Obstetric Forum

Anaesthesia for Caesarean delivery of a malignant hyperthermia susceptible parturient

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The anaesthetic management for Caesarean delivery of a parturient with a strong family history of malignant hyperthermia (MH) is presented. Before surgery an anaesthetic machine that was in regular use was prepared by replacing all rubber or disposable components and flushing with O_2 at 10 $L \cdot min^{-1}$ for one hour. Dantrolene prophylaxis was not used, and the patient received a bupivacaine and fentanyl spinal anaesthestic. Hypotension was treated with ephedrine. Current management of the MH patient no longer mandates a dedicated vapour-free machine, dantrolene is not indicated as pre-treatment, and amide local anaesthetics are considered safe. The role of vasopressors and ergot preparations is less clear.

Cette observation décrit la prise en charge d'une parturiente présentant des antécédents concluants d'hyperthermia maligne (HM) programmée pour une extraction foetale par césarienne. Avant l'intervention, toutes les tubulures en caoutchouc et les composantes jetables d'un appareil d'anesthésie régulièrement utilisé sont remplacées et on y fait circuler de l'oxygène au débit de 10 $L \cdot min^{-1}$ pendant une heure. La patiente n'est pas préparée avec du dantrolène. Elle reçoit une rachianesthésie à la bupivacaïne et au fentanyl. L'hypotension est contrôlée avec de l'éphédrine. La technique de prise en charge actuelle de l'HM ne prévoit plus l'utilisation d'un appareil d'anesthésie exclusif exempt de vapeurs d'agents inhalatoires, le dantrolène sodium n'est plus prescrit en pré-traitement et les anesthésiques locaux de type amide ne sont pas contre-indiqués. Le rôle des vasopresseurs et des dérivés de l'ergot est moins clair.

Since malignant hyperthermia (MH) was first described there have been a number of case reports of MH reactions in obstetrical patients[1-3] and descriptions of management plans for the susceptible parturient.[4-7] Not surprisingly, as our understanding of this condition has evolved, so too has our approach to it. The following case report details our recent experience with a pregnant patient at risk for MH and describes how our management has changed in the light of new information about the condition and its triggering agents.

Case report

The patient was a healthy 29-yr-old G_2P_1 scheduled for elective repeat Caesarean delivery. Four years previously she had had an operative delivery, because of failure to progress, under an epidural anaesthetic using bupivacaine, carbonated lidocaine, and fentanyl. Subsequent to this her niece had an MH reaction during general anaesthesia. Two of her sisters proved to be muscle biopsy positive, but the patient herself had not been tested. She had also had a scar revision under lidocaine infiltration, but had never had a general anaesthetic. She reported a codeine allergy and an aversion to caffeine.

The patient was first seen by a member of the Department of Anaesthesia through the Same Day Admission for Caesarean Clinic one week before her scheduled delivery. The reasons for considering her MH susceptible, and how this would affect management, including the choice of anaesthetic and monitoring, were discussed. She was in favour of regional anaesthesia and agreed to a spinal technique.

The patient was admitted to hospital on the morning of surgery. Preoperative preparation consisted of sodium citrate 30 ml *po* and being fitted with anti-thromboembolic stockings.

One hour before surgery, the operating room was prepared by removing all recognized MH triggering agents from the room, including succinylcholine and the vaporizers from an Ohmeda Modulus II anaesthetic machine.

In addition, the machine was modified by replacing all disposable or rubber elements, such as tubing, face mask, reservoir bags, fresh gas hose, and soda lime with new, unused components. The machine was then flushed with 100% O_2 at 10 L · min⁻¹ for one hour. The resuscitation cart and MH kit were placed in the room. The MH kit contained 20 vials of dantrolene, 20 mg, with more readily available from the main operating suite, as well as chlorpromazine, hydro-cortisone, procainamide, furosemide, and mannitol. Ice was available but was not brought into the delivery room.

Upon arrival in the operating theatre a 14 ga intravenous and a radial artery catheter were inserted after skin infiltration with 2% lidocaine. Other monitors included 3-lead ECG, non-invasive automated blood pressure cuff, pulse oximeter, and a skin temperature probe which was placed under her back. Two litres of normal saline at room temperature were rapidly infused before induction of anaesthesia. The parturient received oxygen by face mask at 10 L · min⁻¹ from a separate flow meter side-mounted on the anaesthetic machine until delivery of the infant.

