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Pain Management for Ambulatory Surgery: What Is New?

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Abstract Safe ambulatory surgery mandates the provision of an anesthetic 'package', or care bundle commensurate with surgery, which enables the patient (or their guardian) to manage their pain at home. Anesthesia providers must therefore plan and implement analgesic regimens that commence in the preoperative phase, continue through the intraoperative and recovery periods and into the outpatient setting. Multimodal analgesia is the mainstay of successful ambulatory surgery analgesia. A combination of opioid and nonopioid analgesics, as well as local or regional techniques is likely to ensure the best patient outcome. There is a clear trend toward more peripheral selective nerve blocks and wound infiltration.

Keywords Surgery: ambulatory · Analgesia: postoperative · Analgesics: systemic · Peripheral nerve blocks · Local infiltration · Perineural catheters

Introduction

Ambulatory, same-day or day stay surgery is now commonplace around the world, with more than 41 million surgeries or invasive procedures occurring annually in the United States [1]. Ambulatory surgery is defined by admission and discharge within the same day, excluding an overnight stay [2•]. In many ambulatory surgical environments, formal admission to a facility providing inpatient care is difficult and may require transfer to another hospital [3].

An absolute requirement for safe ambulatory surgery is the provision of an anesthetic 'package', or care bundle that is sufficient for surgery and will enable the patient (or their guardian) to manage any suitable outpatient analgesic requirements at home [4]. This may include systemic (oral), local, or regional analgesic modalities. The complexity of outpatient analgesia has increased as both the surgical procedures and the patient population have changed [5–8]. Anesthesia providers must therefore plan and implement analgesic regimens that commence in the preoperative phase, continue through the intraoperative and recovery periods and into the outpatient setting [9, 10].

At the heart of the success of ambulatory surgery is achieving 'discharge readiness' in a timeframe commensurate with the day-stay facilities. Guidelines include pain manageable by outpatient measures and written instructions about what to do should complications occur [4].

Analgesic Options for Ambulatory Procedures

As the procedural possibilities for ambulatory surgery expand, so must the analgesic options too. Pain is often the most feared postoperative complication and a significant contributor to unexpected hospital admission or delayed discharge from ambulatory surgical facilities [11]. Adequate pain relief is considered a basic human right and the measurement of pain now constitutes the 'fifth vital sign' [12].

Analgesic needs will be dictated by the surgical procedure. Some procedures lend themselves to topical

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(ophthalmic), local or regional (limb surgery) or systemic analgesic techniques (laparoscopy), or a combination of these. There may also be vastly different analgesic requirement intra-operatively as opposed to post operatively. Multimodal or balanced analgesia can be used to describe both the different applications of analgesia, for example topical, local, regional and systemic options [13], or the systemic co-administration of opioids and non opioids that act at different molecular sites. They are often synergistic and allow improved analgesia with decreased systemic side effects [14]. Multimodal analgesia is the mainstay of successful ambulatory surgery analgesia.

Systemic Analgesia for Ambulatory Surgery

Preoperative Administration

Balanced systemic analgesia ideally commences in the preoperative period.

Acetaminophen may be commenced orally preoperatively. However, postoperative plasma levels are more likely to be therapeutic if acetaminophen is given intravenously intra-operatively [15]. Intravenous acetaminophen has an excellent safety profile in recommended doses of 15 mg/kg in children and 1 gm in adults >50 kg [16]. It also has been shown to achieve higher cerebrospinal fluid levels than oral dosing [17]. Rarely contraindicated, acetaminophen is effective at decreasing postoperative pain scores and morphine consumption [18, 19].

Non-steroidal anti-inflammatory drugs (NSAIDs), including the selective cyclo-oxygenase (COX)-2 inhibitors can be given preoperatively. They decrease both postoperative pain and opioid side effects [20, 21]. However, NSAIDs and COX-2 inhibitors should be avoided in those with preexisting renal failure. Of note, COX-2 inhibitors could be used when there is a history of aspirin sensitive asthma. Soon after their introduction, COX-2 inhibitors were shown to be associated with an increased risk of adverse cardiovascular events when taken long term. Population studies demonstrated a similar cardiovascular risk profile to NSAIDs [22]. The safety and efficacy of single dosing of NSAIDs and COX-2 inhibitors is supported by a recent review [23].

