Review article

Pain management after ambulatory surgery

Girish P. Joshi *

Department of Anesthesiology and Pain Management, University of Texas Southwestern Medical Center at Dallas, 5323 Harry Hines Boulevard, Dallas, TX 75235-9068, USA

Abstract

Numerous studies have reported inadequate pain management after ambulatory surgery. Uncontrolled pain is associated with increased incidence of nausea, anxiety and delirium, prolonged postanesthesia care unit stay, delayed discharge from ambulatory facility, unanticipated hospital admissions and delayed resumption of normal activities. The management of pain after ambulatory surgery poses unique challenges because of the need to balance pain relief with concerns of side effects ans safety. The goal of pain management should be to minimize pain, not only at rest but also during mobilization. Preoperative education of patients regarding the modalities of pain treatment, the pain assessment tools and the degree of pain that they might expect is an important part of pain management. The preemptive and multimodal techniques provide more effective analgersia with reduced incidence of side effects. Local anesthetic techniques should be utilized whenever possible as they are simple, have a high success rate and a low incidence of compilations. Local anesthetic techniques administered before the initiation of the surgery may decrease anesthetic requirements, provide for an earlier recovery and decrease postoperative analgesic requirements. Nonsteroidal antiinflammatory drugs have opioid-sparing effects, which may reduce the incidence of opioid-related side effects. Pain after discharge from the ambulatory facility should be controlled with regular dosing with oral nonsteroidal antiiflammatory drugs and opioid analgesic combination. Oral medications should be administered as early as possible and before the reduction of analgesic effects of parenterally administered drugs. It is important that oral medications are administered at regular intervals rather than on an 'as needed' basis. Regular dosing with pain medications provides superior analgesia as this prevents pain from becoming severe and decreases the incidence of breakthrough pain. Finally, adequate and appropriate application of currently available information and therapies would significantly improve postoperative pain management. © 1999 Elsevier Science B.V. All rights reserved.

Keywords: Ambulatory surgery; Postoperative pain management; Analgesics; Opioids; Nonsteroidal anti-inflammatory drugs; Local anesthetics

1. Introduction

Currently, ambulatory surgery constitutes more than 60% of all surgery performed in the USA. Furthermore, there is an increasing trend towards performing more extensive and potentially more painful surgical procedures on an ambulatory basis. However, one of the most important factors limiting the growth of ambulatory surgery is our ability to provide adequate postoperative pain relief. This has increased interest in finding more effective pain management techniques after ambulatory surgery [1]. Although there is an increased awareness of the importance of effective pain management after ambulatory surgery, numerous clinical studies indicate that postoperative pain is not always effectively treated [2,3]. A study evaluating the quality and severity of pain in patients undergoing ambulatory

* Tel.: +1 214 5907259; fax: +1 214 5906945; e-mail: girish.joshi@email.swmed.edu

surgery reported that 35% of patients experienced moderate-to-severe pain at home in spite of analgesic medication [2].

Inadequate treatment of pain may be due to lack of knowledge and skills or attitudes of healthcare personnel. In addition, pharmacokinetic and pharmacodynamic variability among patients and variability in the patient's perception of pain are important factors resulting in inadequate pain relief. An important reason for inappropriate pain management is inadequate or improper application of available information and therapies. Outpatients undergoing day-case procedures require an analgesic technique that is effective, has minimal side effects, is intrinsically safe, and can be easily managed away from the hospital or surgery center.

2. Consequences of inadequate pain management

The harmful pathophysiological and psychological consequences of unrelieved pain are well-recognized [4]. Uncontrolled pain is associated with increased incidence of: postoperative nausea [5], postoperative delirium [6], prolonged postanesthesia care unit (PACU) stay [3], delayed discharge from an ambulatory facility [7], and unanticipated hospital admissions [3,8]. Furthermore, inadequate pain control may delay resumption of normal activities. Importantly, postoperative patient satisfaction has been shown to be related to the level of pain intensity [9]. In a survey of ambulatory surgery patients, the presence of postoperative symptoms including pain significantly contributed to dissatisfaction with their surgical experience [10]. Patient satisfaction is a major determinant of the success of ambulatory surgery and is among the most important outcomes that can be influenced by adequate pain management. Importantly, in the current atmosphere of managed care, increasing attention has been given to the assessment of patient satisfaction as a way to monitor quality of care in the hospital setting.

3. New concepts in acute pain management

Recent advances in the pathophysiology of acute pain have improved our ability to manage postoperative pain. Laboratory and clinical studies have shown that injury produces prolonged change in the central nervous system function that influences responses to subsequent afferent input [11,12]. Therefore, blockade of afferent input before the surgical stimulation may eliminate central sensitization and prevent amplification and prolongation of postoperative pain. Preoperative administration of opioid or nonopioid analgesics (nonsteroidal anti-inflammatory drugs (NSAID) and local

anesthetics) may reduce the degree of pain and the need for analgesics in the postoperative period. This is termed as 'preemptive' analgesia. Two recently published articles have critically reviewed clinical studies related to the preemptive effects of analgesic treatments [11,12].