With the patient sitting, the subarachnoid space at L_{3-4} was identified with a 27 ga Quincke needle and 1.7 ml hyperbaric bupivacaine 0.75% with 12.5 µg fentanyl were injected. She was positioned supine with the operating table tilted 15° to the left. The maximum height of the block was T_1 bilaterally as measured by loss of temperature discrimination.

Five minutes after the spinal anaesthetic was in place the patient's blood pressure, which had been 120/80 mmHg, decreased to 82/42 mmHg although she remained asymptomatic. Increments of ephedrine to a total of 30 mg were required to return the systolic pressure to above 100 mmHg. No further blood pressure instability occurred.

Twenty minutes after induction of anaesthesia a live female infant was born with Apgar scores of 9 and 9 at one and five minutes. An infusion of 500 ml normal saline containing 20 IU syntocinon was started. The patient tolerated the procedure well, required no further vasopressor, nor any supplemental analgesia. Skin temperature which had been 35.9°C at the start of the case decreased to 35.1°C. Baseline heart rate was 80 beats per minute, increasing to 104 at delivery, but otherwise staying below 100. No arrhythmia was detected. Perioperative laboratory data are summarized in the Table.

After surgery, the patient was transferred to the obstetrical recovery room where she remained for six hours for close observation. As well as routine vital signs, temperature was measured orally every hour until transfer to the ward. She required, and received, no further specific treatment. After an uneventful postoperative course,

TABLE   Laboratory values

	Pre-induction	Post-induction	Recovery room
Haemoglobin (g · L⁻¹)	135	–	109
Creatinine phosphokinase (U · L⁻¹)	214	–	198
K⁺ (mmol · L⁻¹)	4.2	–	3.9
pH	7.40	7.29	7.32
PaCO₂ (mmHg)	31	33	33
HCO₃⁻ (mmol · L⁻¹)	19	16	18
Base excess (mmol · L⁻¹)	−4	−9	−7

she and her daughter were discharged home on the fourth post partum day. She was counselled about the importance of having a muscle biopsy performed in the near future in order to verify her own MH status and to assess her children's risk of susceptibility.

Discussion

This patient was treated as being at risk for MH because of her strong family history. Malignant hyperthermia acts as an autosomal dominant genetic condition with reduced penetrance[8] giving her a 50% likelihood of being MH susceptible.

Perioperative creatinine phosphokinase (CK) levels in this patient were elevated (normal 28–110 U · L⁻¹). One small series suggested that pregnant women have CK plasma concentrations that are within the normal range in the first trimester but show a slight elevation at term, in early labour.[9] Reported CK levels from three parturients of known MH susceptibility were much higher,[4,5,9] but CK can be normal in 60% of MH patients and elevated in 10% of unaffected people.[10] Therefore this woman's CK concentration did not help to clarify her MH status.

Definitive diagnosis of MH susceptibility is obtained by subjecting a muscle biopsy specimen to the caffeine-halothane contracture (CHC) test.[10] The local MH testing laboratory felt that a biopsy taken at the same time as the Caesarean delivery might not provide reliable information, so it was decided to defer testing to a later time. A positive biopsy taken during pregnancy has been reported,[11] but in that instance the test used was a measure of actomyosin adenosine triphosphatase (ATPase) activity which does not have the accuracy of the CHC test.[12]

Previous discussions of anaesthesia for MH susceptible parturients have recommended pre-treatment with dantrolene, the presence of a dedicated, vapour-free anaesthetic machine, epidural anaesthesia choosing ester local anaesthetics, and avoiding vasopressors.[7] When planning the management of this patient we opted to omit prophylactic treatment, we prepared an anaesthetic machine that was otherwise in regular use and performed a spinal using an amide agent and used ephedrine as required.

Dantrolene sodium is a lipid soluble hydantoin analogue which has proved invaluable in the treatment of MH crises, presumably by preventing calcium release from the sarcoplasmic reticulum.[13] It affects skeletal, cardiac, and smooth muscle. The mortality from acute MH crises has decreased from >80% to <10% because of effective management, including dantrolene.[10] Its role as a prophylactic agent in patients who will not be exposed to known triggering agents is less precise.[10] It has marked side effects such as pain on injection, thrombophlebitis, dizziness, diplopia, dysarthria, weakness, nausea, diarrhoea, epigastric discomfort, and a sensation of swollen eyeballs and tongue[13] which are often not well tolerated by patients. In addition, it does cross the placenta[14] and has been implicated as a cause of severe uterine atony.[15] Prophylaxis may be advisable in a parturient who is having a general anaesthetic, or has a history of a previous MH reaction. Only the intravenous route should be used since oral dantrolene is poorly absorbed, especially in the pregnant patient.[16]

The use of the "clean" machine, one that has never been exposed to volatile anaesthetics, has hitherto been considered fundamental in the management of the MH susceptible patient. However, there is a cost of keeping and maintaining a dedicated MH machine, which will rarely be used. In many hospitals where the labour and delivery area is separate from the operating suite either two such machines must be maintained or the one unit must be transported to where the need seems to be greater.

