Controversies in paediatric anaesthesia

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Masseter muscle rigidity

Masseter muscle rigidity (MMR), also known as masseter spasm, is a well-known sign of the rare syndrome malignant hyperthermia (MH). However, in two recent studies one per cent of all children anaesthetized with halothane and paralyzed with succinylcholine developed MMR,^{1,2} that is 100–200 times greater than the incidence of MH in the population.³ Furthermore, 50 to 70 per cent of these patients were biopsy-positive for MH. These alarming statistics have raised concern and generated confusion among paediatric anaesthetists. In order to clarify some of the confusion, I will review the pathophysiology and clinical findings of MMR and discuss its management.

MMR is defined as a transient contracture of the muscles of mastication after administration of succinylcholine. MMR reaches its maximum effect within 30–45 seconds after succinylcholine and lasts only several minutes. This abnormal response to succinylcholine usually is detected first when attempts to insert a laryngoscope into the mouth are *actively resisted* by clenched teeth. Despite vigorous attempts to pry the mandible and maxilla apart with the laryngoscope blade, the mouth opening rarely exceeds 1–2 cm. MMR, which must be differentiated from other causes of limited

excursion of the mandible (listed in the Table), is an active resistance that is quite distinct from the more common finding of "incomplete relaxation of the jaw." A peripheral nerve stimulator may be helpful to verify complete relaxation of the extremities.

Since MMR may be the only sign heralding MH, the diagnosis of MMR should be based on objective findings. In an attempt to test objectively masseter muscle tone, Van der Spek *et al.* measured masseter muscle tone in healthy children anaesthetized with halothane and paralyzed with several muscle relaxants including succinylcholine.⁴ They found that masseter muscle tone increased transiently after succinylcholine but did not increase after non-depolarizing relaxants. Unfortunately, there were no instances of MMR in their study to differentiate the effects of succinylcholine on masseter muscle tone in children with MMR from healthy children. In order to objectively diagnose MMR, a quantitative measure of masseter muscle tone such as that described by Van der Spek *et al.* may prove very useful in the future. MMR remains a subjective diagnosis.

The very high incidence of MMR, 1.0 per cent in children anaesthetized with halothane and succinylcholine, is 10 to 20 times the estimated incidence of MMR at The Hospital for Sick Children in Toronto. Why should the incidence of MMR vary so greatly between centres? The discrepancy may be attributed in part to differences in anaesthetic techniques: in centres with a high incidence of MMR, patients are anaesthetized with halothane and paralyzed with succinylcholine^{1,2} whereas in centres with a low incidence such as ours, they are anaesthetized first with thiopentone, atropine, and succinylcholine and then given halothane. With the former technique, the combination of halothane and succinylcholine is a potent trigger for MH and may be considered an *in vivo* halothane-caffeine contracture test whereas with the latter technique, MH reactions are less frequent because of: (1) the protective effect of thiopentone⁵ and (2) the temporal separation of succinylcholine from halothane. Similar reasoning may account for the low incidence of MMR in adults. The incidence of MMR after succinylcholine in your practice may be reduced by the avoidance of

TABLE Causes of limited excursion of the mandible

Temporomandibular joint disorders
Congenital dysfunction
Inflammatory (infection, arthritis)
Trauma
Post-surgical
Muscle disorders
Malignant hyperthermia (masseter muscle rigidity)
Myotonia
Myopathy/myositis
Integumentary/fascia disorders
Neoplasm
Infection
Post-irradiation
Scleroderma
Freeman-Sheldon syndrome
Arthrogryposis
Trismus pseudocamptodactyly syndrome
Neurological injury
Denervation
Atypical response to succinylcholine
Ineffective succinylcholine

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succinylcholine during inhalational inductions or by the use of non-inhalational induction technique (intravenous, intramuscular, or rectal) when succinylcholine is to be administered.

Management

When MMR is diagnosed, the airway must be secured. Most patients with MMR undergoing elective surgery can be ventilated by mask and 100 per cent oxygen until they have recovered from the anaesthetic. However, if the airway cannot be maintained by mask, then a laryngoscope blade should be inserted between the molar teeth and sustained traction applied to overcome the contracture. If the contracture persists, then dantrolene $2.4 \text{ mg} \cdot \text{kg}^{-1}$ should be infused rapidly.⁶ There is no place for non-depolarizing muscle relaxants in this instance since the defect in MMR is within the muscle cell and not at the neuromuscular junction.

Should anaesthesia and surgery be terminated when MMR is diagnosed? Since 50–70 per cent of these patients are biopsy-positive for MH (usually type K),⁷ it is prudent to stop anaesthesia for all elective surgery and monitor the patient for signs of an MH reaction. However, this practice is not universal. Carroll recently reported a series in which anaesthesia was continued in 14 of 15 patients with MMR: three were given trigger-free anaesthetics and 11 were given halothane.² One MH reaction was diagnosed in the latter group and was treated successfully with dantrolene.

