Anaesthetic Considerations during prolonged Major Abdominal Surgery

Dr. M. Ravishankar

Why talk about major abdominal surgery? If you look in the text books, you will find chapters on Cardiac anaesthesia, Neuro anaesthesia, Obstetric anaesthesia, Paediatric anaesthesia etc. When you read these chapters it is assumed that you have mastered the art and science of anaesthesia for abdominal procedures which forms the fundamental basis. Often you find people getting carried away and start focusing on the above areas during their learning period without really understanding the basics. The very idea of this lecture is to focus on the need to understand the basics of balanced ‘steady state’ anaesthesia for a prolonged period of time so that the stress response to surgery is minimised and physiological responses can be interpreted for taking corrective action at the appropriate time.

Definition

There are no accepted guidelines to call a procedure as prolonged. For practical reasons, we can call it as prolonged if the duration exceeds 4 - 6 hours. It is very arbitrary but acceptable as the adverse effects of the procedure and anaesthesia starts manifesting after about 4 hours.

The Requirement:

The requirements for balanced steady state anaesthesia should consider the components of anaesthesia which form the ‘Triad’; a) Narcosis, b) reflex suppression and c) relaxation. Narcosis includes unconsciousness as well as lack of perception of pain sensation. Reflex suppression includes both autonomic and somatic reflexes. Muscle relaxation adequate to perform surgery should be produced.

All these objectives are usually easily achieved. The patients are usually premedicated with drugs to produce sedation and anxiolysis. Induction of anaesthesia is often performed with intravenous agents and narcotics though inhalational agents can be used for the same. Maintenance of narcotics is done using inhalational agents and
narcotics adequate to suppress the reflexes. Relaxation is produced using neuromuscular blocking agents.

Is that all that needs to be done to have a satisfactory outcome. Just alleviating pain during surgery and maintaining unconsciousness is not enough to achieve an outcome that is contributory for the recovery of the patient after surgery. The goals may be alright to achieve surgical anaesthesia during the surgery, but as anaesthesiologist we should consider the entire perioperative period to achieve satisfactory outcome. For this the focus has to shift from just anaesthesia to encompass other factors, ie., a) Reduction in stress response b) Maintaining near normal homeostasis including O2 delivery and CO2 removal.

Initiation of the stress response is primarily due to afferent nerve impulses combined with release of humoral substances, such as prostaglandins, kinins, leukotrienes, interleukin-1, and tumor necrosis factor from the surgical site. Factors like semi-starvation, infection, and hemorrhage can amplify the response. The neural pathway is probably most important in releasing the classical endocrine catabolic response, while humoral factors are important for the hyperthermic response, changes in coagulation and fibrinolysis, immunofunction, and capillary permeability. The modifying effect of pain relief on the surgical stress response is dependent upon the technique of analgesia. However, the effect on humoral-mediated responses is small, regardless of the technique used.

**SHORT TERM EFFECTS OF ANAESTHESIA**

**Analysis of effect of drugs used in General Anaesthesia:**

The drugs administered intravenously are dependent on metabolism and / or elimination for termination of the effect. Inhalational agents are eliminated unchanged through the lungs and have minimal metabolism. Pharmacodynamic effects are more important while considering inhalational agents whereas both pharmacokinetics and dynamics have to be taken into account for intravenous agents.

**Premedicant drugs:**
**Opioids:** The inclusion of opioids as a component of anaesthesia can reduce the preoperative pain and anxiety, decrease somatic and autonomic responses to airway manipulation, improve haemodynamic stability, lower requirement of inhaled anaesthetics and provide immediate postoperative analgesia. The administration of a opioid, attenuate physiologic responses better when administered prior to, rather than after initiation of noxious stimulation. The timing and dose of supplemented opioid should be tailored to the specific condition of the patient and the expected duration of surgery in order to avoid postoperative pain *vis a vis* respiratory depression. Respiratory depressant effects of opioids are enhanced and/or prolonged when administered with other CNS depressant drugs like inhaled anaesthetics, barbiturates and benzodiazepines.