It has been increasingly apparent that the effectiveness of an individual analgesic may be enhanced by the additive or synergistic effects of multiple analgesic drugs that have different mechanisms of analgesia. The 'multimodal' analgesia techniques consisting of a combination of analgesic regimens including opioids, NSAID, and local anesthetics have assumed increasing importance in the management of postoperative pain. Combining modalities provides more effective analgesia with a reduced incidence of side effects [13].

The demonstration of an increased number of opioid receptors on peripheral nerve terminals in the postinflammatory state has led to the concept of peripheral analgesia [14]. It has been recognized that opioid nociception can be achieved by activation of peripheral opioid receptors. Peripheral administration of smaller, systemically inactive doses of opioids has been reported to provide effective and prolonged analgesia. Effective peripheral antinociception has several advantages, including the need for lower total opioid doses and reduced opioid-related side effects. Many investigators have used an arthroscopic model to evaluate the peripheral analgesic properties of opioids and nonopioid analgesics.

4. Surgical considerations

One of the major considerations in selection of a surgical procedure to be performed on an outpatient basis is the expected degree of postoperative pain associated with the surgery [15]. A study evaluating the pattern of pain after ambulatory surgery found that the type of surgery was a significant predictor of severity of postoperative pain [3]. Almost 50% of patients reporting 24-h postoperative pain had undergone laparoscopic, orthopedic or a urologic procedure. In addition, severe pain was associated with increased duration of surgery.

A reduction in surgical trauma by minimally invasive surgery should reduce the stress response to surgery including postoperative pain and thus facilitate early recovery [16]. Minimally invasive surgery including laparoscopic surgery is one of the rapidly expanding fields of surgery. The major reasons for increased use of laparoscopic procedures include decreased pain, smaller incisions, and decreased length of hospital stay. However, pain after laparoscopic procedures (particularly cholecystectomy) can sometimes be severe and may last for several days [17]. The type of pain after laparo-

scopic procedures differs considerably from that observed after open procedures. Laparotomy results mainly in parietal pain (from the abdominal wall), while laparoscopy causes more visceral pain [18]. In addition, the degree of stretching of the intraabdominal cavity is an important source of postoperative pain. Higher insufflation pressures significantly increase the severity of postoperative pain [19]. Subphrenic and shoulder pain after laparoscopic procedures appears to arise from diaphragmatic and phrenic nerve irritation due to insufflated carbon dioxide. This pain tends to be aggravated by ambulation and may persist for several days after surgery.

It is suggested that pain after laparoscopic tubal ligation is more severe than that after diagnostic laparoscopy [20,21]. The deep pelvic pain after tubal ligation might be due to tubal spasm following their occlusion [20] or due to uterine contractions resulting from prostaglandin release secondary to tubal trauma and ischemia [22]. In patients undergoing open hernia repair, the postoperative pain is from dissection of the spermatic cord (including the cremasteric muscle and any associated fat) and the suturing of the tissues, sometimes with some tension. During laparoscopic hernia repair, there is relatively little cord manipulation and postoperative pain is probably due to the dissection of parietal peritoneal flap off the abdominal wall.

The morbidity associated with surgical procedures has been steadily decreasing in recent decades due to the specific therapeutic strategies focused to prevent or treat specific outcome variables. However, most of these strategies have been focused on unimodal interventions with surgeons focusing on surgically oriented postoperative complications and anesthesiologists focusing on intraoperative and immediate postoperative complications [16]. It is possible that multimodal interventions may lead to a further reduction in the undesirable sequelae of surgical injury with improved recovery and reduction in postoperative morbidity and overall costs [16]. With respect to perioperative pain management, it is important that both anesthesiologists and surgeons join hands to manage pain as a continuum (i.e. preoperative, intraoperative and postoperative).

5. Preoperative considerations

Preoperative psychological factors, anxiety, fear of surgery and anticipation of pain are important factors which may affect patients' experience of postoperative pain [23]. The first step in the management of perioperative pain, which is commonly overlooked, is preoperative patient education regarding the modalities of pain treatment, the pain assessment tools, and the degree of pain that they might expect. Patients have to be made aware that they should expect adequate pain relief and should communicate their analgesic needs. It is necessary to educate patients that it is preferable not to allow pain to become severe, as it is easier to 'control' pain if it is treated at an early stage.