The enhanced efficacy of the combination of acetaminophen and NSAIDs/COX-2 inhibitors compared to either drug alone has been demonstrated [24]. Ong et al. [24] examined 21 randomised controlled trials that showed the NSAIDs/acetaminophen combination to be superior to acetaminophen alone in 17 out of 20 trials (85 %), as evidenced by a 35 % reduction in pain intensity and 38.8 % reduction in analgesia supplementation. Unless contraindicated, all ambulatory patients should receive acetaminophen and NSAIDs regularly

Gabapentinoids, comprising gabapentin and pregabalin, are oral medications increasingly used in multimodal analgesic regimens. Originally used for its antiepileptic properties, gabapentin showed success at decreasing neuropathic pain and has since been extensively trialled in the perioperative setting [25]. A 2013 systematic review concluded that immediate postoperative pain relief was better in patients receiving gabapentin or pregabalin compared to placebo. The gabapentinoids continued to decrease morphine use when given postoperatively. Therefore, a higher preoperative dose (gabapentin 900–1,200 mg, pregabalin 150–75 mg) with 14 days of ongoing postoperative dosing (gabapentin 600 mg tds, pregabalin 150 mg bd) has been suggested. [26] In addition, gabapentinoids decrease preoperative anxiety and opioid associated side effects [27•].

Gabapentinoids may also play a role in preventing central sensitisation. Patients undergoing lumbar discectomy who received pregabalin perioperatively had less pain at three months [28]. A recent systematic review supported the notion that gabapentinoids may prevent the development of chronic pain, but called for larger, better-designed studies [29]. Given the number of day surgeries performed worldwide, a reduction in chronic post surgical pain would have major health care benefits. In the ambulatory setting, consideration must be given to the side effects of gabapentinoids including sedation and dizziness. Care must be taken in the elderly and those with renal dysfunction who are at risk of accumulation of gabapentinoids [30]. Dose reduction based on creatinine clearance is suggested, down to a daily maximum of gabapentin 300 mg, pregabalin 75 mg if CrCl 15 ml/min [26].

The use of gabapentinoids should be patient and procedure specific. They are probably more suited for anxious patients with preoperative chronic pain and to surgical procedures known to have a high incidence of persistent postoperative pain.

Intraoperative Administration

In addition to the simple analgesics discussed above, i.e., acetaminophen and NSAIDs, opioids, dexamethasone, and ketamine are part of the intraoperative analgesic armamentarium.

Remifentanil is a unique synthetic opioid that is broken down by plasma esterases and has a very short context sensitive half-life. Being cleared rapidly from the circulation, it lends itself to infusion e.g., 0.1–0.2 μg/kg/min during intensely stimulating surgery. It may also be administered as a slow bolus of 0.5–1 μg/kg for intense, short stimuli e.g., intubation or abscess incision. Boluses and high infusion rates carry the risks of bradycardia and hypotension, which should be anticipated—as should the development of opioid hyperalgesia, which is relevant to

ambulatory surgery such that adequate postoperative analgesia should be in place prior to awakening [31].

Morphine is the most commonly used longer acting opioid. In patients with significant renal impairment, oxycodone is an alternative for postoperative analgesia. It can be administered intravenously at a dose similar to morphine, but its touted benefits are in relation to oral dosing; lower first pass metabolism and thus better bioavailability [32]. It is equi-analgesic and does not have significant active metabolites; therefore, it is particularly beneficial in patients at risk from morphine-3 and morphine-6 glucuronide accumulation [33]. It is available as immediate release (Oxynorm®) or slow release (Oxycontin®) preparations. As with all opioids, there is abuse potential and the risk of developing opioid-induced hyperalgesia.

Dexamethasone, most commonly used for antiemetic prophylaxis, has shown benefit in terms of reduction in both postoperative pain and time to discharge home [34]. However, routine dexamethasone use has been questioned in recent years for two reasons: (i) concern over corticosteroid-induced hyperglycaemia leading to decreased wound healing and increased wound infection, and (ii) concern over corticosteroid-induced immunosuppression and cancer recurrence

An elegant randomised placebo controlled trial investigated the effect of intraoperative 4 or 8 mg of dexamethasone on blood glucose levels in gynecological surgical patients. Two hundred patients were randomised to six groups (either placebo, 4 or 8 mg dexamethasone, and sampling either early or late). Their results showed that although median blood glucose values rose in the three different medication groups (saline, 4 or 8 mg dexamethasone), there were no significant differences between the groups either at 1–4 h (early group), or 8–24 h (late group). Episodes of hyperglycaemia (defined as >180 mg/dl) did not differ among study groups either. The study was not designed or powered to look at differences in wound healing/infection or pain scores [35].