Hypocapnic hyperventilation has been shown to enhance the postoperative respiratory depression after fentanyl. Possible explanation includes increased brain opioid penetration due to increased unionised fentanyl with hypocarbia. Intraoperative hypercarbia produces opposite effect. Delayed respiratory depression has been reported with most opioids. Mechanism for renarcotisation include augmented release of fentanyl or other opioids from skeletal muscle into systemic circulation on rewarming, shivering, movement or any other condition that enhances muscle perfusion. Reduction in liver blood flow that results from induction of anaesthesia or during prolonged anaesthesia, intraoperative hypotension or haemorrhagic shock will delay the decline of morphine and fentanyl concentration thus prolonging the effect.

**Other premedicant drugs:** Benzodiazepine group of drugs are the most commonly used anxiolytic agents. They have a prolonged action and for some drugs the metabolites are also active. Administration of a single dose does not alter the pharmacodynamics of most anaesthetics. But if used concomitantly during the course of anaesthesia they can significantly alter the cardiovascular and respiratory actions of opioids and inhaled anaesthetics.

**Inducing agents:**

**Thiopentone:** It’s quicker distribution to highly perfused low volume tissues (eg. Brain) and slower redistribution of the drug to lean tissue (eg; muscle) terminates effect of the induction dose. Because of its affinity to fat, relatively large volume of distribution
and low rate of hepatic clearance, thiopental can accumulate in tissues especially if given in large doses or as infusion over a prolonged period.

**Propofol:** It is rapidly metabolised in the liver and excreted by the kidney. After a single bolus injection, whole blood propofol level decreases rapidly as a result of both redistribution and elimination. Elimination half life varied from 1 to 3 hours. Propofol may impair its own clearance by decreasing hepatic blood flow due to its reduction in arterial pressure. Recovery from propofol anaesthesia remains rapid even after prolonged infusions. During maintenance of anaesthesia with propofol infusion systolic pressure remain between 20% and 30% below pre induction levels and context sensitive half life should be considered to understand the recovery.

**Ketamine:** The duration of ketamine anaesthesia is determined by the dose; higher doses produce more prolonged anaesthesia and the concurrent use of the other anaesthetics also prolongs the time of emergence. It’s relatively short duration of action is due its redistribution from the brain and blood to other tissues in the body. Termination of effect after a single bolus administration of ketamine is a result of drug distribution from well perfused to less well perfused tissues. Concomitant administration of benzodiazepines may prolong ketamine’s effect. Ketamine stimulates the cardiovascular system and is usually associated with increase in blood pressure, heart rate and cardiac output.

**Maintenance drugs:**

**Inhalational agents:**

**Effects on CVS:** All modern volatile anaesthetics depress contractile function in normal myocardium. The relative degree of myocardial depression produced by different volatile anaesthetics has been more difficult to establish because simultaneous alterations in sympathetic nervous system activity often complicate the assessment of LV systolic function. Isoflurane and sevoflurane produce less myocardial depression than halothane. Halothane produces more pronounced myocardial depression in ischemic than normal myocardium. Volatile anaesthetic cause direct negative chronotropic action by depressing sinoatrial node activity. Isoflurane increases HR in response to simultaneous decreases in BP.
All volatile anaesthetics cause concentration related decrease in arterial pressure. The mechanisms by which these anaesthetics reduce arterial pressure differ among anaesthetics. Decrease in arterial pressure produced by halothane can be primarily attributed to reduction in myocardial contractility and cardiac output. In contrast, isoflurane and sevoflurane reduce LV afterload while preserving myocardial contractility.

The cardiovascular effects of volatile anaesthetics are altered by duration of anaesthesia. Increases in myocardial contractility and cardiac output and decreases in LV preload and afterload occur after several hours of constant MAC anaesthesia. Recovery from circulatory depression is greatest during halothane anaesthesia and less pronounced during prolonged administration of isoflurane.

Volatile anaesthetics have the potential to produce bradycardia and AV conduction abnormalities because these agents prolong the His-Purkinje and ventricular conduction time. Halothane and to a lesser extent other agents sensitize the myocardium to the arrhythmogenic effects of epinephrine.

Nitrous Oxide causes direct negative inotropic effects, does not substantially affect LV diastolic function. It produces modest increases in pulmonary and systemic arterial pressure via a sympathomimetic effect.

