It’s getting hot in these genes: Malignant Hyperthermia in the Pediatric Patient

By: Ashley Evick, BSN, SRNA
Objectives

• Be able to quickly assess/identify a malignant hyperthermia emergency in the operating room

• Be able to identify symptomology in the pediatric patient and how it can differ from the adult presentation

• Understanding of the treatment process for this emergency, and how it can impact outcomes for the pediatric patient
Case Discussion
History

- 4 month old male
- Wt. 6.48 kg
- NKDA
- No past surgical HX
- No medications
- HX of trigonocephaly and premature birth
- No family HX of surgery
Surgical procedure

- Craniosynostosis
- GA with ETT
- Anticipation of large blood loss
Anesthetic plan

- No premedication (child calm)
- Inhalation induction with N₂O and sevo
- Intubation with ETT
- Rectal temp placed
- 22g, 24g, and 20g IV placed
- A-line placed (took quite a long time)
- Infant on under body blanket, heated circuit used, and room temperature increased

- Remi and precedex gtts used
- 0.9% NS and LR infusing
- Maintained on Sevoflurane
- Upper body blanket placed on infant, in addition to under body blanket
Case progression

- 90 minutes into case
- HR increased to 150s
- BP slight increase
- O₂ saturation decreased to 97%
- EtCO₂ gradually increasing to a peak of 53 (unresponsive to changes in ventilation)
- Temp. increasing 0.1 degree Celsius at a time (child hypothermic to begin 33 degrees Celsius)
Differential Diagnosis

- Gave fentanyl and remifentanil boluses to assure child was not too light
- No change in EtCO₂ with ventilation changes
- ETT in good position and not obstructed
- MALIGNANT HYPERTHERMIA!!!!
## Labs

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Myoglobin in urine: negative
Treatment

- Call for help!!!!
- Sevo stopped, flows increased
- CO2 absorber and circuit changed
- Ice applied to infant, warming blankets turned off, and room temp decreased
- Dantrolene 2.5 mg/kg initial dose
- Insulin R
- Dextrose
- Gttts changed to plasma-lyte
- Remi and precedex gttts ran as anesthetic agents
- Calcium chloride given
- MHAUS called and assisted in treatment plan
- Emergency algorithm guide used
- Versed given
- Subsequent doses of Dantrolene given at 1.5 mg/kg then 1 mg/kg
- Child transferred to PICU and remained on ventilator
Emergency Therapy for MALIGNANT HYPERThERMIA

MH Hotline: 1-800-644-9737 • Outside of the US: 001-303-389-1647

DIAGNOSIS

**Signs of MH:**
- Increasing ETCO2
- Trunk or total body rigidity
- Malignant ventricular tachycardia
- Tachycardia
- Increased temperature (may be in 6 degree increments)
- Myoglobinuria

**Sudden/Unexpected Cardiac Arrest in Young Patients:**
- Presumed hypermetabolism and initiate treatment (see #6)

**Trismus/Masseter Spasm with Succinylcholine**
- Early sign of MH in many patients
- If limb muscle rigidity, begin treatment with dantrolene

**For emergent procedures, continue with non-triggering agents, evaluate and monitor the patient, and consider dantrolene treatment.**
- Follow CK and urine myoglobin for 36 hours.
- Check CK immediately and at 6-hour intervals until returning to normal. Observe for dark or colored urine. If present, administer N-acetyl cysteine and test for myoglobin.
- Observe in PACU or ICU for at least 24 hours

**ACUTE PHASE TREATMENT**

1. **GET HELP. GET DANtROLENE.**
   - Notify Surgeon
   - Discontinue volatile agents and succinylcholine.
   - Hyperventilate with 100% oxygen at flows of 10 L/min or more.
   - Halt the procedure as soon as possible; if emergent, continue with non-triggering anesthetic technique.
   - Don’t waste time changing the circle system and CO2 absorbent.

2. **Dantrolene 2.5 mg/kg rapidly IV through large-bore IV, if possible**
   - To convert kg to lbs for amount of dantrolene, give patient 1 mg/lb (2.5 mg/kg approximately 1 mg/lb).

**CAUTION! This protocol may not apply to all patients; alter for specific needs.**

3. **Dissolve the 20 mg in each vial with at least 60 ml sterile, preservative-free water for injection.**
   - Report until signs of MH are reversed.
   - Sometimes more than 10 mg/kg (up to 30 mg/kg) is necessary.

4. **Bicarbonate for metabolic acidosis**
   - 1-2 mEq/kg if blood gas values are not yet available.

5. **Cool the patient with core temperature >39°C.**
   - Use convection by internal cooling system
   - Intravenous cold saline infusions
   - Other cooling techniques may be applied at clinician’s discretion.

