INHERITED METABOLIC DISORDERS

Surgical Specialty:	All
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Background:

This Case Guide is a broad overview of anesthetic approaches for metabolic disorders. There is a large variety of disorders that have different anesthetic implications; therefore, there are links below to reliable references that provide more specific information about each disorder.

General Considerations

- Metabolic Disorders - a broad category that encompasses hundreds of inherited diseases that alter one's ability to metabolize proteins, fats, or sugars.
- Most metabolic diseases are worsened by physiologic stressors – acute illness, dehydration, surgical stress, and periods of fasting.
- Patients are prone to metabolic crisis due to accumulation of toxic metabolites when pushed into a catabolic state.
    - Signs include metabolic acidosis, hypoglycemia, dehydration, shock, and lethargy.
- Most patients are followed by genetic specialists and carry information about their disease. Consider contacting their genetic specialist prior to the surgical procedure.
- Simplification of Nutrient Metabolism Disorders
    - **Carbohydrate** breakdown/utilization disorders – unable to tolerate or use existing glucose to produce energy, cannot maintain normoglycemia or mobilize glycogen stores.
        - Shift to ketones/fatty acids for energy & develop ketoacidosis.
    - **Lipid/Fatty Acid** Breakdown disorders – Tolerate stress or activity until glycogen/glucose stores are depleted.
        - Cannot shift into lipid/fatty acid breakdown for energy.
    - **Protein** Metabolism Disorders - Tolerate stress or activity until glycogen/glucose stores are depleted.
        - A catabolic state causes the accumulation of toxic metabolites depending on which enzyme is dysfunctional.

Patient Considerations

- Avoidance of catabolic state.
    - Prone to hypoglycemia and metabolic acidosis.
    - Avoidance of prolonged fasting states, first start case is best.
    - Use of dextrose-containing fluids, and close glucose monitoring.
- Associated Comorbidities/Syndromes
    - Facial dysmorphia – large forehead (peroxisomal disorders), coarse facial features & airway anatomic changes (mucopolysaccharidosis), macroglossia (glycogen storage diseases).
    - Neurologic: Developmental delay is common, severity is usually dependent on the type of metabolic disease, and disease progression.
        - *Consider oral midazolam/premedication.*
    - Myopathies: Genetic myopathies are not considered metabolism disorders but there aremyopathic manifestations of metabolic diseases. These include fatty acid oxidation disorders, glycogen storage diseases & mitochondrial diseases. Patients are prone to rhabdomyolysis.
        - Rhabdomyolysis Risk: Anesthesia-Induced Rhabdomyolysis – syndrome with skeletal muscle breakdown after exposure to volatile anesthetics or succinylcholine – result of muscle contraction with unstable sarcolemma.
            - *McArdle (Glycogen Storage Disease V), Carnitine palmitoyl transferase deficiency type 2.*
            - *DMD & Becker's, dystrophin gene associated muscular dystrophies.*
        - Malignant Hyperthermia is a risk of genetic myopathies, not myopathic manifestations of metabolic diseases. Patients at risk for MH include:
            - *RYR1 Receptor Variants, Central core myopathy, Minicore myopathy, King-Denborough syndrome, periodic paralysis.*
    - Cardiomyopathies: dilated or hypertrophic – Pompe's Disease, fatty acid oxidation disorders, organic acidemias, mitochondrial disorders.
    - Hepatic Dysfunction: most prominent in galactosemia, glycogen storage diseases, mitochondrial disease, Wilson's disease, and urea cycle disorders.
        - May have prolonged INR.
        - Liver failure is the result of the progression of many of these metabolic disorders. A liver transplant may be required.
    - Hematologic Abnormalities
        - Pancytopenia – bone marrow suppression in organic acidemias or crowding of marrow by abnormal cells in lysosomal storage disorders.
        - Anemia – a result of disorders of B_{12} transport.

Anesthetic Planning:

Pre-Anesthetic Evaluation

- Additional labs/tests indicated during work-up
    - ***Echocardiogram:*** Advanced stages of Glycogen Storage Diseases, organic acidemias
    - ***Basic Metabolic Panel:*** *If surgery lasts more than 2 hours – glucose, electrolytes*
    - ***Venous Blood Gas and lactate****:Bbaseline metabolic state*
    - ***CBC:*** *Many prone to anemia and/or pancytopenia*

  - ***LFTs & INR:*** *Consider in Wilson's disease, galactosemia, organic acidemias, mitochondrial disorders, urea cycle disorders*
  - ***Ammonia:*** *Urea cycle disorders*
- Discussions to have with surgeon/family
  - Code Status – Situationally dependent – Most of these metabolic disorders may cause early death so this conversation would be dependent on disease progression, and family/patient wishes.
  - ECMO Candidates – Varies significantly depending on the patient & disease progression.