Dexamethasone is known to inhibit natural killer T cell function and could theoretically suppress the body's ability to prevent cancer recurrence postoperatively. The results of a retrospective study on the influence of perioperative dexamethasone on ovarian cancer recurrence did not support a role for dexamethasone in enhancing ovarian cancer recurrence [36].

Given the known advantageous effect of dexamethasone on the prevention of postoperative nausea and vomiting and its ability to decrease postoperative pain and time to discharge readiness [37], studies support the safety of the routine use of a single dose of systemic dexamethasone. It should be considered part of a multimodal regimen aimed at improving postoperative pain, nausea, and vomiting.

Ketamine is an NMDA receptor antagonist. At subanesthetic doses, it is known to be opioid sparing and to reduce opioid related side effects [38]. Studies have confirmed a 37.5 % reduction in early postoperative pain scores (upto 4 h) and a 25 % reduction in late scores (24–72 h) [39]. In addition, it has been shown to reduce opioid requirements and opioid-related adverse events. These benefits are particularly appreciated in opioid tolerant patients. Ketamine is also shown to reduce opioid-induced hyperalgesia and the incidence of persistent postsurgical pain. However, ketamine-related side effects such as blurred vision, diplopia, nystagmus, dysphoria, hallucinations, unpleasant dreams, and psychiatric disturbances are of concern. Side effects may delay discharge in the ambulatory setting, therefore, patient and procedure-specific administration of the appropriate dose of ketamine is key. It is best used at low doses for patients with preexisting chronic pain, where regional techniques are not possible, surgical pain is severe, or when opioid side effects are particularly deleterious, e.g., in patients with a history of severe PONV or obstructive sleep apnoea. The optimal dose remains unknown, bolus doses of 0.2–0.5 mg/kg and infusions of 0.1–0.2 mg/kg/h have been reported [40].

Postoperative Administration

The continuation of systemic medications orally is the most common form of postoperative analgesia. Multimodal regimens that correspond to the severity of the expected pain commensurate with surgery should be available to patients along with written instructions. For example, outpatient laparoscopic cholecystectomy patients could be prescribed regular oral acetaminophen 1 g four times a day, with regular NSAIDs and a rapid acting opioid (e.g., tramadol, codeine, or oxynorm) available if necessary. Appropriate instructions for when and how to increase the dose for break-through pain and/or when to seek help should be clearly outlined. Fixed dosing regimens with multiple medications may simplify self-administration with a tramadol/acetaminophen 37.5/325 mg combination showing effective analgesia and high patient satisfaction after ambulatory hand surgery [41]. However, this approach of fixed dose combination prevents optimal dosing of acetaminophen or may result in the patient consuming opioids unnecessarily.

Peripheral Nerve Blocks for Ambulatory Surgery

Peripheral nerve blockade (PNB) has become increasingly popular with the advent of real-time ultrasound guidance. Regional anesthesia provides the best analgesia both intra- and postoperatively, and ensures earlier discharge from the

ambulatory care unit. The combination of PNB and general anesthesia has many benefits too, including decreased opioid use and associated side effects.

Regional techniques include single shot perineural injections and continuous local anesthetic infusions via perineural catheters. The ideal regional analgesic can be administered prior to induction (if a general anesthetic is to be given), provides a dense sensory block but minimal motor block, has a prolonged duration of action, wears off slowly and is not neurotoxic. Although discharge with an insensate limb may carry risks, it has been shown that in 1,791 patients having 2,382 long-acting peripheral nerve blocks placed for ambulatory surgery, complications relating to the nerve block were uncommon [42].

All current long-acting local anesthetics—bupivacaine, levobupivacaine, and ropivacaine—show wide inter-patient variability. Cox et al. [43] demonstrated supraclavicular block durations of between 892 and 1,039 min with 0.25 and 0.5 % S(−)-(levo) bupivacaine with standard deviations of 250 and 317 min. Ropivacaine has similar duration of action as bupivacaine. In some trials it has been shown to display less motor block, especially in epidural analgesia [44–46]. However, this initially promising point of difference has not translated into clinical practice with peripheral nerve blocks and may only be a product of differing drug concentrations.

Upper Limb Surgery

Shoulder Surgery Postoperative pain after shoulder surgery is common, and can be managed with an effective interscalene brachial plexus block. This is associated with significant side effects including phrenic nerve paralysis approaching 100 %, especially with traditional, high volume blocks [47]. Permanent phrenic nerve dysfunction is rare but can be a devastating injury impeding respiratory function [48]. Supraclavicular brachial plexus blocks are a reasonable analgesic alternative and carry slightly less risk of diaphragm paraesis.

