**Enhanced Recovery After Surgery (ERAS): Anesthetic Considerations; Time to fundamental change in practice?**Dr.V.Thiruchelvan., M.D., D.N.B., Anaesthesiology

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In the 1990s Professor HenrikKehlet initiated ERAS, Enhanced recovery programs (ERPs) or Fast Track programs. ERAS society ( [www.erassociety.org](http://www.erassociety.org)) was formed in 2010, the mission is to develop perioperative care and to improve recovery through research, education, audit and implementation of evidence based practice. The ERAS society had published the guidelines for anesthesia in 2015. The task is to align the practice of Anesthesia before during and after surgery, within the context of ERAS program with the care delivered by surgical team. It is not a topic of discovering new knowledge but rather how to integrate what we already know into clinical practice. Unfortunately large gaps still exist between evidence and practice.Rationally ERAS is not only about faster recovery but also about reducing morbidity and mortality.

**Pathophysiology:**

 Reaction to surgical stress is the metabolic response to injury. Minimizing this stress response is the central mechanism around which is the concept of enhanced recovery based. This response encompasses all elements such as anxiety, fasting, tissue damage, hemorrhage, hypothermia, fluid shift, pain, hypoxia, bed rest, ileus and cognitive imbalance. The injury by surgery can be primary or secondary. Primary injury is by direct trauma or tissue injury by mobilization. Secondary injury is by bleeding, temperature loss and physiological effects of anesthetic techniques. This includes the ill effects of positive pressure ventilation, local blood flow changes by anesthetic drugs, physiological effects of patient positioning, intrabdominal pressure, CO2 pneumoperitoneum.

 Such significant changes in physiological and metabolic homeostasis represent a threat to body and mind. Therefore the more extensive the surgical wound, internal organ manipulation and tissue dissection, the greater is the stress response. This is further amplified by the postoperative complications. An example is MINS (Myocardial injury after non cardiac surgery).

ERAS Anesthetic interventions against insulin resistance: Peripheral and central nervous system acts as a common pathway in triggering the catabolic response to tissue injury. Epidural anesthesia or blockade of major nerves interrupts these pathways and this explains its ability for improved cardiovascular and respiratory outcome after major surgical procedures. Therefore it is possible that most of the metabolic response to injury can be overcome when post-operative feeding is combined with pre-operative carbohydrates and epidural anesthesia.

**Surgical interventions within ERAS programs to minimize stress response:**LAFA study has shown positive benefits when laparoscopic approach is optimized within ERAS protocol. It means rather than the question of laparoscopy versus open approach, the surgical technique that produces less invasiveness, minimal wound trauma, tissue dissection and bleeding should be preferred. Duration of surgery with the ill effects of Pressure, Position and PaCO2 and reduced Cardiac Output can adversely affect outcome. Changing the orientation of incision so that it traverses lesser myotomes and dermatomes, lesser length of incision, muscle splitting rather than cutting, lesser intraoperative blood loss and modern energy sources producing lesser collateral injury can all help. Vital capacity and FEV1 are less affected in transverse incisions. There was a lesser incidence in wound dehiscence and incisional hernias in transverse incisions. In summary laparoscopic approach is recommended in appropriate patients when expertise and resources are available and in open surgeries transverse incisions should be preferred.

**Anesthetic care elements within ERAS program:**

Preoperative elements: 1. preadmission counseling 2. no prolonged fasting 3.fluid and carbohydrate loading 4.no/selective bowel preparations 5. no premedication 6. antibiotic prophylaxis 7.thromboprophylaxis.

Intraoperative elements: 1.usage of short acting anesthetic agents. 2. Mid-thoracic epidural anesthesia / analgesia 3. maintenance of normothermia 4. avoidance of salt and water overload 5. no drain.

Post-operative elements: 1. Mid-thoracic epidural analgesia 2. non opioid oral analgesia/NSAIDs 3.early mobilization 4 .stimulation of gut motility 5. early oral nutrition 6. early removal of Foleys catheter 7.avoidance of salt and water overload 8 .no nasogastric tube 9. prevention of nausea and vomiting 10. audit of compliance and outcome.

While each intervention has a smaller effect all together has a stronger synergistic effect. It is a Multidisciplinary approach and silo mentality is to be avoided.

Preadmission risk stratification: POSSUM scores, LEE index, cardiovascular risk calculator, assessment of functional capacity, risk of acute kidney injury can all help to quantify risk.