When MMR occurs during emergency surgery, the anaesthetic should be converted to a trigger-free technique and the surgery allowed to continue. Intravenous dantrolene must be available immediately in the operating room to treat an MH reaction. With these modifications to the anaesthetic, emergency surgery may then be completed with minimal risk of an MH reaction.

Patients with MMR must be monitored postoperatively in a constant care setting (ICU or recovery room), until all signs of MMR (including jaw pain and stiffness) have resolved. The postoperative management should include continuous axillary and rectal temperature, serum CPK concentrations at 8–12 and 24 hours after succinylcholine, venous (or arterial) blood gases immediately postoperatively and intermittently for 24 hours and urine for myoglobinuria. Intravenous dantrolene is usually not required during this period unless signs of an MH reaction develop. If dantrolene is required, $2.4 \text{ mg} \cdot \text{kg}^{-1}$ should be given as a single rapid intravenous infusion over 10–15 minutes (elimination half-life of 9.8 hours).⁸ This provides a protective blood concentration of dantrolene for approximately five to six hours.⁸ Supplemental doses of dantrolene may be administered as needed in $1 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ increments until all signs of MH have dissipated.

The parents should be counselled about MH and Medic-Alert bracelets ordered for family members. A muscle biopsy should be considered for both the patient and the parents.

Anaesthetic agents in the neonate

In the last 25 years, advances in perinatal care have increased the survival of preterm neonates weighing less than 1000 gm at birth from less than 10 per cent to approximately 50 per cent. With this increase in survival, the numbers of preterm neonates presenting for surgery have also increased. Whereas the low survival of preterm neonates 25 years ago required little more from anaesthesia than a prolonged resuscitation, today anaesthesia for the preterm and full-term neonate undergoing surgery must provide all of the requirements of anaesthesia; i.e., analgesia, attenuation of reflex responses, muscle relaxation, and absence of awareness since recent data have demonstrated that neonates respond to nociceptive stimuli with stress (hormonal) responses, reflex responses and movement.^{9–12} In order to satisfy these requirements, we will consider the inhalational and intravenous agents available for general anaesthesia. Spinal anaesthesia, another technique available for the high-risk neonate, has been the topic of a recent review by Broadman.¹³

Although the inhalational anaesthetic agents halothane and isoflurane are used routinely in paediatrics, their use in preterm and full-term neonates has been discouraged because of reports of profound circulatory depression.¹⁴ These reports were accepted because in the neonate the ventricular compliance is reduced, the cardiac output is heart-rate dependent, the afterload does not decrease appropriately in response to an increase in end-diastolic pressure, and the baroreceptor response is attenuated compared to adults.^{15–17} These differences support the contention that the neonate is vulnerable to circulatory depression. However, contrary evidence is available. Gregory *et al.* measured the MAC for halothane in infants 0–6 months of age and found the MAC to be 1.10 per cent.¹⁸ Because MAC values in neonates and older infants were assumed to be equal, Diaz and Lockhart compared the circulatory responses to equal concentrations of halothane and nitrous oxide in neonates and older infants.¹⁴ They found that hypotension (>30 per cent decrease in blood pressure) occurred significantly more frequently in neonates (70 per cent incidence) than in older infants (30 per cent incidence). They concluded that neonates are more prone to circulatory depression than older infants. Subsequently, we measured the MAC for halothane in neonates and found it to be considerably lower (0.87 per cent) than that of older infants one to six months of age (1.20 per cent).⁹ These MAC values differed by 30 per cent. Based on these measurements, we found that at equipotent (rather

FIGURE

than equal) concentrations of halothane, full-term neonates are no more prone to circulatory depression than older infants.

When the MAC for isoflurane in preterm neonates was measured it was found to be 1.28 per cent in neonates less than 32 weeks gestational age at birth and 1.41 per cent in those 32-37 weeks at birth (Figure).¹² These values are both significantly less than the MAC for isoflurane in full-term neonates (1.60 per cent) and infants one to six months of age (1.8 per cent).¹⁰ Based on these measurements, we have found that at equipotent concentrations of isoflurane, circulatory depression in these two groups of preterm neonates does not differ provided that the anaesthetic is administered in incremental doses and balanced salt solutions or colloids are administered to maintain the systolic arterial pressure ≥ 40 mmHg. In fact, the circulatory responses of preterm neonates are similar to those reported previously in full-term neonates at 1 MAC halothane.⁹ We conclude that volatile anaesthetics may be administered safely in preterm neonates, full-term neonates and older infants and that the extent of circulatory depression is similar in all age groups providing equipotent concentrations of volatile anaesthetics are administered.