Specific or Unique Room Set-up Requirements

- Airway – facial dysmorphisms may cause intubation difficulty
  - Prior airway history is helpful; however, disease progression may worsen the airway and increase intubation difficulty – particularly in mucopolysaccharidosis.
  - Video laryngoscopy/bronchoscopy available.
- Drugs/Infusions
  - D_{10} Normal Saline as maintenance fluids. Avoid hypoglycemia and catabolic state.
  - Avoid LR – particularly in disease states with difficulty metabolizing lactate (organic acidemias, glycogen storage diseases).
  - Total Parental Nutrition - Consider a low protein total parenteral nutrition and/or lipid infusion for longer surgeries. TPN recipes will vary based on metabolic disease.
- Monitors
  - Standard monitors, additional based on surgical procedure and/or patient status.
  - Arterial Line: frequent blood gases, frequent glucose checks, fluid resuscitation, electrolytes in longer procedures.
  - BIS or EEG monitoring if available to minimize anesthetic exposure.
- Blood Availability
  - Dependent on surgical plan, baseline CBC, & bleeding risk – *discuss with surgeon.*
- PICU Bed Availability (if indicated)
  - Dependent on surgical plan & patient status.
- Other Indicated Resources (ex. ECMO standby)
  - Consider preoperative admission for fluids, IV access, adequate dextrose during the fasting period, and preoperative lab testing.
  - Involve the patient's geneticist early.

Intraoperative Considerations:

General

- Regional Anesthesia: may help decrease physiologic stress response to surgical stimulus and spare some exposure to parenteral anesthetics.[2]
  - Amide local anesthetics inhibit carnitine-acylcarnitine translocase – bupivacaine more significantly blocks this enzyme than ropivacaine or lidocaine and therefore should be avoided.[2]
  - Case reports of successful regional blocks using ropivacaine & lidocaine.

Induction

- Avoidance of succinylcholine when possible.[6]
  - Myopathies, elevated baseline creatine kinase levels – risk of malignant hyperthermia or hyperkalemia & rhabdomyolysis.

    - UpToDate Summary Table - Disorders with guidance on volatile anesthetics & succinylcholine use.[6]
- Propofol – Use with caution in mitochondrial disorders and organic acidemias.
    - Boluses for induction and maintenance infusions for short procedures (MRIs etc.) are well tolerated.[1,4]

Positioning
- Reverse Trendelenburg, shoulder roll, optimize oral/pharyngeal/laryngeal axis for intubation.

Maintenance
- Volatile anesthetics at reasonable doses are well tolerated. [4]
    - Isoflurane is preferred if the patient has liver dysfunction.
    - **EXCEPTION: Volatiles are contraindicated in most myopathies (MH risk) and should be avoided in most diseases prone to anesthetic-induced rhabdomyolysis.**[6]
- Dexmedetomidine – tolerated well, although clearance may be prolonged
- Propofol – safe for short procedures, however, blocks mitochondrial respiratory chain and uncouples oxidative phosphorylation and therefore may worsen acidosis.
    - Should be avoided in longer or more traumatic surgeries given risk of causing propofol infusion syndrome.
- Ketamine – reports of successful use, particularly in GSDII/Pompe's to spare cardiac depressant effects of propofol.

Hemodynamic/Physiologic goals
- Tight blood pressure control – avoid anaerobic metabolism and worsening existing organ dysfunction.

Surgical Considerations
- Nondepolarizing muscle relaxants - dependent on baseline hepatic & renal function.
    - Baseline metabolic myopathies may make patients more sensitive.
- Additional considerations are specific to the surgical procedure.

Emergence/Disposition
- Patients are more sensitive to anesthetics; emergence may be prolonged.
- Disposition based on metabolic status and surgery.
    - PACU & discharge is reasonable for smaller procedures/surgeries (MRIs, central line placements).
    - Admission may be required for continued monitoring, fluids, and nutrition.

Post-op Care
- Continue maintenance dextrose fluids until the patient is tolerating adequate enteral nutrition to avoid a catabolic state.

Case-Specific Complications/Pitfalls

Given the large variance of metabolic disorders, it is impossible to make a unified treatment plan that is applicable across types of disorders. Conclusions amongst most of the anesthetic recommendations are made based only on case reports and in-vitro knowledge of drug metabolism.

Helpful Resources

- The patient's genetic specialist is a great resource and patient advocate. They expect to be contacted for help with perioperative care related to genetic disorders.
- **International Classification of Inherited Metabolic Disorders** – large database with description and classification of disorders
- **Orphan Anesthesia** – Database for genetic disease-specific details and their anesthesia/perioperative considerations

References

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