With an increased focus on the concept of preemptive analgesia, preoperative administration of analgesics has been increasingly employed. Preoperative administration of opioid or nonopioid analgesics has been reported to reduce patient anxiety, perioperative analgesic requirements, and pain scores in the immediate postoperative period [24,25]. However, opioid premedication is controversial in the ambulatory setting because it may increase the incidence of opioid-related side effects and delay recovery. Premedication with oral NSAIDs given 60–90 min prior to surgery can reduce the degree of postoperative pain, analgesic requirements, and discharge times [26–28]. However, efficacy of preoperative NSAIDs is presumably dependent on the type and severity of the surgical procedure.

6. Intraoperative considerations

The influence of the anesthetic technique on postoperative analgesic requirements is an important consideration. Opioids still remain the primary analgesic drugs used to achieve perioperative analgesia. Opioids are commonly administered as a part of a balanced anesthesia technique. The use of an opioid-based general anesthetic technique decreased opioid analgesic requirements during the first 4 h after surgery [29]. A recent study suggested that patients receiving smaller doses of fentanyl when body mass index and duration of anesthesia were taken into consideration had a higher incidence of severe pain in the PACU [3]. Not surprisingly, the need to provide analgesia in the PACU has been increased with the availability of shorter-acting anesthetic and analgesic drugs, leading to a more rapid emergence from anesthesia. Shorter-acting opioids such as remifentanil allow faster postoperative recovery, however, it is important that appropriate longer-acting analgesic techniques are utilized to achieve adequate postoperative pain control [30]. However, aggressive use of opioids can increase the incidence of postoperative nausea, vomiting, sedation, and bladder dysfunction which may delay recovery [31]. In addition, opioids are less effective in relieving the pain associated with physical activity such as coughing and ambulation [31]. Therefore, it may be necessary to reconsider the primary use of opioids for perioperative pain relief [32].

Tverskyy et al. [33] evaluated the effects of the type of anesthesia (i.e. general anesthesia, spinal anesthesia, and local anesthesia) on the degree of postoperative pain. They observed that compared with spinal anesthesia or general anesthesia alone, preincisional inguinal field blocks as an adjunct to general anesthesia was

associated with lower pain scores and a longer time to first analgesic requirement. In addition, wound tenderness was lower in patients receiving a field block. These results suggest that peripheral nerve blockade may have a higher efficacy in preventing central hyperexcitability as compared with central blockade.

7. Local anesthetic techniques

Local anesthetic techniques are simple, have a high success rate and a low incidence of complications. Furthermore, epinephrine added to the local anesthetic solution decreases capillary oozing and reduces the risk of postoperative reactionary hemorrhage. When used as adjuvants to general anesthesia, these techniques decrease the intraoperative anesthetic and analgesic requirements and provide for a rapid and smooth recovery. In addition, local anesthetic techniques can be utilized to modulate peripheral mechanisms of nociception and reduce the response to surgical injury (i.e. provide preemptive analgesia). Although the potential benefits of using local anesthetic techniques for postoperative pain relief have been well-recognized, they are under utilized.

Wound infiltration can provide excellent analgesia that may outlast the duration of action of the local anesthetic [34]. Different methods of administration, such as instillation [35–37] or aerosol application [38] of local anesthetics in the surgical wound have also been shown to provide long-lasting analgesia, reduce postoperative analgesic requirements, and facilitate earlier mobilization. The duration of analgesia can be further increased by infusion of local anesthetics through a catheter placed in the layers of the skin [39,40]. Yndgaard et al. [41] reported that subfascial injection of local anesthetics resulted in more effective pain relief when compared with subcutaneous administration. Similarly, injection of local anesthetic at the parietal peritoneum (versus subcutaneous infiltration) provided more reduction in pain scores [42]. This may suggest that pain stimuli are generated primarily in the subfascial layers, rather than the subcutaneous layers. Therefore, it is important that the local anesthetic solution is administered in the appropriate tissue plane.

In patients undergoing laparoscopic tubal ligation procedures, mesosalpingeal infiltration or topical application of local anesthetic directly to the Fallopian tubes has been shown to significantly reduce postoperative pain and cramping [43–45]. Another simple and effective method of reducing the intensity of postlaparoscopic pain is intraperitoneal instillation of local anesthetic drugs. Recent studies have reported significant pain relief after laparoscopic cholecystectomy when 15–20 ml bupivacaine 0.5% with or without epinephrine was administered before and after surgery

into the hepatodiaphragmatic space, near and above the hepatoduodenal ligament and above the gallbladder or gallbladder bed [46,47]. No side effects from bupivacaine 150–200 mg with or without epinephrine were observed. On the other hand, high volumes of local anesthetics in lower concentrations did not provide significant pain relief. It is possible that concentration and the timing of local anesthetic administration are important with this technique of pain relief.

