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PARADIGM SHIFT IN THINKING OF PERIOPERATIVE ANALGESIA

This is a reflection of our quarter century experience at the University of Southern California in Los Angeles which has three multi-disciplinary medical centers with public and private hospitals under one roof. We provide anesthesiology service to approx. 32000 patients per year. LA County USC is the largest trauma center in the western United States. There are approximately 200 ICU beds in all specialties. The Keck School of Medicine is amongst the oldest in the country established in 1885.

Historically we as anesthesiologists have focused our attention on the intraoperative period and to some extent at the immediate postoperative period regarding the patient's experience and analgesia needed for the proposed surgery. Poorly managed pain can lead to complications and prolonged rehabilitation. We use some syringes to anesthetize patient, maintain their hemodynamics, respiratory and vital organ functions by controlling a dial on gas vaporizer or through intravenous fluids and intravenous medications. Towards the end of surgery we use another few syringes to terminate the anesthetic, wake up our patients and provide postoperative opioid analgesia.

The scope of anesthesiology is now being extended into a larger perioperative role. This begins from the time surgeons decides to operate on a patient until the patient has recovered. This means the focus is now on prehabilitation before surgery

which tends to strengthen muscles, manage anxiety and avoid starvation before the catabolic process of surgery. The focus is also on change in analgesic modality of preoperative, intraoperative and postoperative prescription with multi analgesic receptor concept. This also includes use of regional anesthesia and extended duration of regional analgesia with continuous catheters when possible. This approach prevents the acute perioperative pain transitioning to chronic pain. The preponderance of evidence shows that postoperative pain predicts chronic pain. For example, after cardiac surgery, patients with high levels of postoperative pain are 3.5 times more likely to suffer from chronic pain compared to patients with lower postoperative pain levels⁶. The ultimate advantage is improving quality, safety and efficacy with improved outcome perioperatively.

The British journal of anesthesia published a meta-analysis that compared the effectiveness of intramuscular opioids, PCA, epidural analgesia and combined techniques using the aforementioned modalities⁵. The authors found that after IM opioids alone, 67% of patients had moderate and 30% had severe pain. After PCA, 36% had moderate and 10% had severe pain. After epidural analgesia with local anesthetic and opioids, 28% had moderate and 8% had severe pain. When using mixed techniques 30% of patients had moderate and 11% had severe pain. While the epidural analgesia produced the best results,

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it requires an invasive procedure, and still left one out of five patients moderate to severe pain.

Surgeons are now increasingly utilizing preemptive analgesia by infiltrating skin before incision with lidocaine or liposomal bupivacaine. Anesthesiologists utilizes preventive analgesia by using multimodal analgesia techniques. The surgeons have also revised their concept of managing patients postoperatively with early ambulation, minimizing use of nasogastric tubes and wound drains, removing foley catheters early, perioperative venous thrombosis and antibiotic prophylaxis, decreasing use of bowel preparation unless absolutely necessary.

The above paradigm shift decreases recovery time by decreasing hospital length of stay, encourages early ambulation made possible with better analgesia, decreased respiratory depression and better mentation from minimal or no opioid use, all this decreases complications and readmissions. This ultimately leads to better patient satisfaction and improved scores for our doctors and hospitals. The Center for medicare services assess performance of physicians and hospitals on value based measures. Perioperative analgesic management is an important part of these value based measures. These measures are compared to a benchmark consisting of high level of performance at a national level. Each physician and hospital's performance standard must meet a minimum threshold requirement. Institutions are implementing enhanced recovery protocols with a paradigm shift regarding perioperative analgesia across the world.

Prehabilitation

Prehabilitation (15 to 30 days before surgery) as a piece of enhanced recovery protocol can reduce surgical stress, enhance mobilization, maintain postoperative physiological function by delaying the catabolic process and improved muscle strength. This has resulted in faster recovery and shorter length of stay in hospital.

The components of prehabilitation are:

Explain the perioperative program to patient well. Understanding the advantages of the program, gives the patient enthusiasm to cooperate with improved compliance. Medical optimization reduces delay and cancellations of cases on the day of surgery. A visit with physiotherapist for learning isotonic and isometric exercises improves core muscle strength. There is muscle mass loss associated with inactivity perioperatively. If the pain prevents mobility, then muscle mass loss is higher after surgery.

During a visit with Nutritionist, the primary goal is to optimize nutrient stores to combat the catabolic response of surgery postoperatively. This includes additional protein diet and carbohydrate load before surgery. The rationale for the carbohydrate load is to prevent starvation and preserve glycogen stores intact until the start of surgery. If we were to build patient's muscles with high protein diet and improve core strength, then patient starts with excellent muscle build and may not deteriorate below baseline during perioperative period.

Apply Strategies to manage anxiety. Relaxation and breathing exercises along with meditation decreases anxiety.

The thought process for analgesia starts with preoperative per oral dose of analgesics like Gabapentin, Clonidine, Celecoxib and Acetaminophen. Each of these medications has unique receptor affinity with different mechanisms of action and

varying durations of action. Taken alone or in combination, it enhances management of pain with fewer analgesic gaps. With decreased analgesic gaps, the likelihood of severe pain occurring is reduced and high doses of rescue opioids are not needed to control postoperative pain.

