

Pain relief after ambulatory surgery: Progress over the last decade

ABSTRACT

The concept of fast-track or ambulatory surgery appeared to facilitate early recovery and discharge from the hospital and early resumption of normal daily activities after elective surgical procedures as well to reduce the health-care costs. Multimodal/balanced analgesia is an increasingly popular approach for this. The use of conventional modalities including central neuraxial blockade and opioids cannot be extended to patients undergoing fast-track surgery. Hence, an aggressive perioperative analgesic regimen/protocol is required for effective pain relief, with minimal side effects and which could be managed easily by the patient or the relatives at home away from the hospital setting. Pharmacological therapy and regional anesthesia techniques have been utilized for postoperative pain management. The use of perineural, incisional, and intra-articular catheters and local anesthetic administration through elastomeric and electronic pumps is promising approach for effective pain management at home. The key to successful pain management of such procedures requires individually tailored education to patients or caregivers including information on treatment options for postoperative pain and use of multimodal analgesia. This review provides an overview of the current armamentarium of drugs and modalities available for effective management of patients undergoing day care surgeries and sheds light on newer modalities available.

Key words: Ambulatory surgery; local anesthetics; multimodal analgesia; patient satisfaction

Introduction

The concept of fast-track or ambulatory surgery appeared in the early 1990s to facilitate early recovery and discharge from the hospital and early resumption of normal daily activities after elective surgical procedures as well to reduce the health-care costs. Day care surgeries have led to cost containment in the United States to the tune of 15%–30%, while in the United Kingdom, 40% saving in the cost has been observed.^[1] Poorly controlled pain negatively affects quality of life and functional recovery, causes persistent postsurgical pain, and leads to delayed discharge of patient

and unanticipated hospital admissions following surgery.^[2-4] It requires a proactive approach for postoperative pain management for a better outcome, patient comfort and fast and better recovery, and accelerating patient's ability to resume their activities of daily living. Top priorities for successful outcome of such day care procedures are achieving alertness, ambulation, analgesia, and alimentation.^[5] Multimodal/balanced analgesia is an increasingly popular approach for this. It utilizes a combination of opioids and nonopioids which act out on different receptors including central and periphery to control pain.^[6,7] Using excess of opioids leads to excessive drowsiness, sedation, nausea and

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vomiting, pruritus, urinary retention, ileus, constipation, and ventilator depression; hence, using a combination of drugs minimizes these side effects.^[8] Hence, planning postoperative pain relief in day care surgeries should involve selection of drugs and their use in a predefined and strict manner based on the availability of evidence and past experiences.^[9]

The current armamentarium of analgesic drugs and various techniques for managing postoperative pain continues to grow at a rapid pace. However, an increasing number of complex surgical procedures are being done on outpatient basis nowadays, which pose a bigger challenge for clinicians for controlling postoperative pain. The use of conventional modalities including central neuraxial blockade and opioids cannot be extended to such patients. Hence, an aggressive perioperative analgesic regimen/protocol is required for effective pain relief, with minimal side effects and which could be managed easily by the patient or the relatives at home away from the hospital setting.

The first review on this topic appeared in the Indian Journal of Anaesthesia in 2006.^[9] Since then, further advances have been made in this important and ever-expanding area of ambulatory surgery. A number of recent reviews are available,^[1,10-12] but it is important to see how these might be relevant and applicable in the Indian scenario since the last decade or so.

Preemptive Analgesia

Preemptive analgesia is the administration of analgesia before surgical incision. The underlying assumption is that secondary to any peripheral injury or inflammation, there is central sensitization which embraces a number of different and complex neurobiological changes that lead to increase pain sensitivity.^[13] However, the use of preemptive analgesic regimens for control of postoperative pain failed to show any clinically significant advantage over conventional multimodal regimens.