Intraarticular administration of local anesthetics following arthroscopic knee surgery has been shown to reduce postoperative analgesic requirements and facilitate early mobilization and recovery [48]. Although the plasma bupivacaine concentrations after intraarticular instillation of 25–40 ml 0.5% bupivacaine were within a safe range [49,50], some investigators have recommended the addition of epinephrine [51]. With the acceptance of peripheral analgesia, an increasing number of studies have reported the analgesic effects of intraarticularly administered morphine [52]. The dose and volume of morphine injected and the interval between intraarticular injection and tourniquet release are important factors in the success of the intraarticular technique [53]. Intra-articular administration of morphine 5 mg in 25–30 ml dilution provides effective analgesia and decreases analgesic requirements after arthroscopic knee surgery [54,55]. Since local anesthetic agents have a rapid onset of action, there is the possibility that a combination of morphine and bupivacaine would provide for analgesia of an early onset and long duration.

Similar to local anesthetic infiltration or instillation, peripheral nerve blocks are highly effective in reducing anesthetic and analgesic requirements in patients undergoing ambulatory surgery. In patients undergoing inguinal hernia repair, ilioinguinal and iliohypogastric nerves block have been shown to decrease postoperative pain and analgesic requirements [56]. In patients undergoing long saphenous vein stripping surgery, femoral and genitofemoral nerve blocks were associated with faster recovery, lower incidence of postoperative pain, backache, headache, and better patient satisfaction as compared with spinal anesthesia [57].

Orthopedic surgical procedures have been shown to be associated with significant postoperative pain. Therefore, utilization of local anesthetic techniques may be highly beneficial in allowing early ambulation and return to normal function. Shoulder arthroscopy performed under the brachial plexus block using the interscalene approach was found to be safe and effective with shorter hospital stays and fewer overnight hospitalizations [58]. The suprascapular nerve provides sensory fibers to 70% of the shoulder joint, including the superior and posterosuperior regions of the shoulder joint, capsule, and variably the overlying skin [59]. Suprascapular nerve block has been shown to provide

excellent pain relief in shoulder pain disorders [60]. Therefore, suprascapular nerve block may offer a safe alternative to interscalene nerve block. Richie et al. [61] evaluated the efficacy of suprascapular nerve block on the degree of pain and morphine consumption after arthroscopic shoulder surgery. They observed that suprascapular nerve block using 10 ml 0.5% bupivacaine with 1:200000 epinephrine before induction of general anesthesia reduced visual analog and verbal pain scores, as well as decreased the usage of morphine and the incidence of postoperative nausea in the immediate postoperative period and 24-h after surgery. In addition, the duration of hospital stay was also reduced. Because of its efficacy and safety, these authors recommend routine use of suprascapular nerve block as a supplement to general anesthesia in ambulatory shoulder arthroscopic surgery.

With increasing acceptance of the concept of preemptive analgesia, a number of investigators have evaluated the efficacy of local anesthetic blockade prior to surgical incision. Preincisional wound infiltration with lidocaine 1%, 40 ml, was a more effective method of providing postoperative analgesia than infiltration of the wound after inguinal hernia repair [62]. In contrast, other investigators have not found significant differences in pain scores and analgesic requirements between patients who received field block either before or after surgery [63].

Significant pain relief with a lower incidence of side effects can be achieved with the use of multimodal analgesia techniques. Eriksson et al. [64] reported that the application of 5 ml lidocaine gel on the sterilization clips and perioperative administration of ketoprofen 200 mg i.v. provided superior pain relief with reduced analgesic requirements and lower incidence of postoperative nausea and vomiting as compared with the use of local anesthetic or ketoprofen alone. In patients undergoing laparoscopic cholecystectomy, intramuscular administration of meperidine 0.6 mg/kg and ketorolac 0.5 mg/kg prior to induction of anesthesia combined with local anesthetic infiltration into the skin prior to surgical incision was highly effective in relieving postoperative pain and resulted in faster recovery and discharge [65]. Similarly, a combination of field block with bupivacaine and oral papaveretum–aspirin provided superior analgesia compared with either field block or oral papaveretum–aspirin alone [66].

Because of its long duration of action, bupivacaine is the most commonly used local anesthetic to provide postoperative pain relief. Ropivacaine is a new aminoamide local anesthetic with less potential to depress myocardial contractility and conduction and is reported to have a greater sensory-motor separation property. Thus, it may provide superior sensory blockade without the motor blockade. However, no difference in the duration of analgesia was demonstrated between bupivacaine and ropivacaine [67].

