CONTINUING EDUCATION

Malignant Hyperthermia: A Review

Mary Frances Mullins, DNP, RN, CRNA, CPAN, CAPA

Malignant hyperthermia is an uncommon, but potentially lethal condition that may be encountered during the perioperative period. There is wide variability in the manner in which malignant hyperthermia may manifest. For a patient to survive a malignant hyperthermia crisis, prompt recognition and treatment is of paramount importance. Perioperative nurses play a pivotal role in the successful management of malignant hyperthermia. The fictitious case study presented in this paper describes the identification, presentation, pathophysiology, and treatment of a general anesthesia patient with fulminant malignant hyperthermia.

Keywords: *malignant hyperthermia, ryanodine receptor, volatile anesthetics, succinylcholine.*

OBJECTIVES–(1) DISCUSS the pathophysiology of malignant hyperthermia. (2) Identify the pharmacological triggers for malignant hyperthermia. (3) Identify the pharmacological antidote for malignant hyperthermia. (4) Describe the perioperative management of a malignant hyperthermia crisis.

Malignant hyperthermia (MH) is a genetic disorder most often associated with the administration of volatile general anesthetic agents and/or the muscle relaxant succinylcholine. First described in 1960, MH is an uncommon but potentially lethal condition that may be encountered during the perioperative period.[1,2] For a patient to survive an MH crisis, prompt recognition and treatment is of paramount importance. This article will present a fictitious case report of a surgical patient with MH. The incidence and etiology of MH will be described, and the evidence-based practice recommendations for the recognition and treatment of MH in the perioperative setting will be reviewed.

Literature Review

MH is an uncommon pharmacogenic 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.[2,3] Lidocaine and other local anesthetics are not MH-triggering agents.[4] Very rarely, nonpharmacogenetic triggers such as heat and rigorous exercise can precipitate MH.[5] The occurrence of MH is estimated to range from 1:5,000 to 1:50,000-100,000 anesthetics.[6] Children, less than age 15 years, encompass over half of the cases of MH (52%), with males at considerably higher risk than females (2:1).[6]

MH occurs because of a genetic autosomal dominant disorder involving a mutation on the ryanodine receptor (type 1: RyR1)[7] or dihydropyridine receptor.[8] These mutations cause an atypical increase in release of calcium from the sarcoplasmic reticulum of skeletal muscle cells.[7-9] Up to 1:3,000 individuals may be genetically susceptible to MH.[6] Although all ethnic groups are affected, the incidence of MH susceptibility may be significantly higher in the French, Scandinavian, and Japanese populations.[10] Due to pockets of genetically susceptible individuals, reports of MH cases in the United States appear to

Mary Frances Mullins, DNP, RN, CRNA, CPAN, CAPA, Memorial Medical Center, Modesto, CA.

Conflict of interest: None to report.

Address correspondence to Mary Frances Mullins, Memorial Medical Center, 1700 Coffee Road, Modesto, CA 95355; e-mail address: mac3miller2@aol.com or mullinm@sutterhealth.org.

1089-9472/$36.00

http://dx.doi.org/10.1016/j.jopan.2017.04.008

be clustered in Wisconsin, Nebraska, West Virginia, and Michigan.[2] Figure 1 illustrates the main ion channels involved in the initiation of a muscle contraction following neuromuscular impulse transmission. Figure 2 illustrates the ryanodine receptor and its associated proteins.

A molecular genetic blood test may identify MH-susceptible individuals; however, the caffeine-halothane muscle contracture test remains the gold standard for making that determination.[11] The caffeine-halothane muscle contracture test has been the standard diagnostic test for MH since the mid-1970s.[12] Test results depend on the in vitro muscle contracture response of biopsied muscle to graded concentrations of the calcium-releasing agents of caffeine and halothane.[12]

MH may present anytime during general anesthesia (GA) and the early postoperative phase.[13] The earliest signs of MH are tachycardia and an increase in the level of end-tidal carbon dioxide ($ETCO_2$), along with muscle rigidity.[13,14] Masseter spasm may occur, especially after succinylcholine administration.[6]

Unrestrained skeletal muscle hypermetabolism secondary to altered intracellular calcium homeostasis potentiates cellular hypoxia.[15] This is manifested by increasing acidosis that can lead to vital organ failure. If the acidosis is not corrected, ensuing myocyte death and rhabdomyolysis result in life-threatening hyperkalemia.[6]

Core body temperature may rise dramatically, but it is not always an early sign of MH.[16] When hyperthermia occurs, it is frequently marked by a rapid increase in temperature at the rate of 1 to 2°C every 5 minutes.[17] Severe hyperthermia leads to excessive oxygen consumption and a markedly increased production of carbon dioxide, which can ultimately result in fulminant uncompensated mixed respiratory and metabolic acidosis.[6]

Other signs of MH may include cardiac dysrhythmias, disseminated intravascular coagulation, hypocalcemia, hyperphosphatemia, mottled skin, and myoglobinuria.[10] However, it should be noted that the clinical presentation and initial signs of MH are greatly variable.[18] Some people may exhibit only one or just a few symptoms of variable intensity.[19] This can make it difficult to confidently diagnose MH.[20]

Treatment of MH should be initiated as soon as the disorder is suspected. Treatment comprises calling

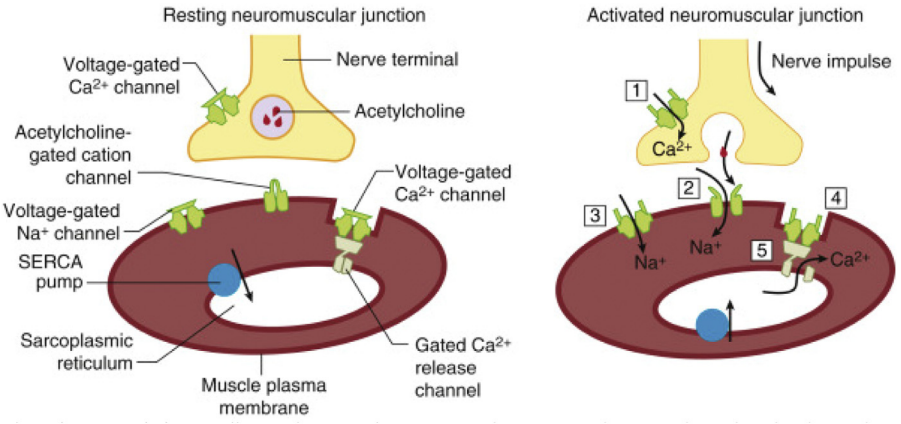

Figure 1. Key ion channels involved in neuromuscular transmission and excitation-contraction coupling. Nerve impulses arriving at the nerve terminal activate voltage-gated Ca^{2+} channels (1). The resulting increase in cytoplasmic Ca^{2+} concentration triggers the exocytosis process of acetylcholine. Binding of acetylcholine to postsynaptic nicotinic acetylcholine receptors (nAChRs) activates an integral nonselective cation channel that depolarizes the sarcolemma (2). Depolarizing the sarcolemma to threshold activates voltage-gated Na^+ channels (3), which initiates action potential impulses that propagate deep into the muscle through the transverse tubule system. Within the transverse tubule system, L-type voltage-gated Ca^{2+} channels sense membrane depolarization and undergo a conformational change (4). A physical link between the $\alpha 1$ subunit (Ca_V 1.1) of the dihydropyridine receptor (DHPR) and the ryanodine receptor (RyR1) is the means by which the electrical signal is transferred from the T tubule to Ca^{2+} release from the SR (5). Reprinted with permission from Elsevier. This figure is available in color online at www.jopan.org.