Gabapentin and Pregabalin are anti convulsants with anti hyperalgesic and anxiolytic properties and efficacy with neuropathic pain also seems to be very promising for perioperative pain relief. Gabapentin decreases excitatory neurotransmitter release at the spinal cord level thereby decreasing central sensitization which occurs with noxious stimulus⁴. A single preoperative dose of 600 to 1200 mg Gabapentin or repeated doses at 8 hour intervals for up to a few days after surgery is recommended.

Clonidine in the doses of 50 to 200 micrograms po dose does reduces perioperative pain and anxiety via its α -2 agonist action. Alpha-2 agonists have sedative and analgesia sparing effects via central actions in the locus ceruleus and in the dorsal horn of the spinal cord.

Nonsteroidal and nonselective anti-inflammatory agents like (NSAIDs) help control postoperative pain but have bleeding concerns. Cyclooxygenase (COX)-2 selective inhibitors like Celecoxib offer peripheral pain relief benefits of nonselective NSAIDs but with fewer GI effects and bleeding concerns.

Acetaminophen per oral dose and rectal suppositories have varying analgesia depending on their bioavailability with first pass through the liver. This centrally acting agent is one of the most popular drugs for the treatment of pain and fever. Unlike NSAIDs it is considered to have no anti-inflammatory activity, does not produce untoward GI or cardio renal effects. Unlike opiates it is almost ineffective in intense pain and has no depressant effect on respiration. The mode of action has been a mystery until few years ago. It produces the analgesic effect by direct inactivation of cannabinoid CB-1 receptor in brain and spinal cord which leads to increased levels of endogenous cannabinoids. Moreover it inhibits cyclooxygenases in the brain. The intravenous use of acetaminophen (paracetamol) intraoperatively and during the immediate postoperative time frame has been a key component of the enhanced recovery protocols.

Latest NPO guidelines suggest that dehydration and starvation should be reduced before surgery³. We allow non-fatty meals up to 6 hours before surgery and clear liquids 2 hours before surgery. This used to be a norm for pediatric patients, so why not for adults? There is evidence that when clear liquids are given 2 hours prior to induction, there is decreased acidity and lower residual volume of liquid in the stomach.

Appropriate preoperative recommendations are given for alcohol and smoking restrictions in elective surgeries.

Intraoperative

The goal is not to rely on our traditional opioids as analgesics, but replace with analgesics that use multiple receptors to avoid analgesic gaps. Moderate doses of multiple medications reduce complications when compared to high dose opioid monotherapy. Attention to appropriate fluid administration is the key to reducing bowel related delay in recovery.

Goal directed fluid therapy is the new area of attention during intraoperative period. The usual response to hypotension in most cases is fluid replacement until blood pressure returns to normal.

When the heart and kidneys are good, it works. Postoperatively during 48 hours to 72 hours period, fluid returns to the central circulation and is eliminated by kidneys and pumped well by the healthy heart without perioperative ischemic events or failure. But this excess fluid accumulation for 48 hours causes GI tract edema and resultant decrease in bowel movements, extending postoperative paralytic illness. Appropriate fluid balance is the goal. The adverse outcome occurs with organ dysfunction in both the hypovolemic situation leading to myocardial infarction, acute kidney insufficiency and volume overload. This leads to reduced oxygen diffusion at the tissue level, pulmonary edema and bowel dysfunction. Instead of using invasive intraoperative central lines for close monitoring, noninvasive continuous stroke volume variation measurements are gaining traction.

Anesthetic optimization via short acting inhalation and intravenous agents help recovery, and a less drowsy patient allows for better assessment of pain and early interventions to control it.

Intraoperative multimodal analgesia could be a combination of multiple modalities. Use of regional anesthesia, IV Ketamine as NMDA antagonist², Dexmedetomidine as an alpha-2 agonist, Ketorolac as NSAID, Acetaminophen, Lidocaine as sodium channel antagonist could all offer additional opioid sparing therapies.

Preventing intraoperative hypothermia and improved glycemic control prevents perioperative complications.

Postoperative

Manage pain, hemodynamics, and respiratory function, assess the risk of nausea and vomiting with appropriate treatment. Early ambulation aided by adequate analgesia, Physiotherapy consults to regain strength with regular exercise. Early removal of tubes, drains and catheters reduces infections and improves mobility of the patient. Early feeding improves gut motility and chewing gum stimulates bowel function. Alvimopan can be used for opioid induced ileus. New Kappa opioid receptor agonists appear promising with reduced complications compared to our usual μ -opioid receptor agonist agents.

The evidence in these studies (monitoring mortality, morbidity, length of stay and hospital readmissions) supporting

enhanced recovery protocols are increasing when compared to traditional management, especially in colorectal cases¹. Unless contraindicated, patients must now receive multimodal analgesia for perioperative pain management. No one theory alone will be able to block the pain pathway and reduce the consequences of surgery. We need to take a more balanced therapeutic approach to manage pain perioperatively.

Research transparency

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Declaration about financial and other relations

All authors took part in elaboration of article conception and writing the script. The release script was approved by all authors. The authors did not get the honorary for the article.

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