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 (Ca^{2+}) 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 ($ETCO_2$)
    - Tachycardia with or without increase in blood pressure
    - Muscle rigidity which may manifest as masseter spasm after exposure to the triggering agent

- Respiratory acidosis

2. *Late signs*:
   - Increase in core temperature
   - Mixed metabolic and respiratory acidosis
   - Rhabdomyolysis leading to hyperkalemia
3. Electrolyte imbalance: hypocalcaemia and *hyperphosphatemia*
   - Cardiac dysrhythmias
   - Acute Kidney injury due to myoglobinurea
   - Disseminated intravascular coagulation may occur as a sequelae

A. 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.

2. *Medical management with i.v. Dantrolene:*
   - The dose of Dantrolene is 2-3mg/kg every 5 min until the achievement of an end tidal CO_2 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.

3. *Management of hyperthermia*:
   Active cooling with cold i.v. fluids, icepacks, and decreasing the operating room temperature should be done.

B. 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.

C. 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.

D. Continued monitoring:

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

E. 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.