An important limitation in the use of local anesthetic techniques when utilized to achieve postoperative pain relief is the short duration of action of the presently available local anesthetic drugs which may lead to an increased perception of pain after the recovery from the neural blockade. Although continuous irrigation of the surgical wound may provide prolonged analgesia, irrigation of all parts of the wound may be technically difficult. In addition, motor blockade might predispose to injury and render postoperative neurological assessment difficult. Availability of longer-acting, slow-release preparations with incorporation of local anesthetics or opioids in liposomes or microspheres, should enhance the efficacy of local anesthetic techniques [68,69]. There is a need for the development of more effective methods for continuous irrigation and to evaluate the efficacy of local anesthetic techniques as a part of multimodal analgesia. Refinement and development of new block techniques and approaches may provide superior postoperative pain relief with improved patient safety. Furthermore, well-designed studies are necessary to clarify the clinical significance of the timing of local anesthetic blockade and the dose and volume of local anesthetics.

8. Nonsteroidal anti-inflammatory drugs

The NSAIDs have become increasingly popular in the management of perioperative pain because of their opioid-sparing effects and increased acceptance of the concept of multimodal analgesia. Of importance, NSAIDs are associated with a lower risk of postoperative nausea and vomiting, thereby improving patient comfort and allowing for an earlier discharge. The analgesic properties of the NSAIDs have been attributed to a decrease in the inflammatory response to surgical trauma and reduced peripheral nociception by inhibition of cyclooxygenase and a decrease in the synthesis of prostaglandins [70]. There are also recent reports describing the central modulation of painful stimuli by NSAIDs [71]. The controversies in the perioperative use of NSAIDs have been recently reviewed [72].

In the ambulatory setting, many studies have reported reduced postoperative pain and opioid requirements with intraoperative or postoperative use of NSAIDs either alone or in combination with opioids [73–75]. However, NSAIDs have a weaker analgesic property as compared with opioids or local anesthetics and also appear to exhibit a 'ceiling effect' [76] and therefore, may not provide adequate analgesia when used as sole analgesic. Despite these deficiencies, NSAIDs may decrease the risk of breakthrough pain because of their more prolonged duration of action and are valuable adjuvants when used in combination with

opioids and local anesthetics. Combination of hydrocodone (7.5 mg) and acetaminophen (750 mg) were found to be as effective in the management of pain after arthroscopic surgery as ketorolac (10 mg) orally [77]. The adjunctive use of ketorolac (30 mg) i.v. reduced pain scores and the need for additional analgesics in adult patients undergoing inguinal hernia repair using general anesthesia with field block [78].

Concerns have been raised regarding the side effects of NSAIDs such as gastric irritation, gastrointestinal bleeding, impaired coagulation, and renal dysfunction following their perioperative use [79]. It has been shown that short term use (24–72 h) of NSAIDs do not increase the risk of gastrointestinal side effects, provided the contraindications of these agents such as a history of peptic ulcer disease are observed [80]. Although no significant increase in blood loss have been reported after the use of NSAIDs in the perioperative period [81], they should not be used in patients with preexisting coagulation defect or those undergoing procedures with extensive tissue dissection (e.g. surgery involving skin flaps). Clinically significant renal dysfunction with the use of ketorolac has been reported only in patients with pre-existing renal dysfunction, hypovolemia, cardiac failure, sepsis, cirrhosis of the liver, and use of other nephrotoxic drugs [81]. Recent studies have reported that ketorolac administered for 5 days or less did not increase the incidence of acute renal failure or gastrointestinal and operative site bleeding [82,83]. Finally, NSAIDs should be used with caution in clinical situations where prostaglandins have proven therapeutic benefits, such as circulatory insufficiency, myocardial ischemia, and coronary vasospasm [84].

9. Immediate postoperative considerations

Adequate postoperative analgesia without side effects is necessary to facilitate discharge after outpatient surgery. Pain in the PACU should be treated quickly and effectively with small doses of potent, rapidly acting opioid analgesics. Fentanyl has a faster onset time, and its use may provide more rapid pain control and avoid unnecessary extra doses of opioids which may be administered when a drug of slower onset (i.e. morphine) is used. Claxton et al. [85] compared the analgesic efficacy and the incidence of opioid-related side effects of equipotent doses of morphine (1–2 mg) and fentanyl (12.5–25 μg) repeated every 5 min. These authors concluded that morphine and fentanyl in equipotent doses are comparable in treating postoperative pain in the PACU. However, the regimen did not provide rapid analgesia, as it took 20 min to achieve a significant decrease in baseline pain scores and 40 min to achieve VAS pain scores of less than 40 mm. Morphine provided more sustained analgesia than fentanyl,

but it was associated with a higher incidence of nausea and vomiting after discharge home [85]. On the other hand, patients receiving fentanyl required additional oral analgesia during phase II recovery (i.e. after discharge from the PACU but before discharge home). Therefore, these authors suggested that if fentanyl is used to provide analgesia in the PACU, oral analgesics should be administered as supplements to provide more prolonged pain relief.