**Optimization of pre-existing health conditions:**

Alcohol: who defined alcohol abusers as ingesting more than 36gms of ethanol or equivalent of 3 standard drinks / day. They have increased risk of bleeding, wound infection, impaired immune and cardiac function and impaired metabolic stress response. 4 weeks abstinence is needed to reduce these risks and 8-12 weeks for return to normal.

Smoking:

Apart from co existing conditions smoking per se impairs wound healing. This can be improved with 4 weeks abstinence from smoking pre operatively. NRT (Nicotine Replacement Therapy), Varenicline, antidepressants like Bupropion can help. Encouraging is not enough, individual counseling and pharmacological support should be offered to every patient who are smoking and or alcoholic.

Optimization of Cardiovascular illnesses, Anemia, Asthma, COPD and Diabetes prior to surgery should meet international standards.

**Nutrition:**Data from Vanderbilt University has shown that preoperative nutritional deficiency is a strong predictor of 90-day mortality. In one study the complication rate was as high as 80% in patients with poor nutrition. The definition of “severe” nutritional risk as per the European Society of Parenteral and Enteral Nutrition (ESPEN) is the presence of one or more of the following: weight loss >10% to 15% in 6 months, body mass index <18.5 kg/m2 or a serum albumin of <30 g/L. Treatment includes prolonged parenteral or in combination with enteral nutrition with dietician guidance depending on the severity of the problem and GI function.

**Anemia:** anemia is associated with postoperative morbidity and mortality. It should be identified and treated before surgery. This avoids adverse effects from anemia and or transfusion. In cardiac surgery patients it has been shown that there is no strong evidence to prove the benefit of preoperative transfusion in terms of surgical outcome and, other blood management measures didn’t reduce the total transfusion requirements. There is no evidence to suggest advantages of preoperative transfusion over intra operative transfusion. The focus should always be on reducing further intra operative blood loss.

**Thromboembolism prophylaxis:** patients at risk of VTE should receive preoperative thromboprophylaxis with either LMWH or Heparin combined with mechanical methods. Patients should discontinue oral contraceptives pre operatively. Consideration should be given to stopping HRT.

**Antibiotic prophylaxis and skin preparation:** Routine IV antibiotics 1 hour prior to skin incision should be given for gynaecological/oncological surgery, the dose being repeated if surgery prolongs or with significant blood loss. For skin preparation Chlorhexidine-alcohol solution is preferred to povidone iodine solution.

**Mechanical bowel preparation (MBP):** The aim of MBP is to reduce solid fecal content, to reduce bacterial load and ultimately to reduce the post-operative complications. But MBP liquefies the fecal content which may increase the possibility of intra operative spillage and it is almost impossible to reduce the bacterial load due to the presence of vast number of microorganisms. A meta-analysis with nearly 2000 patients had found that MBP is associated with increased incidence of anastomotic leaks, wound infections, intra-abdominal abscesses and extra digestive complications. Routine mechanical bowel preparation should not be used even when bowel resection is planned.

**Preoperative fasting guidelines:**

Many guidelines allow administration of solid foods upto 6 hours and clear fluids upto 2 hours prior to surgery but patients are commonly asked to fast from midnight. But the evidence for this practice is lacking. A recent 22 RCTs had revealed that there is no evidence to suggest that shorter fluid fast guideline results in an increased risk of aspiration, regurgitation or related mortality compared with standard fasting from midnight practice policy. Rather fasting from midnight inhibits insulin secretion promotes the release of catabolic hormones. It increases insulin resistances, decreases intravascular volume especially in patients with mechanical bowel preparation. Imaging studies have confirmed the safety of clear fluids up to 2 hours before induction showing complete gastric emptying time within 90 min. preoperative administration of clear complex carbohydrates (CHO) like maltodextrin 100 gms (800 ml of 12.5% solution) the night prior to surgery and 50 gms (400 ml of 12.5% solution) 2 to 3 hours prior to surgery has shown number of advantages. It reduces catabolic state induced by surgery, reduces insulin resistance by 50%, it shifts cellular metabolism to a more anabolic state, maintains glycogen reserves, decreases protein breakdown and improves muscle strength. However the safety of preoperative CHO drinks remains to be established in patients with documented delayed gastric emptying time, gastro intestinal motility disorders and patients undergoing emergency surgeries.