Impact of Pain after Day Care Surgery

Pain after surgery causes extreme discomfort, sleep deprivation, postoperative nausea and vomiting, and delayed discharge. Currently, day care surgeries are being done on healthy young adults, but now, elderly patients with multiple comorbidities and pediatric patients are also being included. Acute pain may affect early return to work, increase consumption of health resources, could be harmful in patients with ischemic heart diseases or those with chronic respiratory conditions, and also may lead to the development of chronic pain if left untreated.^[2]

Intensity of Pain after Day Care Surgery

Most common complication after day care surgery is pain. Among outpatients discharged, 30%–40% suffer from moderate-to-severe pain during first 48 h of surgery.^[14,15] Similar results have been shown by two large Swedish surveys, as well as patients undergoing laparoscopic cholecystectomy (65% patients had moderate pain and 25% had severe pain), laparoscopic gynecological procedures (only 60% patients had satisfactory pain relief), or cataract surgery shown significant pain postoperatively.^[16-20] Studies conducted in pediatric patients reveal that more than half of children experience significant pain after discharge.^[21-23] Inappropriately treated pain may lead to the development of chronic pain conditions. With time, the pain intensity decreases, but it is severe enough to disrupt normal routine of patient. Furthermore, certain types of surgeries such as urological, orthopedic, dental, cholecystectomy, hernia repair, and breast surgery cause more severe pain and require more analgesia.

Barriers for Pain Management in Day Care Surgeries

Despite having varied modalities for pain management, there is dissatisfaction on patient's behalf for pain control. The commonest factor responsible is lack of proper information provision and communication from clinicians; studies reveal that only 15% of patients have written instructions on discharge from clinicians regarding pain control regimen rest receive only a verbal command. The other factors include lack of access to analgesics, lack of compliance on patients and relatives part, misconceptions regarding use of analgesics, reluctance to report postoperative complications and acceptance of pain on part of patient as an inevitable consequence of surgery.^[24-27] For improving the quality of pain control and facilitating recovery after surgery, there is a need to educate patient and family members about the importance of continuing medications after discharge from the hospital.

A large category of nonopioid analgesics are used as adjuvants before, during, or after surgery to facilitate the recovery process and provide adequate analgesia after ambulatory surgery: nonsteroidal anti-inflammatory drugs (NSAIDs), acetaminophen, COX2 inhibitors, ketamine, dextromethorphan, alpha 2 agonists, dexmedetomidine, gabapentin, pregabalin, glucocorticoid steroids, magnesium, and use of local anesthetics and regional nerve blocks. However, the clear benefit of these approaches for ambulatory pain management must be balanced against the cost of equipment and the resources required and safe management of patients using these techniques outside the hospital. The

choice of an appropriate pain management protocol by pain care physicians should be based on the important factors such as patient's comorbidities, psychological conditions, exposure to analgesics, the operative site, and surgical procedure done. The use of multimodal analgesic regimens is still undermined; there is lack of adherence to the guidelines for control of pain. An editorial by White highlights the issues related to extensive reliance on opioids and discontinuation of pain regimens postoperatively and refers to this phenomenon as a disconnect between scientific advances and lack of implantation in clinical practice.^[28] Literature search suggests that using a rational combination of different nonopioid analgesics as part of multimodal regimen provides effective pain control. Only the most common agents used are reviewed here.

Nonsteroidal Anti-inflammatory Drugs

These have anti-inflammatory, antipyretic, and analgesic properties. Parenteral preparations of NSAIDs include diclofenac, ketorolac, and piroxicam. These are recommended as part of multimodal analgesia for postoperative pain and are given for mild-to-moderate pain. Mechanism of action involves blocking the synthesis of prostaglandins by inhibiting COX-I and II, thereby reducing production of acute inflammatory mediators and reducing peripheral nociception and central response. Preoperative administration of NSAIDs decreases tissue prostaglandins and hence reduces primary and secondary hyperalgesia, suggesting their role in preemptive analgesia.^[29] The reports suggest that parenteral NSAIDs possess analgesic properties comparable to traditional opioid analgesics without opioid-related side effects.^[30,31] Studies have found that ketorolac provides improved postoperative analgesia and patient comfort compared to fentanyl.^[32] Furthermore, ketorolac is superior to local anesthetic infusion of bupivacaine in supplementing epidural patient-controlled analgesia (PCA) with hydromorphone in patients undergoing thoracotomy.^[33] Compared to tramadol, ketorolac produces comparable analgesia and 68% decreased incidence of nausea and vomiting after maxillofacial surgeries.^[34] Similarly, diclofenac given preoperatively has been shown to reduce pain and opioid requirement 24 h after laparoscopic surgeries.^[35] In arthroscopic surgeries too, diclofenac produces comparable results to fentanyl.^[36] In pediatric patients, diclofenac reduces the incidence of postoperative crying and restlessness.^[37] Furthermore, oral ketorolac was found to be superior to acetaminophen in bilateral myringotomy surgeries.^[38] In inguinal hernia repair surgeries, ketorolac had comparable pain control compared to caudal block given with bupivacaine; there was better recovery and shorter time to void early ambulation and early discharge.^[39]

Despite having a great potential to reduce postoperative pain, these agents are not free of side effects. Their side effect profile includes potential for gastrointestinal mucosa bleed and damage and damage to renal tubules and platelet dysfunction.