10. Pain control after discharge from the ambulatory facility

Oral opioids or NSAIDs either alone or in combination are frequently used to provide postoperative pain relief at home. The rapid recovery associated with the availability of short-acting anesthetic drugs make it possible for patients to tolerate oral medications in the early postoperative period. Oral medications should be administered as early as possible, and before the reduction of analgesic effects of parenterally administered drugs. It is important that oral medications are administered at fixed intervals rather than on an 'as needed' basis. Regular dosing with pain medications provides superior analgesia as this prevents the pain from becoming severe and decreases the incidence of breakthrough pain. Recently Litman et al. [86] reported the successful use of oral patient-controlled analgesia by placing a limited number of analgesic tablets by the patients' bedside and giving them some degree of independence and self-control over their postoperative treatment.

When used orally, larger doses of opioids are required to achieve comparable analgesic effects because of the extensive hepatic metabolism also known as the 'first pass' effect. Codeine and its derivatives are the most commonly used oral opioid analgesics after ambulatory surgery. Compared to morphine, codeine and its derivatives have a higher oral bioavailability. Oxycodone and hydrocodone are orally active derivatives of codeine with higher analgesic potency. Controlled release preparations of oxycodone have a longer duration of action and less side effects than the older formulations and have been shown to be effective postoperatively [87]. Controlled-release preparations should provide superior pain relief because they allow greater convenience, improve patient compliance, and provide uninterrupted nighttime sleep.

Mild to moderate postoperative pain can be treated with oral combinations of opioids with NSAIDs that may prove more effective than either drug alone and may reduce their side effects. In addition, the use of NSAIDs with opioids may reduce healthcare costs by decreasing the costs associated with opioid therapy and opioid-related side effects [31,88]. However, unaccept-

able adverse effects of high doses of NSAIDs may limit their daily analgesic dose. Therefore, use of NSAIDs and opioid combination during the daytime and controlled-release formulations of opioids for the night may provide more cost-effective analgesia.

11. Noninvasive techniques

In recent years, there has been an increased interest in noninvasive approaches for administering analgesics because of their potential benefits in the management of pain following ambulatory surgery. Investigators have evaluated the use of oral transmucosal fentanyl [89], transnasal sufentanil, fentanyl, and meperidine [90–92], transdermal fentanyl and sufentanil [93,94], and morphine iontophoresis [95]. These alternative methods of opioid administration are simple, easily accessible, avoid the first-pass hepatic drug metabolism and provide for a rapid onset of action.

Development of a spray bottle with safety measures similar to a patient-controlled analgesia device may be used to self-administer opioids nasally. A recent study reported that patient-controlled intranasal analgesia using fentanyl provided postoperative pain relief as effective as intravenous patient-controlled analgesia [96]. A patient-controlled analgesia system using iontophoresis of opioids may also provide effective analgesia and would be advantageous in ambulatory patients. However, there is the potential for an increase in opioid-related side effects. Therefore, the role of these analgesic techniques in the outpatient setting remains to be investigated.

12. Non-pharmacologic techniques

In recent years there has been an increasing interest in the management of pain using non-pharmacological techniques because they avoid the side effects produced by opioid and non-opioid analgesics and, thus, may be beneficial for ambulatory surgery. These techniques include cognitive behavioral strategies such as relaxation and distraction therapy, preparatory information, or positive reinforcement and physical strategies such as the application of heat or cold, massage, exercise, rest, or immobilization. Other non-pharmacological approaches such as transcutaneous electric nerve stimulation (TENS), acupuncture, acupuncture-like transcutaneous electric nerve stimulation (ALTENS), and percutaneous electrical nerve stimulation (PENS) have also been used for treatment of postoperative pain. Although these non-pharmacologic techniques have convincing theoretical bases, their clinical efficacy remains to be proven [1]. Furthermore, these non-pharmacologic techniques may not be efficacious as sole

strategies and should be utilized only in combination with pharmacologic treatment. These techniques are encouraged in the clinical practice guidelines proposed by the Agency for Health Care Policy and Research. To improve the efficacy of these techniques, it is necessary that they are discussed with the patients preoperatively.

