution must be used with volatile anesthetics because mitochondrial patients may potentially be hypersensitive.

4. Caution must be used with muscle relaxants in those mitochondrial patients with a preexisting myopathy or decreased respiratory drive.

5. Mitochondrial patients may be at a higher risk for propofol infusion syndrome and propofol use should be avoided or limited to short procedures.

6. One should consider slow titration and adjustment of volatile and parenteral anesthetics to minimize hemodynamic changes in mitochondrial patients.

7. Local anesthetics are generally well-tolerated in patients with mitochondrial defects.

8. There is no clear established link between malignant hyperthermia and mitochondrial disease.

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