For day case shoulder surgery, a low volume (5 ml versus the traditional 20–30 ml), ultrasound-guided interscalene block will decrease phrenic nerve involvement while providing adequate analgesia upto 6 h postoperatively [49]. Alternatively, the combination of suprascapular and axillary nerve blocks (Shoulder Block) provides analgesia to the joint capsule and overlying skin while avoiding the risks of both interscalene and supraclavicular approaches [50].

Forearm and Hand Surgery Peripheral nerve blocks are ideal for surgery to the forearm and hand. Axillary brachial plexus blocks capturing the median, radial, ulnar +/− the musculocutaneous within one needle entry point are most commonly performed. Selectively blocking individual nerves distally provides excellent analgesia to the innervation area. Quick onset anesthesia conditions with 2 % lidocaine plus epinephrine in the axilla can be supplemented with peripheral long-acting local anesthetic blocks targeting individual nerves under ultrasound guidance. Ultrasound has revolutionised single target nerve blocks, with approaches above, below and at the elbow facilitated by the real-time imaging. Both in and out of plane techniques are acceptable and allow access to nerves at most sites, although blocking the ulnar nerve within its passage around the medial epicondyle should be avoided.

Lower Limb Surgery

Safe ambulation is a consideration when performing lower limb blocks. The concentration of local anesthetic may be reduced in an attempt to minimise motor block. However, there is a real danger of motor block leading to delayed mobility or altered proprioception resulting in falls.

Femoral nerve blocks are excellent at providing analgesia to the inner thigh and knee, but the motor block of the knee extensors may contribute to falls [51]. More peripheral blocks have evolved: (i) adductor canal blockade of the saphenous nerve, which will anesthetise the medial aspect of the leg from the knee to the foot with less motor block.; (ii) infrapatellar nerve block, a purely sensory block of the anterior capsule of the knee [52]. Following arthroscopy, patients receiving infrapatellar block with 10 ml 0.5 % bupivacaine showed an improvement in pain scores but not opioid usage compared to those receiving placebo [53].

Sciatic nerve blocks are useful for anterior cruciate ligament reconstruction using hamstring graft, as well as for ankle and foot surgery. Proximal approaches will cause significant leg weakness, whereas blockade at 10–12 cm above the popliteal fossa, provides analgesia to the lower leg while permitting ambulation with crutches [54].

Trunk Surgery

Paravertebral blockade in breast surgery has gained in popularity due to ultrasound guidance, and ongoing concerns that systemic anesthetics may modify disease progression in breast cancer [55, 56]. As the sole technique with sedation, or in addition to propofol total intravenous anesthesia, unilateral paravertebral blockade provides excellent analgesia to the chest wall and may improve the quality of recovery compared to sevoflurane general anesthesia [57].

In the ambulatory setting of ‘simple breast surgery’ a continuous paravertebral infusion in addition to single shot blocks, did not improve pain, nausea, or mood scores or hasten return to normal activity [58]. It appears that the low pain scores of breast conserving surgery (<3 on a 0–10 scale) do not warrant ongoing infusions, and these should

be reserved for more invasive surgery, e.g., mastectomy with immediate reconstruction [58].

The transversus abdominis plane (TAP) block provides effective analgesia to the lower abdomen and inguinal region. When used for laparoscopy, TAP blocks resulted in less early and late pain at rest, particularly when, but, administered preoperatively [59]. Whether TAP blocks are superior to ilioinguinal/iliohypogastric blocks or infiltration techniques following open hernia repair is debatable [60–64]. It is, however, clear that some local anesthetic placed within the correct plane will improve postoperative pain scores compared to no local anesthetic.

Novel Formulations and Adjuncts to Single-Shot Nerve Blocks

Liposomal bupivacaine (Exparel®) was approved by the FDA in 2011, for wound infiltration use in haemorrhoidectomy and bunionectomy [65]. While effective compared with placebo, it has not yet been demonstrated to have significant improvements over standard bupivacaine after total knee arthroplasty or mammoplasty [66]. A single study of liposomal bupivacaine in femoral nerve blockade showed large intersubject variability in 14 volunteers [67]. Currently perineural liposomal bupivacaine use is off label. Further studies with liposomal local anesthetics are needed. It is conceivable that liposomal bupivacaine would make its way into regional anesthesia practice gradually from subcutaneous wound infiltration through fascial plane blocks to specific nerve blocks.