**Continued on the other side...**

**POST ACUTE PHASE**

A. **Observe the patient in an ICU for at least 24 hours, due to the risk of recurrences.**
B. **Dantrolene 1 mg/kg orally 4-6 hours or 0.25 mg/kg/hr by infusion for at least 24 hours and sometimes longer as clinically indicated.**
C. **Follow vital signs and labs as above (see #7)**
- Frequent ABGs as per clinical signs
- CK every 8-12 hours; less often as the values trend downward

E. **Counsel the patient and family regarding MH and further precautions; refer them to AHAUS.**
- Fillout and send in the Adverse Medical Reaction to Anesthesia (AMRA) form (www.amra.org) and send a letter to the patient and his/hers physician. Refer patient to the nearest Crisis Center for follow-up.

**NON-EMERGENCY INFORMATION:**

AHAUS
1 North Main Street
PO Box 1060
Seekonk, MA 02771
Phone: 1-800-644-4287
Fax: (401) 947-7900
Email: info@ahaus.org
Website: www.ahaus.org

**CAUTION! This protocol may not apply to all patients; alter for specific needs.**
Benefits of an Algorithm

- An algorithm was used during this case
- Kept everyone on track
- Made sure every task was completed
- User friendly manual in every OR
The Normal Muscle Contraction and Relaxation Cycle
Skeletal Muscle Contraction

- Sliding filament theory
- Multiple steps
1. CNS produces an action potential transmitted down axon of alpha motor neuron

2. Activated voltage gated Ca channels in the NMJ

3. Ca influx causes vesicles to fuse with membrane and release AcH

4. AcH diffuses across synapse and binds/activates nicotinic AcH receptors opening Na/K channels

5. Na rushes in and K trickles out this triggers an action potential

6. Action potential spreads through the muscle depolarizing
7. Voltage gated Ca channels are activated in T-tubule membrane this also activates ryanodine receptors to release Ca from the sarcoplasmic reticulum.

8. Ca binds to troponin C on actin thin filaments on myofibrils modulating tropomyosin.

9. Troponin allows tropomysin to move unblocking sites.

10. ATP binds to myosin releasing actin allowing movement of the crossbridge.
Skeletal Muscle Relaxation

- While the previous steps are occurring calcium is actively pumped back into sarcoplasmic reticulum
- The tropomyosin changes confirmation and blocks binding sites
- The contraction ceases
What is Malignant Hyperthermia??

- Potentially life-threatening complication of anesthesia
- Autosomal dominant genetic disorder of ryanodine receptor gene (RYR1)
Some Statistics

• 1:2,000 occurrence
• May even be 1:500
• With dantrolene, mortality has decreased from 70%-80% to 6.5%-16.9%
• 1:5,000 to 1:10,000 with children
What is the role of the RYR₁ receptor??

- Known as the skeletal muscle calcium release channel
- Protein in the membrane of the sarcoplasmic reticulum
- Various mutations have been noted
What is happening???

- Causes uncontrolled increase in skeletal muscle oxidative metabolism, overwhelming oxygen supply and removal of carbon dioxide, this reaction releases heat and causes acidosis and circulatory collapse.

- See next slide for illustration.
Signs of Malignant Hyperthermia

- elevated temperature
- increases HR
- increased RR
- acidosis
- hypoxia
- rigid muscles
- rhabdomyolysis
- myoglobin in urine
- CK elevation
What are the triggers??
Testing for MH

- Caffeine halothane contracture test
- In vitro contracture test
- 2 g muscle for biopsy from quadriceps test within 5 hours of testing
- Tested 3 times for each test agent
- 4 centers in US: Bethesda, MD; Davis, CA; Minneapolis, MN; Winston-Salem, NC
Testing Continued

**HALOTHANE TEST**

- Halothane (3%) is administered.
- Normal muscle will not change its baseline by more than 0.5 grams (half a box).

**CAFFEINE TEST**

- Abnormal muscle is indicated by any response >0.2 gram evoked by 2 mM caffeine.
- In the graph below, 1 mM caffeine evokes an increase of 0.6 gram, and at 2 mM a further 1.8 gram.
Testing continued
Genetic testing

- Centers within the United States:
  - Pittsburgh, PA
  - Marshfield, WI
Can the presentation be different in pediatric patients???
Differences in pediatrics

• A study analyzed 264 records: 35 in the youngest age group (0-24 months), 163 in the middle age group (25 months-12 years), and 66 in the oldest group (13-18 years).
• Sinus tachycardia, hypercarbia, and rapid temperature increase were more common in the oldest age cohort. Higher maximum temperatures and higher peak potassium values were seen in the oldest age cohort.
• Masseter spasm was more common in the middle age cohort.
• The youngest age cohort was more likely to develop skin mottling and was approximately half as likely to develop muscle rigidity. The youngest age group also demonstrated significantly higher peak lactic acid levels and lower peak CK values. The youngest subjects had greater levels of metabolic acidosis.

