**MALIGNANT HYPERTHERMIA (MH)**

**Malignant Hyperthermia**

Malignant Hyperthermia is a pharmacogenetic disorder that causes hypermetabolism by skeletal muscle in susceptible patients on exposure to volatile anesthetic gases such as Desflurane, Isoflurane, Sevoflurane, Halothane, and/or the depolarizing skeletal muscle relaxant succinylcholine

Rarely, non-pharmacogenetic triggers such as heat and rigorous exercise can precipitate MH.

**Incidence:**

Incidence is estimated at 1:10,000 and 1: 150,000 of all general anaesthetics.

**Pathophysiology:**

MH occurs because of a genetic autosomal dominant disorder involving a mutation on the ryanodine receptor (type 1: RyR1) or the dihydropyridine receptor. This mutation causes an uncontrollably high release of calcium (Ca2+) from the sarcoplasmic reticulum of skeletal muscles after exposure to the triggering agent which causes prolonged muscular contractions and a hypermetabolic reaction.

The signs of the hypermetabolic reaction include tachycardia, hypercarbia, severe rhabdomyolysis, muscle rigidity, mixed metabolic and respiratory acidosis and even mortality if treatment is delayed.

**Recognition**

Malignant hyperthermia manifests with the following signs:

1. *Early signs*:

* Increase in the level of end-tidal carbon dioxide (ETCO2)
* Tachycardia with or without increase in blood pressure
* Muscle rigidity which may manifest as masseter spasm after exposure to the triggering agent
* Respiratory acidosis

1. *Late signs*:

* Increase in core temperature
* Mixed metabolic and respiratory acidosis
* Rhabdomyolysis leading to hyperkalemia

1. Electrolyte imbalance: hypocalcaemia and *hyperphosphatemia*

* Cardiac dysrhythmias
* Acute Kidney injury due to myoglobinurea
* Disseminated intravascular coagulation may occur as a sequelae

1. **Immediate management:**

**The principle of management of malignant hyperthermia employs taking measures to stop the reaction and prevention and management of sequelae of malignant hyperthermia**

After calling for help three approaches need to be followed:

1. *Removal of the triggering agent*:

* Turn off the vaporizer
* Provide 100% supplemental Oxygen at a flow rate of 10L/min or more
* Insert activated charcoal filters on both inspiratory and expiratory limbs of the circuit
* Increase the minute ventilation of the patient to a level twice or thrice the baseline.

1. *Medical management with i.v. Dantrolene:*

* The dose of Dantrolene is 2-3mg/kg every 5 min until the achievement of an end tidal CO2 of <45mmHg and a core temperature of <38.5oC.
* Maximum dose of Dantrolene initially is <10mg/kg. However, if 10mg/kg of Dantrolene has been used then re-evaluation of the condition for other possible diagnosis should be considered. If the diagnosis of malignant hyperthermia is likely, then administration of i.v. Dantrolene should be continued.
* Dantrolene administration for prevention of recurrence of malignant hyperthermia is not recommended. In case the reaction reoccurs within 6 hours, i.v. Dantrolene is to be administered at a dose of 1mg/kg and if the reaction reoccurs after 6hours, a dose of 2 to 3mg/kg should be used.

1. *Management of hyperthermia*:  
   Active cooling with cold i.v. fluids, icepacks, and decreasing the operating room temperature should be done.
2. **Prevention and management of complications:**
   * + - Management of Acidosis: Hyperventilation and administration of Sodium Bicarbonate to treat acidosis
       - Management of Hyperkalemia: Insulin should be used with simultaneous administration of Glucose and Calcium Gluconate.
       - Management of myoglobinurea and prevention of acute kidney injury: A urine output of >2ml/kg/hour should be maintained with i.v. fluids and Sodium Bicarbonate can be administered to alkalinize the urine.
       - Management of arrhythmias: Correction of electrolyte imbalance, use of short acting anti-arrhythmic agents and management according to PALS guidelines should be done
       - Management of DIC: Transfusion of Platelets, fresh frozen plasma and cryoprecipitate is to be done. Tranexamic acid should not be used.
       - Compartment syndrome: Monitoring of peripheral oxygen saturation with clinical examination of limbs should be conducted periodically. Prompt treatment with fasciotomies should be considered if compartment pressures are high.
3. **Post Malignant hyperthermia management:**

* If the reaction has been controlled with control of signs and achievement of treatment goals, then the surgery should be conducted under i.v. anaesthesia
* Patient should be shifted to PACU and then ward if the reaction was terminated successfully with no metabolic derangement or need for i.v. Dantrolene.
* If there is need of Dantrolene or if the patient has developed complications of malignant hyperthermia, then the patient needs to be admitted to the ICU or HDU.

1. **Continued monitoring:**

* Core & peripheral temperature
* ETCO2, SpO2, ECG
* Invasive blood pressure, CVP
* Monitor for acute renal injury and compartment syndrome

1. **Investigations:**

* ABGs
* CBC
* Electrolytes
* Creatinine
* Creatinine Kinase
* Coagulation studies
* Liver enzymes may be elevated 12-36hrs post reaction

**Anaesthesia for Malignant hyperthermia susceptible patients:**

**A** *Anaesthesia machine preparation*: Change circuits, disable or remove vaporizers, flush machine at a rate of 10 L/min for 20 minutes. Continue to use high gas flow rates to prevent rebound phenomena.

*Anaesthesia*:  Use local or regional anesthesia but general anesthesia with non-triggering agents is acceptable. Safe drugs include barbiturates, benzodiazepines, opioids, nondepolarizing neuromuscular blockers and their reversal drugs, and nitrous oxide.

**B** **B**ody temperature monitoring.  
**C**  **Ca**pnography: **C**lose monitoring for early signs of MH.  
**D**  **D**antrolene available. **D**ischarge, if no problems, after 2.5 hours.

*References:*

* + - 1. Mullins MF. Malignant hyperthermia: a review. Journal of Peri Anesthesia Nursing. 2018 Oct 1;33(5):582-9.
      2. Yang L, Tautz T, Zhang S, Fomina A, Liu H. The current status of malignant hyperthermia. Journal of biomedical research. 2020 Mar;34(2):75.
      3. Hopkins PM, Girard T, Dalay S, Jenkins B, Thacker A, Patteril M, McGrady E. Malignant hyperthermia 2020: Guideline from the Association of Anaesthetists. Anaesthesia. 2021 May;76(5):655-64.