**Effects on Liver:** Up to 80% of halothane is eliminated / cleared from the body by exhalation, and 20% is metabolised in the body. Metabolism is entirely by liver both oxidatively and reductively by cytochrome P450. Oxidative metabolites are inorganic bromide, chloride and trifluoro acetic acid. Trifluoro acetyl intermediate is thought to play a role in liver toxicity. Reductive path which occur in presence of hypotension and hypoxia produces reactive metabolites, difluorochloro ethylene, trifluoro chloroethane and free radicals; possibly these are responsible for halothane hepatitis.

One study showed a significant increase in plasma Glutathione S transferase (GST) concentration 3 hours after halothane anaesthesia, with a secondary peak occurring after 24 hours. Peak at 3 hours is a result of alteration in the hepatic blood flow and oxygenation. Secondary peak is thought to be a result of toxic effects of metabolites. The incidence of liver injury caused by isoflurane is less than that of halothane and it correlates with the extent of their oxidative metabolism (halothane 20% and isoflurane
Studies have shown mild elevations in post operative levels of liver transaminases after sevoflurane anaesthesia.

**Effect on Kidney:** All anaesthetic techniques and agents tend to decrease GFR and intra operative urine flow. Halothane and isoflurane with N₂O induces mild to moderate reduction in RBF and GFR primarily as a result of their effects on central circulation (myocardial depression, peripheral pooling).

The potential nephrotoxicity of volatile agents is due to their metabolic breakdown to free fluoride ion, which cause a tubular lesion that results in loss of concentrating ability and polyuric acute renal failure. Methoxyflurane is rarely used in clinical practice today because of its association with polyuric renal failure resulting from high levels of inorganic fluorides. Patients with levels of inorganic fluoride < 50 micromol / L had no evidence of renal injury. Levels of 50-80 micromol / L (2.5 to 3 MAC hours of methoxyflurane) were associated with moderate injury and levels of 80 – 120 micromol / L (> 5 MAC hours of methoxyflurane) with severe injury. It was associated with mortality when inorganic fluoride levels were higher than 120 micromol / L.

Isoflurane is not associated with fluoride associated nephrotoxicity. However, during prolonged anaesthesia for about 19 MAC hours, peak plasma fluoride levels can be much higher after isoflurane administration than after halothane administration. Because the other toxicities are comparatively less, isoflurane is effective for prolonged anaesthesia.

Prolonged anaesthesia with sevoflurane 1-4% with N₂O in patients with normal hepatorenal function is associated with rise in serum inorganic fluoride that may exceed 50 micromol / L. Fluoride level falls very quickly after cessation of anaesthesia because of its low blood-gas solubility and its rapid elimination.

Compound A, a vinyl ether formed by degradation of sevoflurane at low flow through carbondioxide absorbents is capable of inducing renal injury. Baralyme is associated with higher compound A production than soda lime. The presence of potassium and sodium hydroxide in the composition of the absorbent is primarily responsible for the production of compound A. Introduction of absorbents without these
hydroxides has the safety of sevoflurane in closed circuit anaesthesia. The relationship between compound A formation, biochemical injury and clinically relevant renal dysfunction remains unclear and unproven. Under condition of prolonged sevoflurane exposure in which renal changes have been observed, these changes have been transient only. FDA recommends a fresh gas flow of at least 2 L / min to inhibit compound A formation and its rebreathing and to enhance its washout (This recommendation is likely to change with the present available evidence using the newer absorbents).

**Toxic effects:** N₂O is the only anaesthetic reported to produce haematologic toxicity and neurotoxicity with long term administration. Both toxicities are the result of the interaction of N₂O with vitamin B₁₂ and the disruption of several pathways in one carbon chemistry. Megaloblastic bone marrow changes are seen after 12 hours of exposure with 50% N₂O in healthy patients; after 24 hrs of exposure, changes are marked. Evidence also suggests that bone marrow changes are preventable by pretreating patients with large doses of folinic acid.

**Neuromuscular blocking drugs**

Long acting neuromuscular agents and its 3 OH metabolites are excreted through the kidney. In prolonged anaesthesia its clearance is decreased. Duration of action is significantly prolonged by hypothermia, volatile anaesthetic agents and hepatic and renal dysfunction in prolonged anaesthesia.