(Nelson, 2013)
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A Published Case Report

The Case:

- 7-year-old boy with cholesteatomas underwent tympanoplasty.
- Three previous anesthetics with sevoflurane induction and maintenance with propofol infusion were not associated with MH symptoms.
- No family history of MH or muscle disease
- A minor rise of end tidal CO₂
- Increased rectal temperature
- Rhabdomyolysis and his father’s positive IVCT results

Discussion:

- MH-susceptible patient responds differently to various agents
- Atypical MH forms are problematic
- It is possible that the speed of onset reflects the rate of increase of the intracellular Ca²⁺ concentration, which depends on the particular drug used, its concentration in muscles and any number of physiological variables that dictate the efficacy of Ca²⁺ homeostatic processes in each patient.

(BONCIU, 2007)
Another Case Report

- Two cases of MH triggered by sevoflurane:
  - First Case: 6 year old girl stabismus repair 30 min after induction, etCO2 was over 60 mmHg. Muscle rigidity of legs and elevation in temperature. Maximum esophageal temperature was noted to be 40.4 degrees Celsius. CK was 252 post-op and 1690 the next day.
  - Second Case: 1 year and 9 month boy undergoing accessory ear resection. Sevoflurane used. 40 min after induction temperature was 38.6 degrees Celsius, HR 191, and oxygen saturation 93%. Muscle rigidity of the legs was noted. Highest temperature was 39.3 degrees Celsius. Both parents had no history of MH.

(Kinouchi, 2001)
Preparing for the MH patient

Per MHAUS:

- Anesthetic vaporizers are disabled by removing, or taping in the “OFF” position.
- Some consultants recommend changing CO2 absorbent (soda lime or baralyme).
- Flow 10 L/min O2 through circuit via the ventilator for at least 20 minutes.
- During this time a disposable, unused breathing bag should be attached to the Y-piece of the circle system and the ventilator set to inflate the bag periodically.
• Use new or disposable breathing circuit.
• Use the expired gas analyzer to confirm absence of volatile gases, as some newer machines are not so easily cleaned of volatile agents.
• Newer anesthesia “work stations” may require up to 60 minutes for purging residual gases; consult manufacturer’s information and information on the MHAUS website.
• Adding commercially available charcoal filters to the circuit will remove anesthetic gases and therefore obviate the need for purging the system as described. However, the filters should be replaced every hour.
MH cart

- Dantrolene
- Sterile water for injection USP
- Sodium bicarbonate
- Dextrose 50%
- Calcium chloride (10%)
- Regular insulin
- Lidocaine for injection (2%)
- Refrigerated cold saline solution
- Equipment: NGT, IV, syringes, temp probes, CVP kits, transducers, blood collection supplies
Dantrolene

- 36 vials should be available in each institution where MH can occur.
- Diluted at the time of use with 60 ml sterile water for injection (without a bacteriostatic agent).
- The vial is shaken until the solution is clear.
- It is mandatory to get dantrolene to its effective site, the skeletal muscle.
- MHAUS advises that the sterile water be stored in 100 ml vials, not bags, to avoid accidental IV administration of this hypotonic solution.
MH emergency treatment

- Call MHAUS
- Discontinue volatile agents and succinylcholine
- Get help and notify surgeon;
- Dantrolene Sodium for Injection 2.5 mg/kg rapidly IV through large-bore IV
- Bicarbonate for metabolic acidosis
- Cool the patient
- Dysrhythmia treatment
- Hyperkalemia treatment
- Follow: ETCO₂, electrolytes, blood gasses, CK, serum myoglobin, core temperature, urine output and color, and coagulation studies.
New innovations

• Carbon absorber
• Single Use
• Do not have to remove vaporizers or soda lime
How to Use: Proactive use

• Turn the fresh gas flow up to 10 l/min for 90 seconds
• Place one of the Vapor-Clean canisters on the inspired port of the anesthesia machine and the other canister on the expired port of the anesthesia machine.
• Replace the breathing bag and connect a new breathing circuit between the patient and the Vapor-Clean canisters
• Maintain fresh gas flows at 10l/min for duration of the case
• Hook your patient up
• The Vapor-Clean filters are good for up to 12 hours. If your case goes longer than 12 hours, swap the filters for a new pair
How to Use: With MH episode

- Turn the anesthetic gas off
- Place the Vapor-Clean filters between the machine and the breathing circuit
- Turn the fresh gas flow up to 10 l/min
- The Vapor-Clean filters are good for 1 hour. If your case goes longer than 1 hour, swap the Vapor-Cleans for a new pair
- Shorter time is due to concentration of gas both on the patient and in the anesthesia machine
- Removing the vaporizers or soda lime is optional
- Treat the patient as prescribed by MHAUS
How to anesthetize the MH patient?

- Should be first patient of the day
- Prepare machine as discussed
- TIVA
- Can use NMB other than succ
Take Home Message

• Kids can present with MH differently than adults
• If MH is suspected treat with MH protocols
• Early interventions have the best outcomes
• Think with every kid (patient) this can happen
References


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• Shinkaruk KS, Nolan K, Crossan M; Preparation of the Datex-Ohmeda Aestiva anesthetic machine for malignant hyperthermia cases, Anesthesiology 2008; 109 A279


Thank You

Questions?