**Premedication:** Routine use of preoperative long acting sedatives within 12 hours of surgery to allay patient anxiety should be avoided, because it can delay recovery. However short acting anxiolytics and analgesics may be used prior to regional procedures and insertion of IV lines.Even short acting benzodiazepines are to be avoided in elderly.

**Perioperative fluids and Hemodynamic management:**

Surgical Injury releases inflammatory mediators and catabolic hormones; this produces salt and water retention, preservation of intravascular volume and blood pressure, gluconeogenesis, shunting of blood from splanchnic to vital organs. Our mechanisms to excrete excess salt and water are correspondingly inefficient. Studies have shown post-operative complications are increased when weight gain in post op period exceeds 2.5 kg (2.5 l of fluid). Physiological effects of Anesthesia including positive pressure ventilation, usage of vasoactive drugs and regional anesthesia all can adversely affect vasomotor tone & intravascular volume.

Preoperative fluids: Avoidance of prolonged preoperative fasting and mechanical bowel preparation, allowing complex carbohydrate drinks upto 2 hours prior to surgery can substantially reduce intraoperative fluid requirements. However preoperative deficits should be replaced by individualized strategies rather than based on some textbook recipes.

Intraoperative fluids: Intraoperative need can be met with basal balanced crystalloid solution at the rate of 3 ± 2 ml/kg/hr (restrictive approach). 0.9% saline solutions should be avoided for routine use for they are associated with kidney injury (hypercholeremia), risk of hyperkalemia, metabolic acidosis, prolonged hospital stay and increased 30 day mortality. Usage of 0.9 % saline may be preferably restricted to patients with alkalosis, hypocholeremia( vomiting or prolonged nasogastric suction) and neurosurgical patients. Crystalloid excess increases pulmonary complications, prolongs ileus and delays recovery and substantial weight gain > 2.5kg should be avoided. Pharmaco vigilance risk assessment committee has recommended that HES should be used only for acute blood loss induced hypovolemia where crystalloid alone is not sufficient. HES should be used at the lowest effective dose for the shortest period of time targeted to hemodynamic goal.

There are two approaches in fluid therapy;one is administering balanced crystalloids solutions to cover the needs derived from salt water homeostasis. Here aim is to maintain the patient in near zero fluid balance.Since large veins acts as a capacitance vessel, there is a range (green zone) in fluid balance within which cardiac output and tissue perfusion can be adequately maintained. An experienced anesthesiologist can keep the patient in this comfort zone throughout the surgery and in immediate post op period. Another one is Goal directed fluid therapy (GDFT). In GDFT IV fluids are administered to treat objective evidence of hypovolemia, to improve intravascular volume and thereby circulatory flow. GDFT can be based on TOD (Trans esophageal Doppler), Pulse pressure variation (PPV), stroke volume variation (SVV) and pulse contour wave analysis. TOD will try to put the patient in the best part of their individualized frank starling curve. Pulse contour analysis will aim to minimize stroke volume variations during respiratory cycle. Surprisingly in two recent RCTs, GDFT showed no benefits to low risk patients treated within ERAS protocol. However GDFT is recommended in high risk patients and where there is large intravascular fluid loss or blood loss > 7ml/kg or a SIRS response.Arterial hypotension is to be treated first with IVF. If stroke volume is not improved then vasopressors should be considered. If contractility is less (cardiac index < 2.5l/min) inotropes should be considered. Regular fluid challenges without endpoints in otherwise healthy persons may lead to harm.

Postoperative period: early oral fluids and solids are encouraged. If patient can take oral fluids routine IVF should be stopped after PACU discharge. In the absence of surgical loss patients are encouraged to drink 25 to 35 ml/kg/day of water.

**Depth of anesthesia monitoring**:

Traditionally anesthesiologists are using clinical signs to monitor depth of anesthesia to prevent awareness. Recently many devices are used in this regard, most importantly by BIS(Bispectral Index). Recently they are used not just to avoid awareness but to titrate the minimum amount of anesthetic drugs needed so that unnecessary complications can be avoided. Usage of BIS not only reduces the incidences of awareness but also reduces the amount of anesthetics given with faster immediate recovery. Studies have shown that maintaining End tidal volatile agent concentration of 0.7 to 1.3 MAC is as equal as maintaining BIS between 40 to 60 in preventing awareness. It is to be noted that studies have shown for patients with BIS <45 during surgery death rate was increased by more than 1.24 times. Short acting anesthetic agents like sevoflurane or desflurane or continuous target controlled infusions of propofol are preferred. To summarize anesthetic depth must be monitored with End tidal volatile agent concentration (0.7 to 1.3 MAC) or BIS (40 to 60). BIS levels < 45 must be avoided especially in elderly patients.A lung protective ventilation strategy with 5-7ml/kg tidal volume and 4-6 cm H2O of PEEP is recommended to avoid post-operative pulmonary complications.