It has been shown that a machine in regular use can be made safe for the MH patient. McGraw and Keon[17] flushed Ohmeda Modulus II machines in which halothane had recently been used with 100% oxygen at a flow of 12 L · min⁻¹, and found that the concentration of volatile agent decreased to undetectable levels within six minutes. Beebe and Sessler,[18] using gas chromatography, measured halothane concentrations of <1 ppm after changing the circle circuit and fresh gas hose and flushing the machine for 5 minutes with 100% O_2 at 10 L · min⁻¹. The Updated Technical Bulletin for Malignant Hyperthermia[19] from the American Society of Anesthesiologists advises a 10 L · min⁻¹ oxygen wash-out through the machine for 20 min, as well as changing the tubing, fresh gas hose, and the CO_2 absorbent before using it on an MH patient.

Monitoring of these patients should be directed at identifying the early manifestations of MH, namely tachycardia, arrhythmias, and increasing CO_2 production. Muscle rigidity and increase in temperature, also signs of MH, may be delayed or absent.[10] Standard monitors are ECG, blood pressure, temperature, capnography and pulse oximetry. Central temperature monitoring provides a more accurate indication of core temperature than skin temperature which tends to be lower and is influenced by external factors and by vasoconstriction. However, oesophageal, tympanic, or rectal probes may be impractical in the patient under regional anaesthesia. A well placed skin probe can adequately measure temperature trends. In the patient undergoing general anaesthesia capnography will detect increasing CO_2. A nasal catheter placed in an awake patient in order to measure CO_2 may be uncomfortable and easily displaced, although respiratory rate may be easier to follow. With this patient we opted to place an arterial line since we intended to draw a number of blood samples. If precipitation of an MH crisis seems unlikely, arterial and central venous monitoring is probably unnecessary.

Malignant hyperthermia crises in awake patients not exposed to pharmacological triggers are extremely rare in humans, but have been reported.[20] Presenting signs may be those of sympathetic hyperactivity such as cardiac abnormalities, sweating, and tachypnoea.

Prior to Caesarean delivery prophylaxis against aspiration is mandatory. Non-particulate antacids, H_2 blockers, and metoclopramide are all considered safe in MH, but the latter is contraindicated in patients with the neuroleptic malignant syndrome.[16]

In a patient such as this, regional anaesthesia is the better choice. The hazards of general anaesthesia in pregnancy, namely increased risk of aspiration and intubation difficulties are well recognized.[21] If general anaesthesia is unavoidable, a technique that avoids known MH triggers is necessary. This would require rapid-sequence induction with thiopentone and a non-depolarizing muscle relaxant such as atracurium, and nitrous oxide and a narcotic for maintenance. Reversal of the neuromuscular blocking agents is not contraindicated, but dantrolene may cause prolonged muscle weakness.[16]

In choosing between spinal and epidural anaesthesia, the epidural route has been advocated because of the belief that the incidence of hypotension, and therefore the need to consider vasopressors, is reduced.[16] Our local experience is that, by using elastic stockings and aggressive fluid loading, the degree of hypotension and use of ephedrine does not differ between patients receiving subarachnoid or epidural anaesthesia for Caesarean delivery.[22]

Amide local anaesthetics were originally proscribed in MH patients on theoretical grounds based on their in vitro ability to increase calcium efflux from sarcoplasmic reticulum.[23] However, this class of drugs has been used extensively in MH patients without demonstrable adverse reactions.[24] As a result, the Malignant Hyperthermia Association of the United States (MHAUS) issued a policy statement in 1985 stating that amide local anaesthetics were considered safe in MH patients.[25] Based on this,

and since bupivacaine gives a better quality spinal anaesthetic than an ester such as tetracaine,[26] we did not hesitate to use the amide agent.