Acetaminophen

It is the safest and most cost-effective nonopioid, and its concurrent use with NSAIDs proves to be more superior than used alone. It is available as oral, rectal, and intravenous preparations. The optimal dosing regimen in children is 30–40 mg/kg given preoperatively followed by maintenance dose of 15–20 mg/kg every 6–8 h postoperatively. Intravenous formulations have reduced PCA morphine consumption by 22%–46% in patients undergoing major orthopedic procedures.^[40,41] Rectal acetaminophen has also been used in conjunction with NSAIDs as a part of multimodal fast-track surgery.

COX 2 Inhibitors

Selective COX 2 inhibitors have less pronounced effect on platelet function with low risk of associated bleeding. These are used as adjuvants for minimizing pain during perioperative period. The use of celecoxib and rofecoxib as preemptive analgesics has also been evaluated by many studies. A study revealed that celecoxib when used in a dose of 400 mg was found to be equivalent to acetaminophen during otolaryngologic procedures.^[42] In a study conducted by White *et al.* in patients undergoing outpatient laparoscopic procedures, patients received 400 mg of celecoxib in immediate postoperative period followed by 200 mg twice a day for additional 3 days. Celecoxib reduces postoperative pain, and opioid requirement also leads to better patient satisfaction and recovery scores.^[43] Both pre- and postoperative administration of these agents resulted in significant opioid-sparing effects, reduced adverse events, improved quality of life, and increased patient satisfaction. However, due to adverse cardiovascular events, rofecoxib was withdrawn from the market. The newer agent etoricoxib has been found to have rapid and long-lasting pain relief when used in patients undergoing dental surgery.^[44]

Ketamine/Dextromethorphan

Ketamine is a noncompetitive NMDA receptor antagonist. It modulates central sensitization induced by incision and tissue damage; it also possesses preemptive analgesic properties. Used in small doses (0.1–0.2 mg/kg), it has opioid-sparing effects, less incidence of adverse events, and better patient

and physician acceptance.^[45] A single bolus of ketamine (0.1–0.15 mg/kg) intravenous has significant opioid-sparing effects after painful orthopedic and intra-abdominal procedures. Furthermore, the use of intramuscular ketamine in a dose of 0.1 mg/kg has been shown to decrease the swallowing-evoked pain during tonsillectomy procedures in pediatric patients.^[46-49] It has a definitive role in preventing opioid-induced hyperalgesia in patients who require high dose of opioids for postoperative pain control. Another NMDA antagonist is dextromethorphan; it inhibits the wind up and NMDA-mediated nociceptive responses in dorsal horn neurons. It has been shown to enhance opioid, NSAIDs, and local anesthetic-induced analgesia. Premedication with 150 mg of oral dextromethorphan has been shown to reduce PCA morphine requirements in early postoperative period after abdominal hysterectomy procedures.^[50] Also, in patients undergoing laparoscopic cholecystectomy or inguinal hernia repair surgeries, use of 90 mg oral dextromethorphan improved patients well-being and reduced analgesic consumption, pain intensity, sedation, and hyperalgesia.^[51]

Alpha 2 Adrenergic Agonists

Dexmedetomidine is an alpha 2 adrenergic agonist. It has significant anesthetic- and analgesic-sparing effects. The most common side effect is sedation and bradycardia. When used for premedication, intravenous dexmedetomidine (1 µg/kg) reduces patient anxiety, sympathoadrenal responses, and intraoperative analgesic requirements.^[52] Similarly, administration of dexmedetomidine as 1 µg/kg intravenous bolus followed by 0.4 µg/kg/h infusion was associated with 66% reduction in PCA morphine use in early postoperative period in patients undergoing major surgeries.^[53]