13. Future considerations

Numerous studies are investigating novel techniques to provide effective pain relief with minimal side effects. New interest has been focused on the peripheral treatment of surgical wounds and controlling the local inflammatory response to minimize postoperative pain. Intraoperative infusion of low-dose adenosine has shown to reduce anesthetic requirements, decrease the need for analgesics, and reduce pain scores in the postoperative period [97]. Multimodal analgesic regimens with combinations of opioids, NSAIDs, α_2-adrenergic antagonists, and N-methyl-D-aspartate receptor antagonists (e.g. ketamine) are being investigated. Similar to the peripheral effects of opioids, the analgesic efficacy of intraarticular administration of NSAIDs have also been investigated. Ketorolac 60 mg when administered along with bupivacaine 0.25% through the intraarticular route provided significant analgesia after knee arthroscopy [98]. Intraarticular tenoxicam (20 mg) (NSAID) reduced oral analgesic requirements during the first day after knee arthroscopy but did not alter patient's perception of pain [99]. However, one of the concerns with the use of intraarticular NSAIDs is the possibility of reduction in chondrocyte biosynthesis and cartilage destruction [100].

Recent experimental studies report that cholinergic systems can modulate pain perception and transmission. Neostigmine, an anticholinergic drug, can cause hyperpolarization of neurons, reduction in the release of pronociceptive neurotransmitters, or activation of the nitric oxide–cyclic guanosine monophosphate pathway and thereby, might provide peripheral antinociception by elevating endogenous acetylcholine. Intraarticular administration of neostigmine (500 μg) has been reported to reduce pain scores and time to first use of analgesics [101].

Improvements in the patient-controlled analgesia techniques and availability of smaller non-electronic on demand delivery systems may facilitate pain management with parenteral analgesics in the ambulatory setting. The subcutaneous route of patient-controlled analgesia (SC-PCA) administration may be a practical alternative to the intravenous route in the treatment of postoperative pain following ambulatory surgery because maintenance of intravenous access is not required. Continuous subcutaneous infusion or SC-PCA has been evaluated with morphine, hydromorphone,

and oxymorphone [102]. Use of SC-PCA with morphine following outpatient hemorrhoidectomy provided effective pain control, had high patient acceptance, and was cost-effective [103]. Recently, Rawal et al. [104] reported effective pain relief after outpatient surgical procedures with self-administration of local anesthetic solution using a elastometric balloon pump used at home. The efficacy and safety of the patient-controlled analgesia techniques depends upon proper programming of these devices and improved education of patients so that they are able to use the therapy in a rational manner. The role of these analgesic techniques in the outpatient setting needs to be clarified by further investigation and clinical experience with focus on patient outcome and cost-effective related issues.

With increased stress on multimodal interventions, the importance of the treatment of multiple causes of postoperative pain has been emphasized. It has been suggested that infection of hemorrhoidectomy wounds may influence postoperative pain and analgesic requirement through inflammatory swelling and edema. Administration of metronidazole in patients undergoing day case hemorrhoidectomy has been shown to decrease the degree of postoperative pain on days 5–7, increase patient satisfaction and allow for an earlier return to work [105]. A recent study reported that administration of an antispasmodic drug such as glycopyrrolate (0.3 mg) i.v. at induction of anesthesia significantly reduced pain scores in the immediate postoperative period, decreased the requirements for analgesics, and improved the quality of recovery after day-case laparoscopic sterilization using clips [106].

14. Summary

Despite substantial advances in our understanding of the pathophysiology of acute pain and the availability of newer opioid and non-opioid analgesics, as well as new techniques of drug administration, postoperative pain after ambulatory surgery is not always effectively treated. The goal of pain management should be to minimize pain, not only at rest but also during mobilization. Furthermore, there should be an increased focus on the prevention of breakthrough pain which may occur after the patient has left the ambulatory facility. Pain management is a dynamic process which includes frequent patient assessments and adjustments of the analgesic regimen, and knowledgeable treatment of the side effects. The management of pain after ambulatory surgery poses some unique challenges. The most important task for practitioners is the ability to balance pain relief with concerns about safety and side effects. Importantly, adequate and appropriate application of currently available information and therapies would significantly improve postoperative pain management.

There should be an increased emphasis on multimodal techniques of providing analgesia. Local anesthetic techniques should be utilized whenever possible because they not only decrease the requirements for anesthetic agents and provide for an earlier recovery but also decrease the analgesic requirements in the postoperative period. Despite the relatively short duration of action of local anesthetic techniques, they reduce pain in the immediate postoperative period until it can be controlled with oral analgesics. Pain after discharge from the ambulatory facility should be controlled with regular dosing with oral NSAID–opioid analgesic combinations which should avoid the occurrence of breakthrough pain and provide for superior analgesia. Well-designed studies evaluating the cost-effectiveness of various analgesic techniques are necessary to assist practitioners in decision-making.

References

[1] Joshi GP. Postoperative pain management. In: White PF, editor. Anesthesia for Ambulatory Surgery. Boston, MA: Little Brown, 1994:113–126.

[2] Rawal N, Hylander J, Nydahl PA, et al. Survey of postoperative analgesia following ambulatory surgery. Acta Anaesthesiol Scand 1997;41:1017–22.