**Neuromuscular blockade and monitoring:**

Moderate Neuro muscular blockade certainly facilitate surgical work. Indeed adequate level of anesthesia without muscle relaxants can produce moderate to excellent surgical conditions for certain surgeries. But it is essential that at the end of surgery Neuro muscular function must be restored to preop levels and residual muscle paralysis must be avoided. Maintenance of normothermia is essential in this regard. In clinical trials it has been demonstrated that there is risk of aspiration and hypoxic events if TOF < 0.9.Several studies have shown that Clinical assessment and qualitative assessment (TOF, double burst suppression and tetanic stimulation) are not reliable in detecting residual paralysis even when sugammadex is used. Quantitative methods like mechanomyography(gold standard), acceleromyography provide accurate information. Therefore when using muscle relaxants neuromuscular function must be monitored and TOF >0.9 is to be ensured before extubation. Reversing the neuromuscular blockade with acetylcholine esterase inhibitors or sugammadex is strongly recommended.

**Oxygen during Anesthesia:** Oxygen is a drug; it has its own complications and is to be used with indication. Hyperoxia can produce damage due to the production of oxygen free radicals. A Meta-analysis including PROXI trial have shown two sub groups of patients benefitted by high FiO2, patients undergoing GA and patients having colorectal surgery.The study also shown that high FiO2 can reduce the incidence of late PONV in selected group of patients.High FiO2 may reduce surgical site infections. On the other hand PROXI trial has shown reduction in long term survival in cancer patients and poorer neurological outcome in cardiac arrest patients who received high FiO2. To summarize 100% O2 can be used during preoxygenation before GA and for short periods to prevent hypoxia. Otherwise FiO2 should be titrated to produce normal oxygen saturations and prolonged periods of hyperoxia should be avoided.

**Intraoperative hypothermia**

It is defined as a core temperature of < 36 degree Celsius. The incidence is 50% to 90%. In general anesthesia it is because of redistribution of heat from core to periphery and temperature falls up to 0.5 to 1.5 degree Celsius in the first 30 minutes after induction. Preventing hypothermia reduces wound infections, cardiac complications, bleeding & transfusion requirements, hastens post anesthetic recovery and improves overall survival. Therefore in the context of ERAS if the duration of surgery exceeds 30 min active warming devices are strongly recommended. It includes forced air warming systems, circulating water garments and warmed IV solutions. Patient should be rewarmed to 35.5 to 36 degree Celsius before emergence from anesthesia and shivering should be prevented (mepiridine 0.25 to 0.5 mg/kg or cloinidine 1 to 2 ug/kg can be used).

**Intraoperative glycemic control:**

Any major injury including surgery disrupts metabolic homeostasis and causes insulin resistance, also known as diabetes of injury. For every decrease in intraoperative insulin sensitivity by 20%, the risk of serious complications was more than doubled after open heart surgery. Evidence is mounting that even a moderate increase in blood glucose may be associated with worse outcome.

Patients in ward having Preoperative FBS > 7 mmol/l or PPBS > 11.1 mmol/l have an 18 times increase in in hospital mortality. Even elevated preoperative HbA1c has shown to predict post op complications. However mere associations between two variables, glucose levels and clinical outcome don’t predict direct cause and effect relationships. Most agree that when random blood sugar exceeds 10 mmol/l it should be treated. The author of one review suggested that “it seems prudent to control blood glucose to a reasonable level preoperatively” and acknowledged that “recommendations for exact targets cannot be made”. In summary blood glucose levels is to be kept as close to normal as possible without compromising safety. ERAS elements that reduce insulin resistance like preoperative carbohydrate, midthroacic epidural, early feeding and good post op pain relief are recommended. Larger observational dataset has shown thatDelaying surgery to correct hyperglycemia has not been shown to improve surgical outcome.

**Pain management:**

Multimodal evidence based procedure specific standardized analgesia regimens with minimal side effects with the aim of achieving important ERAS milestones such as early mobilization and early oral feeding should be considered.