Sympathomimetic and parasympatholytic agents have also been listed as drugs to avoid in the MH susceptible patient, perhaps because MH reactions are accompanied by sympathetic hyperactivity[16] and because these agents may aggravate established crises.[10] There is some laboratory evidence supporting, but not proving, these concerns. Fatal MH reactions in pigs have been triggered by noradrenaline, when given in combination with propranolol, and by phenylephrine.[27] In another study ephedrine increased halothane induced contraction in vitro in muscle from MH susceptible patients, but adrenaline, noradrenaline, and isopreterenol did not.[28] However, given the lack of direct clinical evidence of detrimental effects, when the choice is either to allow hypotension to persist in a parturient with the known risks to her and to the fetus, or to use vasopressors prudently while closely monitoring the patient, rational use of ephedrine to normalize the blood pressure seems to be the better alternative.

Use of an intravenous oxytocic agent after delivery of the infant during Caesarean section to improve uterine tone and decrease blood loss is routine in our institution. Oxytocin in considered safe in MH.[16] Similar to vasopressors, ergot preparations are contraindicated because of their α-sympathomimetic properties.[5] The use of methylergonovine and prostaglandin $F_{2\alpha}$ has been reported in an MH susceptible parturient,[15] but that patient had already received dantrolene. Until further evidence regarding their safety becomes available, the possible risks of these agents versus the hazards of persistent uterine atony must be considered in a woman at risk for MH.

In addition to conducting a safe anaesthetic for the pregnant MH patient, it must be remembered that the infant may also be at risk for MH. Two case reports[29,30] detail possible MH reactions including elevated CK levels in neonates whose mothers had received general anaesthesia for Caesarean delivery. Since susceptibility could be inherited from the father, if a family history suggests MH on the father's side, this should be taken into account when planning the anaesthetic. If triggering agents which cross the placenta are used one must watch for signs of neonatal MH.

Since the CHC test is at present the best indicator of MH susceptibility, patients must be counselled on the importance of having the test performed. Parents who have previously resisted having a muscle biopsy performed may be more willing to undergo the procedure to ascertain if their children might be affected. If a child of an MH susceptible parent is being adopted the information that the infant may be at risk must be given to the social service agency handling the case.

Conclusion
The principles of managing the MH susceptible patient have not changed; namely, providing a rational, safe anaesthetic, eliminating exposure to agents known to trigger reactions and monitoring for signs of a possible reaction. What has changed is our understanding of what extra precautions may prudently be required and what is considered safe in terms of drugs and preparation of the anaesthetic equipment. The benefit of reviewing and modifying our approach to the patient is that we can eliminate unnecessary precautions and treatments, utilize the anaesthetic machines already in operation instead of maintaining special equipment, and continue to use preferred, first choice drugs and techniques.

COMMENTARY

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To date, most of the cases of MH described in the literature have occurred during anaesthesia or in the recovery room. In a recent review of 503 published cases of MH, 488 were associated with general anaesthesia. The others included six associated with illicit drug use, five associated with neuroleptic agents, one with other drugs, one from an assault and one from an over-the-counter drug combination.[31] It should be noted that there was some doubt as to the diagnosis in most of the cases that occurred outside the operating room. There were no cases of MH associated with regional anaesthesia.

Malignant hyperthermia in pregnancy is rare. Although labour can be very stressful, there are no reported cases that are unrelated to general anaesthesia.[31] However, MH has occurred in a parturient[3] during Caesarean section and perhaps also in a neonate.[29]

In the past seven years 19 patients, who either were MH susceptible or had a family member who was MH susceptible, delivered at Women's College Hospital, Toronto. Two of these had had a positive muscle biopsy, two had a history very suggestive of an MH reaction in the past, and the rest had a positive family history of MH or a family member who had had a positive biopsy. Interestingly, four patients were referred because the husband was MH susceptible and there was concern for the neonate. Of these, most delivered vaginally with epidural analgesia but two had no analgesia. All the Caesarean sections were performed under regional anaesthesia. None of the patients had an MH reaction.

At our institution, the approach to the MHS parturient is similar to that described in the case report. All patients are seen in the Obstetrical Consult Clinic when they are identified by the obstetrician as MH susceptible.