Gabapentin

It is a structural analog of gamma-aminobutyric acid, it is a well-known anticonvulsant that has analgesic properties, and it is used in the treatment of chronic neuropathic pain as well an adjuvant for management of acute postoperative pain. Preoperative administration of 600 mg gabapentin was found to cause significant reduction in postoperative pain and tramadol consumption on the 1st postoperative day, with decreased incidence of nausea and vomiting in patients undergoing mini-laparoscopic cholecystectomy.^[54]

Role of Regional Anesthesia in Day Care Surgery

In many day care procedures, regional anesthesia techniques are preferred as these provide better and prolonged

analgesia, no sedation, less postoperative nausea and vomiting, reduction of surgical stress, early discharge, and negate the effects of general anesthesia. Due to the above-mentioned benefits, regional anesthesia has been a part and parcel of enhanced recovery protocols.^[55] However, literature search shows conflicting data as to whether regional anesthesia offers significant benefit over general anesthesia for day care surgeries. There are a large cadre of peripheral nerve blocks which can be utilized for ambulatory surgeries to provide intraoperative and extended postoperative analgesia over a limited field with minimal side effects. The mechanism of action of local anesthetics involves modulation of pain at the peripheral level by inhibiting transmission of nociceptive impulses from the site of injury.^[56] The major limitation of peripheral nerve blocks is repeated administration of drugs. This can be overcome by extending blocks in the form of perineural, incisional, or intra-articular catheters using patient-controlled regional analgesia techniques. These are technically more feasible, easy to use, patient friendly, and can be safely managed at home. Catheters are attached to either electronic or elastomeric pumps which are prefilled with local anesthetics and are preprogrammed to release desired and fixed amount of drug. Patients are taught how to use these at home and to recognize the side effects and complications and to report immediately, patients who have indwelling catheters are regularly monitored by the respective hospital acute pain management services, and they are telephonically interviewed each day to know the safe delivery of services by such devices.^[57-59] Regional anesthesia techniques cause minimal physiological trespass and can be used for all age group of patients including pediatric and high-risk elderly patients. The use of peripheral nerve blocks has extended the indications of day care surgeries to complex and major procedures such as shoulder repair, hysterectomy, and knee and shoulder reconstruction. For continuous peripheral nerve blocks, catheter is inserted percutaneously in the vicinity of nerves supplying the area of surgery involved via which local anesthetics are provided using either electronic or elastomeric pumps. Capdevila *et al.* conducted a multicenter randomized trial which included 83 patients who were scheduled to undergo elective ambulatory acromioplasty/hallux valgus surgery.^[60] They received either interscalene or popliteal nerve block using 0.5% ropivacaine. 24 h after surgery, patients were discharged home; one group received patient-controlled intravenous analgesia using morphine and other received perineural 0.2% ropivacaine either as continuous or as continuous plus bolus dose. It was found that patients in ropivacaine group had lesser time to 10 min walk and their daily activities were optimized while patients in morphine

group had increased incidence of nausea and vomiting, sleep disturbances, dizziness, and decreased patient satisfaction scores.^[60] Evidence suggests that continuous peripheral nerve blocks provided at home improve postoperative analgesia, sleep quality, and patient satisfaction while decreasing supplemental opioid requirements and opioid-related side effects. A large number of randomized controlled trials have demonstrated the safety and efficacy of incisional catheter regional anesthesia techniques in surgeries (cesarean section, inguinal hernia repair and hysterectomy, and orthopedic surgeries), but more studies are required in this area to demonstrate the efficacy of postoperative catheter infusions in day care patients.^[61-63]

Intra-articular drug administration for arthroscopic surgeries has gained wide popularity due to the simplicity of procedure, for providing anesthesia and extended postoperative analgesia. Local anesthetics along with myriad group of adjuvants such as ketamine, alpha 2 agonists, NSAIDs, and opioids have been used in different permutations and combinations. Intra-articular drug administration has been used invariably for a number of joint surgeries such as knee, shoulder, ankle, wrist, and metatarsophalangeal and temporomandibular joints.^[64] A systematic review was conducted which included 20 trials with 895 patients on use of intra articular local anesthetic for control of post operative pain after knee arthroscopic surgeries. Of these, 12 studies showed improvement in pain relief. Although the review suggested weak evidence for decreasing postoperative pain for a short duration, it suggested that it might be clinically beneficial for day care surgeries.^[65] Another systematic review and meta-analysis was conducted in which single-dose administration of intra-articular bupivacaine in knee arthroscopic surgery was evaluated. It included 28 trials involving 1560 patients; evidence suggested that single-dose administration of local anesthetic was effective for postoperative pain relief, but still high-quality randomized trials are needed to establish its safety and efficacy.^[66]