**Thoracic Epidural Analgesia(TEA):**

TEA (T6-T11) analgesia is the gold standard for open abdominal surgeries. A recent met analysis has shown that TEA is associated with 40% reduction in mortality. Instituting it before and maintaining it throughout surgery TEA reduces the need for anesthetics agents, muscle relaxants and opioids. TEA provides better static and dynamic analgesia, accelerates recovery of GIT function, reduces insulin resistance and has positive impact on cardiovascular and respiratory complications. Opioids when added to local anesthetics improve the quality of post op analgesia. The usage of low dose bupivacaine (o.1 mg/ml) and lipophilic opioids like fentanyl (3ug/ml) has been shown to produce optimal analgesia with minimal side effects. Epidural morphine (0.02mg/ml) can be preferred for long midline incisions. Adding adrenaline (1.5 to 2.0 ug/ml) improves post op analgesia especially during mobilization and coughing. Analgesic efficacy of epidural clonidine is inconclusive with the added risk of hypotension and sedation. Epidural infusions are to be continued until 48 to 72 hours until the recovery of GI functions and gradually tapered off.

Other options are intra thecal morphine, IV lignocaine infusions, continuous wound infusions of local anesthetics and TAP blocks.

**Postoperative delirium:**

It is under estimated and underdiagnosed. It is defined as a state of altered consciousness, orientation, memory, thought, perception, behaviour and possibly sleep pattern which develops acutely and shows a fluctuating clinical course. It can be in three forms, hyper active hypo active and mixed form. It’s a symptom of acute cerebral dysfunction. Instead of being strictly a binary phenomenon which is either present or absent, it can present in varying degrees. It increases the length of hospital stay, mortality and long term cognitive dysfunction. Preventive measures include avoidance of precipitating factors like prolonged fasting time, disturbances in sleep wake cycle, delirogenic medications like benzodiazepines and atropine. Psychotic symptoms must be treated with neuroleptics like low dose haloperidol or atypical neuroleptics. If there is a need to use sedatives non benzodiazepines like alpha 2 agonists are to be preferred to benzodiazepines.

**PONV: ( Prevention and Treatment)**

Within an ERAS program it mainly includes use of antiemetics, usage of Total Intravenous anesthesia with propofol instead of using volatile agents. Other measures that may influence PONV include avoidance of Nitrous oxide, reduction in preoperative fasting, carbohydrate loading, adequate hydration, high inspired FiO2, the usage of regional anesthesia techniques and NSAIDs over opioids. There are many classes of antiemetics like serotenergic, dopaminergic, cholinergic and histaminergic. But none when used alone is effective in reducing the PONV by more than 25%. Therefore combination therapy with 2-3 antiemetics in addition to propofol based TIVA has the greatest likelihood of reducing the PONV. A 5-HT3 antagonist should be the first choice since it is the only category that has been well studied for existing PONV. Examples include Ondansetron 4 mg IV along with droperidol 0.625 to 1.25 mg IV at the end of surgery. If PONV is present post operatively it should be treated with a different class of antiemetics.

**Nasogastric tubes:**

There is strong evidence that routine nasogastric tubes for all laparotomies should be avoided. If inserted during surgery to evacuate air it is to be removed before anesthesia reversal. The complications include fever, oropharyngeal complications, pulmonary complications, enhanced gastro esophageal reflex and higher incidence of vomiting. Even death and other serious complications were reported. There appears to be no beneficial effect by prophylactic nasogastric tubes even for gastro duodenal and pancreatic surgeries. Nevertheless patients with delayed gastric emptying can present with vomiting and fatal aspirations if not promptly treated with nasogastric tubes. Therefore if the patient fails to progress within 2 to 5 days in post op period with delayed gastric emptying naso gastric tubes should be inserted.

Growing evidences from several RCTs, systematic reviews and meta-analysis has shown that there are significant benefits if ERAS pathways are followed. However there are major difficulties in introducing these evidence based guidelines into practice. Many states that they never heard of ERAS, while some say inadequate interdisciplinary support is a major impediment. Even the simple measures discussed above still represent fundamental changes in practice therefore difficult to achieve. The ERAS team consists of pre admission staff, dieticians, nurses, physiotherapists, social workers, occupational therapists and doctors. All should be familiar with ERAS principles and motivated to achieve its targets.

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