Fentanyl is the most commonly used intravenous analgesic for anaesthesia in neonates. The recommended dose of fentanyl is $10-50 \mu\text{g} \cdot \text{kg}^{-1}$.²⁰⁻²³ This dose of fentanyl is adequate for one to three hours depending on the type of surgery. Fentanyl should be administered in incremental doses while the systolic arterial pressure and heart rate are monitored carefully. If hypotension does occur, it should be corrected with balanced salt solutions

or colloids ($5-15 \text{ ml} \cdot \text{kg}^{-1}$). When the circulatory effects of fentanyl were compared to those of isoflurane and halothane in preterm neonates, the extent of hypotension did not differ significantly among the three anaesthetics.²² Because bradycardia and chest wall rigidity may occur in neonates who receive fentanyl, atropine and a neuromuscular blocking drug are recommended.

Nitrous oxide is avoided in preterm neonates for two reasons: (1) the presence of bowel obstruction, and (2) the risk of hypoxaemia during intentional borderline arterial saturation (85-90 per cent).

There remains no doubt that with this new information regarding the anaesthetic requirements for volatile anaesthetics and fentanyl in preterm neonates, anaesthesia for these patients can and should be administered.

The fasting dilemma

The preoperative fast is considered an essential prerequisite for all elective surgery. However, few agree on the duration of fasting in paediatrics. To clarify the controversies about fasting, we will review our understanding of fasting guidelines in paediatrics.

At The Hospital for Sick Children, the standing NPO orders state that solids, formula and breast milk may be given until 0200 hours and clear fluids until 0400 hours on the day of surgery. If clear fluids are required after 0400 hours, then the anaesthetist must specifically order these fluids. In a recent informal survey of fasting orders in 30 paediatric institutions in the USA and Canada there was little agreement on the duration of fasting after clear fluids in any age group. Is there any scientific evidence to recommend a specific duration of fasting?

The objectives of the preoperative fast are to minimize the gastric fluid volume, and maximize the gastric fluid pH. Meakin *et al.* recommend a minimum fasting period of four hours to minimize gastric fluid volume.²⁴ Manchikanti *et al.* found that the gastric fluid pH correlated with the duration of fasting in adults and children, although the coefficient of correlation was not reported.²⁵ Côté *et al.* reported that seventy-six per cent of fasting children are at risk for severe pneumonitis.²⁶ To determine whether gastric fluid volume or pH correlates with the duration of fluid fasting in children, we measured the gastric fluid volume and pH in 40 children whose duration of fluid fasting varied from two to eight hours.²⁷ We found no correlation between volume or pH and the duration of fasting. We concluded that fluid fasting periods in excess of two hours are not associated with any increase in patient safety. It should be noted that fasting periods less than two hours have not been studied.

How long should breast-fed infants be fasted before elective surgery? There is little data on gastric fluid

volume and pH in breast-fed infants. According to the informal survey cited above, breast-fed infants are fasted four hours in 50 per cent of institutions and six hours in 33 per cent of institutions. Since both breast milk and cow's milk precipitate in acidic medium (forming a suspension of particulates) and since proteins and fats delay gastric emptying, the duration of fasting after milk should be greater than that after clear fluids.

Two factors known to affect the severity of pneumonitis following gastric fluid aspiration are the pH and the volume of the fluid aspirated. A gastric fluid pH < 2.5 and a volume > 0.4 ml·kg⁻¹ predispose to severe pneumonitis although the former factor is considered more important.²⁸ Fasting does not reliably increase the gastric fluid pH > 2.5 and decrease the fluid volume < 0.4 ml·kg⁻¹ in children.²⁷ In order to reduce the severity of pneumonitis after aspiration, pharmacologic interventions to increase the gastric fluid pH (>2.5) and decrease gastric fluid volume (< 0.4 ml·kg⁻¹) are required.

Goudsouzian and Young recently found that 2.0 mg·kg⁻¹ oral ranitidine one to four hours before surgery significantly decreased gastric fluid pH in children.²⁹ Recently, we compared ranitidine and metoclopramide: we found that ranitidine 2.0 mg·kg⁻¹ with or without 0.1 mg·kg⁻¹ metoclopramide given orally four hours before surgery significantly increased gastric fluid pH and decreased gastric fluid volume.³⁰

In summary, the optimal fasting regimen for infants and children remains to be established. Preliminary data indicates that the duration of fasting may be safely reduced to two hours after clear fluids and that oral ranitidine pretreatment may be given to reduce the risk of severe aspiration pneumonitis. Further clinical trials are needed to validate these data. The question of optimum solid fasting regimen remains to be answered.

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