Elastomeric pumps have also been used to provide analgesia. Serra *et al.* described their experience of using intravenous elastomeric pumps using a combination of different drugs (tramadol, haloperidol, ibuprofen, and dexketoprofen) for 48 h postdischarge. The authors found that 80% of patients were discharged home pain free, 40% patients experienced no pain, and 50% showed a visual analog scale score of 1–3. Patients who had received peripheral nerve blocks had better pain control; withdrawal of pump was required in 1.1% of patients. Overall 99.5% of patients had satisfactory pain control.^[67]

Role of Ambulatory Pain Specialist

Unmet need for optimum pain control in ambulatory setting requires the specialist services of ambulatory pain specialist. The concept which has recently emerged in developed countries is yet to incept in developing nations. Ambulatory pain specialist plays an important role in developing standard of care for treatment of postoperative pain, identifies at-risk patients, provides consultation for pain care, utilizes early rescue techniques, implements multimodal analgesia, takes care of complications, plans the discharge medications, and follows up for effective control of pain.^[68]

Future Directions

Advances in pain management for ambulatory surgery might include introduction of extended-action epidural morphine, iontophoretic, intranasal, transmucosal, and transdermal drug delivery systems and development of local anesthetic encapsulated in lipophilic membranes which allow sustained release and prolonged action, but their potential in ambulatory surgery pain management is yet to be established.^[69] In Patient-controlled intranasal analgesia intranasal opioid (fentanyl) is delivered as powder or saline form through nasal spray or in nebulization form. There occurs extensive and rapid absorption via nasal mucosa. There are a few trials reporting its administration for acute postoperative pain management, but its effectiveness and safety for pain management for ambulatory surgery needs to be investigated.^[70,71] In patient-controlled transpulmonary analgesia, aerosolized liposome encapsulated fentanyl (YM BioSciences Inc., Ontario, Canada) benefits via rapid and extended analgesia for acute pain management, but it is still under trial for safety and efficacy for human use.

The success of day care surgery depends on both postoperative pain control and minimizing side effects. An important aspect rests with educating the patient about pain, the need to control pain, and different ways to reduce pain. This approach reduces the anxiety on the part of patient and adds to reduce postoperative pain. With the advent of newer technology and modalities for pain control and economic pressure burdens, there is a visible need on behalf of health-care professionals to provide better outpatient care and lesser duration of hospitalization without compromising on quality of patient care. Despite the progress, more studies are required to develop multimodal analgesic protocols which will cater to the surgical and individual patient needs. Upcoming approach should be the development of procedure-specific evidence-based pain management protocols which could be easily implemented in fast-track surgeries.

Last but not the least is forthcoming role of multimodal perioperative care pathways; the enhanced recovery after anesthesia protocols. These protocols cater to the pre-, intra-, and postoperative care of the patients and hence provide better patient care, reduce the stress to surgery, and lead to shorter hospital stay and cost savings. The key elements involved are preoperative patient counseling, nutritional optimization, standardizing anesthesia and analgesia regimens, and early mobilization.^[72] Eras has been successfully implemented for ambulatory anorectal and sleeve gastrectomy surgeries and will eventually open up new ventures for ambulatory care anesthesia.^[73,74]

Conclusion

With the advent of better and newer technology for surgical procedures and newer anesthesia drugs which have high potency and shorter duration of action, day care surgeries are emerging out successfully. The key to successful pain management of such procedures requires individually tailored education to patient or caregivers including information on treatment options for postoperative pain and use of multimodal analgesia. Effective pain control aims at patient safety and comfort with simultaneously decreasing complications and providing early rehabilitation. Regional anesthesia techniques, especially peripheral nerve blocks, are an emerging and promising concept in the field of day care surgery.

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