During prolonged surgery with neuromuscular monitoring, frequent stimulation of the nerve may produce a lasting antagonism of neuromuscular blockade in the stimulated muscle, which may no longer be representative of other muscle groups.

**AFFERENT NEURAL BLOCKADE**

Epidural anaesthesia and analgesia have the potential to reduce or eliminate the perioperative physiologic stress responses to surgery and thereby decrease surgical complications and improve outcomes.

Afferent neural blockade with local anesthetics is the most effective technique for reducing the endocrine-metabolic response, but only in operations in the lower part of the abdomen, probably because of insufficient afferent blockade during thoracic epidural
analgesia. Systemic opiate as well as non-steroidal antiinflammatory drugs administration, exert only a small modifying effect on the response. Low-dose combined analgesic regimens may provide total pain relief, but exert no important effect on the stress response. In summary, pain alleviation itself may not necessarily lead to an important modification of the stress response, and a combined approach with inhibition of the neural and humoral release mechanisms is necessary for a pronounced inhibition or prevention of the response to surgical injury.

"Preemptive analgesia" describes the concept of decreasing pain perception and overall analgesic needs after surgery by use of a drug regimen capable of inhibiting CNS sensitization before the application of painful stimuli.

4 large studies involving high-risk (eg, aortic reconstruction) surgery patients have reported significant reductions in cardiac morbidity associated with use of intraoperative and postoperative epidural anaesthesia/analgesia using local anesthetics plus opioids. In addition, intraoperative epidural administration of local anesthetics blunts the physiologic hypercoagulable surgical stress response and modifies the perioperative hypercoagulable state. This occurs via several mechanisms, such as blockade of sympathetic efferent signals, enhanced fibrinolytic activity, and systemic absorption of local anesthetics.

**EFFECTS ON VENTILATION**

Induction of general anaesthesia is consistently accompanied by a significant decrease in FRC which usually causes decrease in compliance. Positioning and increased airway resistance are also contributory to decrease in FRC. In the absence of any complicating factors, it does not seem to decrease progressively during anaesthesia.

Pulmonary morbidity in the postoperative period has been attributed to the type of anaesthetic agent and physiologic perturbations of the pulmonary system. Thoracic epidural analgesia/anaesthesia (TEAA) can reduce the incidence of postoperative atelectasis, pneumonia, and hypoxemia by directly influencing these variables. Perhaps the most profound effect of major abdominal and thoracic surgery on pulmonary function is a reduction in the functional residual capacity (FRC) due to diaphragmatic dysfunction, decreased chest wall compliance, and pain-limited inspiration. As a result, FRC decreases
by at least 20% after abdominal surgery, reaching its lowest point at 24-48 hours and not returning to normal until 1 week. On the other hand, TEAA with a local anaesthetic and general anaesthesia when compared with IV-PCA and general anaesthesia resulted in a 27% increase in the FRC and an overall improvement in pulmonary outcome. Reflex inhibition of the phrenic nerve after major surgery also causes measurable impairment of diaphragm contractility that continues 5-7 days postoperatively. The reflex inhibition is not affected by the use of systemic or epidural opioids. However, TEAA with a local anaesthetic disrupts the reflex arc and permits normal diaphragm function.

During prolonged anaesthesia, some parts of lung may be continually dependent and below the left atrium and therefore in zone 3 or 4 condition. Being in a dependent position, the lung is predisposed to accumulation of fluid. Coupled with excessive administration, conditions sufficient to promote transudation of fluid into the lung are present and will result in pulmonary edema and decreased FRC and reduced alveolar gas exchange. The reduced FRC may be restored to normal or above normal by the application of PEEP.

Dry anaesthetic gases and poor systemic hydration reduce the mucociliary flow by decreasing the viscosity of secretion and slowing the ciliary beat. High FiO2 decreases the mucociliary flow. Inflation of an endotracheal tube cuff suppresses tracheal mucus velocity. Halothane reversibly and progressively decreases but does not stop the mucus flow over an inspired concentration of 1 to 3 MAC. The halothane induced depression of mucociliary clearance was probably due to depression of ciliary beat.