If the patient is undergoing a trial of labour, the nurses inform anaesthesia when the patient is admitted to hospital. This allows time for the anaesthetist to talk to the patient and make the necessary preparations. Temperature monitoring is problematic in these patients. Most prefer to ambulate in early labour and do not wish continuous monitoring of any sort. In our institution, the temperature is monitored hourly unless there is a complication demanding more frequent readings. Fortunately, the awake patient feels unwell and fatigued if she develops a high fever[20] and will be able to report these symptoms. We maintain a drug cart on the labour floor which contains 160 mg dantrolene, with more available from the operating room. In addition, we ensure that sufficient ice, cold intravenous solutions and equipment to initiate invasive monitoring are accessible, if required. We also have a vapour-free anaesthetic machine although flushing the standard anaesthetic machine with oxygen, as was done in this case, is probably all that is necessary. Finally, the succinylcholine is removed from the top of the anaesthetic table. The room is not used for other cases until the patient has safely delivered. As with any parturient, epidural analgesia is offered. In the MHS patient, there is the added benefit of stress reduction although stress has not been reported to trigger an MH reaction in labour. Having an epidural catheter *in situ* may reduce the chance of requiring a general anaesthetic should an obstetrical emergency arise.

For elective Caesarean section, we strongly encourage the patient to have regional anaesthesia. Axillary temperature is monitored continuously throughout surgery and the recovery period. Increases in respiratory rate and end-tidal CO_2 monitored via nasal prongs, along with changes in pulse oximetry and ECG, should alert the anaesthetist to an incipient MH reaction, making invasive monitoring unnecessary. Venous gases for pH can be drawn at intervals through an indwelling venous cannula in the forearm. In this circumstance, venous blood has the advantage of reflecting pH in the muscle.

The use of prophylactic dantrolene is controversial. Apart from the unpleasant side effects of weakness and nausea, dantrolene has been associated with postpartum atony.[15] We would therefore only use it in severely reactive patients who are undergoing general anaesthesia.

After surgery, the patient is observed in the recovery room for four to six hours and then monitored on the floor with routine vital signs every four hours. Since these patients receive spinal opioids, the respiratory rate is recorded on the ward at hourly intervals. Instructions are left for the nurses to notify the anaesthetist if there is a fever above 38.5°C that is unresponsive to acetaminophen.

In summary, this case report describes the management of a relatively common problem in obstetrical anaesthesia practice, the potentially MH susceptible parturient. Fortunately, many of the earlier controversies have been resolved in favour of using common, effective agents (amide local anaesthetics), and causing the patient the least amount of discomfort and inconvenience (narrow indications for prophylactic dantrolene). While it is true that MH reactions in pregnancy are extremely rare, the drugs and equipment necessary to treat a reaction should be readily available.

COMMENTARY

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Several years ago, Crawford wondered whether the pregnant patient was in some way protected from MH.[32] His conjecture was based on the paucity of accounts of MH in pregnant women, a fact which still persists. Possible reasons for this low incidence are the greater use of regional anaesthesia for Caesarean section, compared with other surgery, and an under-reporting of cases due to fears of litigation. As triggering agents (succinylcholine and volatile anaesthetic agents) are commonly used in combination for emergency Caesarean section, one would still expect more reported cases.

Much has changed in the management of the MHS parturient since we first reported our experience.[7] There is still a dilemma as to whether or not awake MH reactions occur during labour. Development of a fever and/or tachycardia in the labouring MHS parturient will ultimately cause concern about MH. It is important to remember that fever is more likely due to sepsis or epidural analgesia in labour[33,34] than due to an MH reaction in an awake patient. The same applies to tachycardia which may result from pain, anxiety or fever.

Use of a clinical grading scale[35] to predict MH susceptibility helps determine the relative importance of a single sign or symptom. It relies on the anaesthetist evaluating the appropriateness of these signs for the patient's status. It also identifies those patients who should undergo muscle biopsy, based on their history.

Management of general anaesthesia for emergency Caesarean section (fetal distress or severe maternal haemorrhage) in the MHS parturient is always a concern.

There is the need for rapid muscle relaxation for tracheal intubation and, as succinylcholine is contraindicated, Dr. Lucy suggests the use of atracurium. Vecuronium, 0.25 mg · kg⁻¹, might be a better choice as it produces less hypotension and tachycardia.[36] Obviously, if difficulty with intubation is anticipated awake intubation should be performed. The volatile anaesthetic agents are also contraindicated so it is necessary to protect the patient from recall of intraoperative events. This can be accomplished with either a propofol infusion or low-dose midazolam. The best solution to the problems of recall and muscle relaxation is to avoid general anaesthesia by early identification of the MHS parturient and placement of an epidural prior to the need for Caesarean delivery. For the patient with fetal distress, spinal anaesthesia can be rapidly induced.

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