Single-shot nerve blocks with available long-acting local anesthetics provide upto 16 h of analgesia. Ambulatory patients who experience moderate to severe pain after the blocks have worn off—often after they have gone home—are limited to enteral simple analgesics and opioids, thereby only delaying their exposure and possible development of opioid side effects. Advances have been made into adjuncts that prolong block duration.

Perineural dexamethasone has been demonstrated to increase median block duration by 37 % and thus to decrease postoperative pain scores [68]. In addition, it has been shown that both intravenous and perineural dexamethasone extended ropivacaine and bupivacaine block duration [69, 70]. Animal studies have demonstrated that dexamethasone did not increase the neurotoxicity of ropivacaine when added at a concentration of 66 μg/ml to a 24 h infusion, but significantly increased neurotoxicity at 133 μg/ml [71••]. Thus limiting perineural dexamethasone concentrations to 66 μg/ml, and taking into account any systemically administered dexamethasone upto a maximum of 4 mg per patient is suggested by Williams et al. [72] in a recent editorial.

Perineural clonidine at doses of 100–150 μg prolongs the duration of sensory blocks by upto 100 min. It can produce significant systemic side effects such as bradycardia and hypotension which appear to be limited with doses upto 150 μg. A meta-analysis did not find sufficient evidence to support its use in continuous infusions [73], but it may preferentially prolong sensory block over motor block, especially when used with ropivacaine [74]. It has not been shown to be neurotoxic in animal studies [75].

Dexmedetomidine in regional anesthesia is an off licence application which underwent limited investigation. A recent systematic review of its use in neuraxial and perineural blockade showed that its addition may prolong the duration of PNB by over 4 h. Thus dexmedetomidine may be faciltatory, but currently there is insufficient safety data available to support such use [76].

Perineural Catheters

Continuous perineural infusions of local anesthetic solutions provide excellent localised analgesia, prolonged dynamic pain relief, facilitate postoperative mobilization and thus have been associated with high patient satisfaction [77–79].

Although the safety and efficacy of home based continuous peripheral nerve blocks following limb surgery is well established, their use has been limited to a few centers [80]. Secure pumps for drug delivery and well-motivated patients are basic requirements. Written instructions with healthcare provider contacts as well as appropriate rescue analgesia prescriptions should be provided with clear information about catheter removal. This may be performed by the patient, their family doctor or day care facility [81].

Local Infiltration Analgesia for Ambulatory Surgery

Local infiltration of the surgical field is considered the cornerstone of multimodal analgesia and should be performed whenever possible. Despite common belief, systemic toxicity or wound healing and infection are not major concerns.

The analgesic efficacy of high volume, dilute local anesthesia infiltration has been extensively investigated in hip and knee arthroplasty as part of enhanced recovery after surgery programmes. A systematic review of high volume local infiltration (HVLI) for hip arthroplasty found evidence of analgesic efficacy [82]. Some observed no additional reduction in acute pain from HVLI when added to an oral multimodal regimen [83]. This attributes credit to multimodal analgesia rather than demonstrating the inefficacy of HVLI. Although HVLI provides postoperative analgesia, it is not clear if it is better or more cost effective compared to peripheral nerve blocks [84•]. Although traditionally inpatient procedures, well-selected patient

population are now offered unicompartmental and total hip arthroplasty on an outpatient basis in some centers [85–87].

Clearly, when used in adequate doses, wound infiltration in day surgery can be incorporated into a multimodal analgesic regimen without major complications and could have potential cost saving benefits [88].

Single injections have limited durations. In order to prolong the duration of analgesia, intermittent top-up injections and continuous infusions through catheters placed at the time of surgery have been employed. These techniques are very much procedure and site specific. For example, wound infusions after breast surgery have obviated the use of paravertebral catheters, whereas infusion pumps following open inguinal hernia repair lack sufficient evidence [89].

Conclusion

With the advances being made in day-case surgical capabilities, analgesia for these procedures needs to evolve to meet the procedure-specific requirements for satisfactory postoperative pain relief. No single modality (drug or site of administration) is sufficient and a combination of systemic, local, and regional techniques using simple analgesics, opioids and local anesthetics will give the best patient outcome. Improvements in local anesthetic preparation allowing prolonged selective sensory blockade have the potential to further enhance postoperative analgesia.

Compliance with Ethics Guidelines

Conflict of Interest Kathryn Hagen and Gabriella Iohom declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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