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MALIGNANT HYPERTHERMIA – AN UPDATE FOR PERIOPERATIVE NURSES

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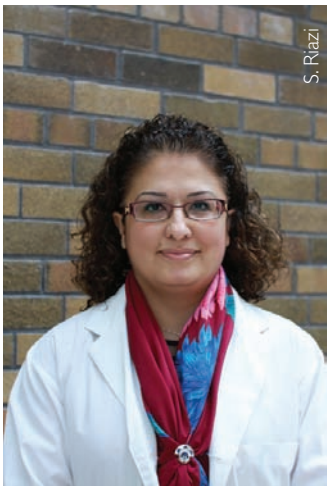
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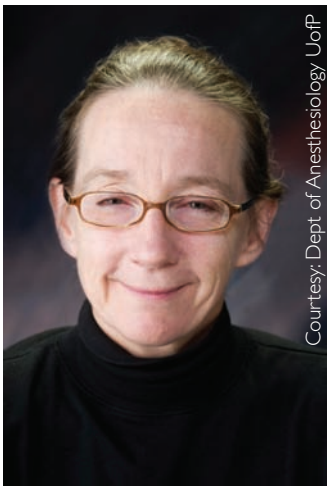
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ABSTRACT:

This article is a summary of the "Updates on Malignant Hyperthermia" presentation given at the 2015 ORNAC National Conference in Edmonton. It presents the facts known about malignant hyperthermia (MH) including definition, anesthetic and non-anesthetic triggers for MH, signs and symptoms, and treatment of MH. It also discusses the care of an MH susceptible patient while undergoing an elective surgery.

What is malignant hyperthermia (MH)?

Malignant hyperthermia (MH) is a potentially fatal disorder of the skeletal muscles.[1] It is most often triggered by volatile anesthetics and/or succinylcholine leading to a potentially fatal hypermetabolic crisis in individuals with malignant hyperthermia susceptibility (MHS).[2,3] The hypermetabolic reaction includes a surge in intracellular calcium, increased and sustained actin-myosin interaction ultimately resulting in rigidity, increased core body temperature, increased production of carbon dioxide, and increased oxygen consumption. This process can lead to exhaustion of energy supplies in muscle. Subsequent break down of skeletal muscle cells leads to hyperkalemia, acidosis, myoglobinuria and increased creatine kinase (CK). Acidosis and hyperkalemia can cause life threatening arrhythmia and cardiac dysfunction.[4]

Major complications of MH include cardiac arrhythmia and dysfunction, renal failure, disseminated intravascular coagulation (DIC), pulmonary edema, central nervous system injury, and death.

Most MHS individuals carry a mutation or variant in ryanodine receptor type -1 gene or, much less commonly, in the dihydropyridine receptor gene.[5,6] These genes encode proteins that are essential in excitation-contraction coupling and the release of calcium into the cytoplasm of skeletal muscle cells. Up to 40 or 50% of MHS patients do not, however, carry any mutations or variants in the above two genes.7-11 Research is ongoing to explore other genes involved in MH.

The incidence of MH has been reported to vary with anesthetic exposure from less than 1/50,000 to 1/250,000 anesthetics,[12,13] but the frequency of the involved gene in the population at large is estimated at 1/2000 to 1/3000.[14,15] There are some areas in Canada, such as Quebec and eastern Ontario, with a higher incidence of MH reactions than other geographic regions. This is most likely due to a cluster of MHS people that live in these areas and pass on the condition to their descendants. MH has a variable penetrance, meaning that a MHS person may not experience MH on every anesthetic. Studies have shown that some MHS patients may have up to 4-5 uncomplicated anesthetics before experiencing an MH reaction.[4]

What are the triggers for MH?

The medications that can potentially trigger MH are volatile anesthetics (e.g. Desflurane, Sevoflurane, Isoflurane) and a depolarizing muscle relaxant (succinylcholine).[3]

There are an increasing number of reports of the sensitivity of MHS individuals to exercise- and heat-induced rhabdomyolysis and these events are profiled as non-anesthetic-induced MH-like reactions.[16,21] It has been suggested that MHS individuals should have a plan for treatment of personal heat illness and consider avoiding strenuous activities in a hot environment.

An MH cart, as well as the standard crash cart, should be brought into the room where the patient is being treated.

What is the treatment for MH?

Treatment of MH reaction includes cessation of triggers, supportive measures (i.e. cooling down the patient, treating hyperkalemia and acidosis, hyperventilation) and administration of intravenous dantrolene as rapidly as possible.

An MH cart, as well as the standard crash cart, should be brought into the room where the patient is being treated. An MH cart contains dantrolene, sterile water to put dantrolene powder as a solution for injection, and syringes for injection. Charcoal filters may be added to an MH cart, that will be used in the OR, because these filters rapidly remove inhalation anesthetic from the breathing circuit.

Sodium bicarbonate, dextrose 50%, insulin (refrigerated), and calcium chloride can also be found in MH crash carts. Cooling blankets or ice packs may be used to cool down the patient. A foley catheter will be inserted to monitor diuresis. As part of the ongoing management an arterial catheter will be inserted for regular monitoring of carbon dioxide, electrolytes (especially potassium), and pH. Blood should be obtained for documentation of coagulation function and renal function. CK should be measured, as soon as practical, and repeated at least daily until a constant level is observed.