A recent meta-analysis of randomized controlled clinical trials assessed improvements in pulmonary outcomes comparing systemic opioids, epidural opioid, and epidural local anesthetic. They found that the use of epidural opioids, compared with systemic opioids, was associated with significantly less atelectasis and a reduced incidence of pulmonary complications. However, epidural local anesthetics significantly reduced the incidence of pulmonary complications, atelectasis, and pneumonia and raised the postoperative partial pressure of oxygen even higher. Subsequently, a meta-analyses of 141 randomized trials found a 39% reduction in pneumonia and a 59% reduction in respiratory depression (both P < 0.001) in patients treated with TEAA using local
anesthetic, compared with patients treated with general anaesthesia and PCA. A review of 462 surgical cancer patients managed with either epidural analgesia or systemic opioids found a distinct advantage with TEAA.

Hypocapnia is considered to be produced by passive hyperventilation by anaesthesiologist or ventilator. Hyperventilation and hypocapnia may cause decrease in cardiac output by

- increase in intrathoracic pressure
- withdrawal of sympathetic nervous system activity
- increased pH that decrease the ionized calcium which may in turn decrease the inotropic state of heart.

EFFECTS ON THERMOREGULATION:

Inadvertent hypothermia during anaesthesia is by for the most common perioperative thermal disturbance.

Factors that contribute to decrease in temperature during surgery are:

1) Anaesthetics induced impaired thermoregulation.
2) Exposure to cold operating room environment
3) Administration of cold I.V. fluids
4) Drug induced vasodilatation
5) Body cavities exposed to ambient temperature.
6) Heat is required to warm and humidify inhaled gases.

Hypothermia during anaesthesia develops with a characteristic pattern. An initial rapid decrease in core temperature results from a core to peripheral redistribution of body heat. This redistribution is followed by a slow linear reduction in core temperature for 2-4 hours that results from heat loss exceeding heat production. After 3-5 hours of anaesthesia core temperature generally reaches plateau and remain virtually constant for the duration of surgery. Beneficial effect of hypothermia is protection against cerebral ischemia and hypoxia.
Complications due to hypothermia are

- reduced drug metabolism and delayed recovery.
- Impaired coagulation due to cold induced platelet dysfunction.
- Wound infection by impaired immune function and triggering thermoregulatory Vasoconstriction.
- Physiological stressful postoperative thermal discomfort.

Intraoperative hypothermia can be minimized by

- Technique that limits cutaneous loss to the environment as a result of cold operating rooms (Forced air warming)
- Warm I.V. fluids.
- Warm blankets
- Humidified anaesthetic gases.

**EFFECTS ON FLUID BALANCE:**

The induction of anaesthesia, onset of mechanical ventilation, fluid shift and stress responses induced by surgical trauma, all lead to redistribution of water, protein and electrolytes. The choice of fluid and rate of administration must be adjusted to achieve physiological goals. The total fluid requirement is composed of compensatory intravascular volume expansion, deficit replacement, maintenance fluids, restoration of losses and substitution for fluid redistribution (ie) third space losses.

Central volume expansion: Intravascular volume usually must be supplemented to compensate for venodilation and cardiac depression caused by anaesthesia. It is corrected with 5-7 ml/kg of balanced salt solution before or simultaneous with onset of anaesthesia.

Maintenance fluid: (2ml/kg) The onset of surgical stimulation and to a smaller extent, onset of anaesthesia elicit changes in catecholamines, cortisol and growth hormone leading to hyperglycemia. So the fluid used for volume maintenance should not contain dextrose.
Deficit: The fluid deficit equals the maintenance fluid requirement multiplied by the hour since last intake plus unexplained preoperative external and third space losses.

Losses: External losses (eg: blood, ascitic fluid) should be replaced to maintain normal blood volume and normal composition of ECF volume. Evaporation from exposed viscera is entirely water, but the electrolyte is left behind, leading to a need for free water. The amount evaporated is directly proportional to temperature and exposed surface area and inversely proportional to relative humidity.