Dantrolene is a muscle relaxant that can reduce myoplasmic calcium and therefore can treat the cause of the MH reaction. Since the introduction of intravenous dantrolene the morbidity and mortality of MH have been significantly reduced. The recommended dose is 2.5 mg/kg as initial bolus, and repeating up to a total dose of 10 mg/kg or more until all signs of MH have resolved.

Literature shows that delay in administration of dantrolene can significantly increase complications of MH.[4]

Signs and Symptoms

Based on signs of MH and laboratory test measurements a clinical grading scale (CGS) has been created to estimate the likelihood that the adverse event is an MH reaction. The CGS ranks an event using score counts for generalized and masseter muscle rigidity, increase in CK, hyperthermia, unexplained tachycardia, family history, acidosis and response to dantrolene.[22] The likelihood of an individual's MH susceptibility may, however, be difficult to estimate if MH-triggering drugs were withdrawn early in the reaction or if some elements of the CGS were not documented. Most of the signs and symptoms of MH are, however, nonspecific and shared with diseases that are more common than MH. Unless the CGS score is equal to, or above, 35 MH can be difficult to recognize based on only clinical observations.

The two diagnostic tests available are genetic testing and the caffeine halothane contracture test (CHCT). Genetic testing has a relatively low sensitivity of about 50-60%.[11] CHCT has sensitivity and specificity of 97% and 78% respectively.[23]

Genetic testing, as mentioned earlier, examines the RYR1 and CACNA1S genes for changes from normal.

CHCT is an invasive test and requires surgery to harvest a piece of muscle from the thigh and test the muscle contracture response to caffeine and halothane (a volatile anesthetic). Thresholds are set and patients whose muscle contracts beyond the thresholds, in response to either or both agents, are called positive (MHS).[24]

Currently there are four centers in the US and only one center in Canada (Toronto General Hospital) that perform CHCT. Based on the authors' observations of referrals received in Canadian centers, over a 3 year period, incidence of MH reaction can be estimated at 50 cases annually in Canada. The number of active MH diagnostic centers in Canada and USA has continued to decrease from over 20 in 1990 to 5 in 2015. Please visit www.mhaus.org for an updated list of CHCT biopsy testing centers.

An individual who is diagnosed as MHS, or has a family member who had an MH reaction, should not be given any volatile anesthetic or succinylcholine.

The majority of MHS patients have normal muscle histomorphology. Histopathological examination of the muscle samples is not, therefore, diagnostic for MH and is mainly performed to rule out other muscular diseases.[25] Sudden and quick MH episodes may exhaust muscle glycogen.

How are MH susceptible patients treated?

An individual who is diagnosed as MHS, or has a family member who had an MH reaction, should not be given any volatile anesthetic or succinylcholine. They should be given total intravenous anesthesia (TIVA). The anesthetic should be designed to be "stress free". The anesthetic machine and ventilator should be flushed, according to the manufacturer's manual or published literature,[26,27] to clear residual volatile anesthetics prior to use for the MHS patient. Application of charcoal filters will speed the removal of volatile anesthetics from the machine.[28] If it is possible to apply regional anesthesia this is generally considered to be an appropriate technique. There is no role for prophylactic dantrolene. MHS patients who are given trigger-free anesthetic, and do not demonstrate any sign of MH in the first hour postoperatively, can be discharged the same day and do not need to be hospitalized for MH susceptibility.[29]

Epidural block is recommended for labour pain for an MHS patient. Regional anesthesia can also be used in case of the need for caesarean section. Upon admission of such a patient into the labor and delivery floor, an OR should be designated for emergency and the anesthesia gas delivery machine should be prepared according to the MH guidelines. A pregnant woman with a partner who is MHS should also be treated as an MHS due to the potential MHS status of the fetus.[30]

What are the available resources?

There is only one MH diagnostic center in Canada and it is located at Toronto General Hospital (https://pie.med.utoronto.ca/mh). At-risk individuals from all provinces are referred to this center for genetic counselling and CHCT.

Malignant Hyperthermia Association of United States (MHAUS) is a non-profit patient-advocacy association with a mission "to promote optimum care and scientific understanding of MH and related disorders". As part of the preparation for an MH reaction they provide posters with information on how to treat an MH crisis. In addition they offer transfer of care guidelines to help the health care team prepare action plans for moving MH crisis patients from an ambulatory center, or office-based facility, to a nearby hospital's emergency room.31 They also provide materials on how to perform an MH mock drill in different types of institutes.

MHAUS' Professional Advisory Council members vet and post answers to frequently asked questions on their website at www.mhaus.org. Information includes details on stocking an MH cart, machine preparation, temperature monitoring in an anesthetized patient, and more. Recent cases have illustrated the fact that failure to monitor core temperature increases the risk of death from MH.[32]

A list of all active biopsy centers, as well as a "Roadmap to Answers about MH" (a resource for communication between healthcare providers and their patients) is also posted on the website. Please visit the site for additional resources and up-to-date information on MH.

ORNAC Standards pertaining to this article can be found in the Operating Room Nurses Association of Canada (ORNAC) (October 2015) *Standards, Guidelines, and Position Statements for Perioperative Registered Nursing Practice* (12th edition). Section 5, pg 300, Standard 5.4.

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