Redistribution: (so called third space losses) primarily results from tissue edema and transcellular fluid displacement. The composition of third space loss is equivalent to ECF volume electrolyte concentration plus a smaller amount of protein. Balanced salt solution is the most appropriate replacement fluid. The volume redistributed correlates roughly with the degree of tissue manipulation. Major surgery requires an additional 4-6 ml/kg/hr

The fluid replacement during prolonged surgery cannot be exact. The above mentioned values are approximations based on previous studies. If the requirements are calculated and administered taking all the factors into account, it could be a better approximation towards normal and body can easily compensate for excess. The aim of fluid therapy is to produce a urine flow of 50 – 80 ml/h and the CVP maintained between 6-9 mmHg with the heart rate and blood pressure maintained in the acceptable range.

**EFFECT ON ACID BASE BALANCE:**

Life is an acidogenic process and stress of prolonged surgery and anaesthesia can increase the systemic acidosis (Lactic acidosis). There is also constant derangement of glucose utilisation, increased resistance to insulin and electrolyte changes.

Iatrogenic causes for metabolic disturbances include manipulation of strong ion difference (SID) by administration of electrolyte or osmolite balanced solutions. Hyperchloremic acidosis is frequently seen due to large volume administration of 0.9% saline solution. It is also associated with acute normovolemic haemodilution with 5% albumin solution or 6% hetastarch (both formulated in normal saline): chloride gain is here; serum sodium may stay the same or even increase.
Dilutional acidosis refers to a condition in which there is an alteration in the relative quantity of sodium and chloride in free water: serum sodium decreases. This can occur from administration of sodium poor fluids. Excessive administration of hypotonic fluids such as 5% dextrose leads to an expansion in free water, hyponatremia and acidosis. Metabolic alkalosis is caused by chloride loss caused by removal of chloride from GIT by continuous suctioning.

Anaesthesiologist should understand the effects of fluids on acid base disturbances in prolonged anaesthesia. Hypotonic and dextrose containing fluid should be avoided. If large volume resuscitation is expected, balanced buffered solutions such as Ringers Lactate, normal saline or plasmolyte are recommended. If the patient is on continuous nasogastric suctioning, normal saline should be administrated until base deficit returns to zero. Care must be taken to avoid hypokalemia, hypocalcemia, hypomagnesemia, and hypophosphatemia.

To summarise:

Maintenance of normal homeostasis during prolonged anaesthesia is a challenge for the anaesthesiologist. Paediatric and geriatric age group have less tolerance and reserve even in the absence of medical problem. There are reports of delirium and cognitive function impairment in the elderly. There is often positional edema, more so on the face and tongue and sometimes pressure necrosis when the patient is lying supine for several hours, especially if there is a low flow state for some time.

It is important to pay attention to details regarding pharmacokinetics and dynamics of the drugs that are used and adjust the dosage according to the patient condition and the duration of the procedure. When the planned procedure is long, should we use long acting or short acting drugs? Most people prefer to use long acting drugs to have sustained well controlled effect over time. The disadvantage is the lack of control on reversibility if the procedure is cut short. While using long acting drugs considerable thought should be given to the dose and timing so that the lingering effects are minimal at the end operative and post operative period.

The use of intraoperative epidural anesthesia combined with postoperative epidural analgesia is associated with reduction in the incidence and severity of
perioperative physiologic perturbations and postoperative morbidity. In most cases, thoracic epidural anesthesia/analgesia with local anesthetics administered throughout the perioperative period, beginning before surgical stimulation and continuing for 24-72 hours postoperatively, is essential to maximize these surgical outcome benefits.

Monitoring should be appropriate for the type of surgery that may include direct arterial pressure monitoring, CVP, SpO2, EtCO2 and NMT monitoring. It is important to measure the ABG, blood sugar, haematocrit and electrolytes at frequent intervals and correct them. If the blood loss is more than anticipated replacement should be appropriate and coagulation factors should be monitored.

The anaesthesiologist is responsible for the safety of the patient and providing the surgeon with ideal operating conditions. He/she has to be prepared mentally for a long anaesthetic, choose the drugs judiciously and take very basic precautions like fixing the ETT securely, adjust the cuff volume, warming and humidification of the inspired gases, warming of the IV fluids and maintenance of body temperature. It is a good idea to use mechanical ventilation intraoperatively and if necessary postoperatively as well.

Lastly there is the fatigue factor. Anaesthesiologist can get fatigued, loose concentration and sometimes be more hypothermic than the patient. It is good to have a colleague with the same wavelength assisting you.