[3] Chung F, Ritchie E, Su J. Postoperative pain in ambulatory surgery. Anesth Analg 1997;85:808–16.

[4] Kehlet H. Surgical stress: the role of pain and analgesia. Br J Anaesth 1989;63:189–95.

[5] Anderson R, Krohg K. Pain as a major cause of postoperative nausea. Can Anaesth Soc 1976;J 23:366–9.

[6] Lynch EP, Lazor MA, Gellis JE, et al. The impact of postoperative pain on the development of postoperative delirium. Anesth Analg 1998;86:781–5.

[7] Chung F. Recovery pattern and home-readiness after ambulatory surgery. Anesth Analg 1995;80:896–902.

[8] Gold BS, Kitz DS, Lecky JH, et al. Unanticipated admission to the hospital following ambulatory surgery. J Am Med Assoc 1989;262:3008–10.

[9] Jamison RN, Ross MJ, Hoopman P, et al. Assessment of postoperative pain management: patient satisfaction and perceived helpfulness. Clin J Pain 1997;13:229–36.

[10] Tong D, Chung F, Wong D. Predictive factors in global and anesthesia satisfaction in ambulatory surgical patients. Anesthesiology 1997;87:856–64.

[11] Dahl JB, Kehlet H. The value of pre-emptive analgesia in the treatment of postoperative pain. Br J Anaesth 1993;70:434–9.

[12] Woolf CJ, Chong M. Preemptive analgesia—treating postoperative pain by preventing the establishment of central sensitization. Anesth Analg 1993;77:362–79.

[13] Kehlet H, Dahl JB. The value of 'multimodal' or 'balanced analgesia' in postoperative pain treatment. Anesth Analg 1993;77:1048–56.

[14] Stein C. The control of pain in peripheral tissue by opioids. New Engl J Med 1995;332:1685–90.

[15] Meridy HW. Criteria for selection of ambulatory surgery patients and guidelines for anesthetic management: a retrospective study of 1553 cases. Anesth Analg 1982;61:921–6.

[16] Kehlet H. Multimodal approach to control postoperative pathology and rehabilitation. Br J Anaesth 1997;78:606–17.

[17] Alexander JI. Pain after laparoscopy. Br J Anaesth 1997;79:369–78.

[18] Joris J, Thiry E, Paris P, et al. Pain after laparoscopic cholecystectomy: characteristics and effect of intraperitoneal bupivacaine. Anesth Analg 1995;81:379–84.

[19] Wallace DH, Serpell MG, Baxter JN, et al. Randomized trial of different insufflation pressures for laparoscopic cholecystectomy. Br J Surg 1997;84:455–8.

[20] Edwards ND, Barclay K, Catling SJ, et al. Day case laparoscopy: a survey of postoperative pain and an assessment of the value of diclofenac. Anaesthesia 1991;46:1077–80.

[21] Davis A, Millar JM. Postoperative pain: a comparison of laparoscopic sterilization and diagnostic laparoscopy. Anaesthesia 1988;43:796–7.

[22] Brodie BL, Casper RF. Prostaglandins mediate postoperative pain in falope ring sterilization. Am J Obstet Gynecol 1985;151:175–7.

[23] Payne FB, Ghia JN, Wilkes NC. The relationship of preoperative and intraoperative factors on the incidence of pain following ambulatory surgery. Ambul Surg 1996;3:127–30.

[24] Kiss I, Killan M. Does opiate premedication influence postoperative analgesia? A prospective study. Pain 1992;48:157–8.

[25] Pandit SK, Kothary SP. Intravenous narcotics for premedication in outpatient anaesthesia. Acta Anaesthesiol Scand 1989;33:353–8.

[26] Comfort VK, Code WE, Rooney ME, et al. Naproxen premedication reduces postoperative tubal ligation pain. Can J Anaesth 1992;39:349–52.

[27] Rosenblum M, Weller RS, Conrad PL, et al. Ibuprofen provides longer lasting analgesia than fentanyl after laparoscopic surgery. Anesth Analg 1991;73:255–9.

[28] Gillberg LE, Harsten AS, Stahl LB. Preoperative diclofenac sodium reduces post-laparoscopy pain. Can J Anaesth 1993;40:406–8.

[29] Taylor E, White PF. Does the anesthetic technique influence the postoperative analgesic requirements. Clin J Pain 1991;7:139–42.

[30] Yarmush J, D'Angelo R, Kirkhart B, et al. A comparison of remifentanil and morphine sulfate for acute postoperative analgesia after total intravenous anesthesia with remifentanil and propofol. Anesthesiology 1997;87:235–43.

[31] Kehlet H, Rung GW, Callesen T. Postoperative opioid analgesia: time for a reconsideration? J Clin Anesth 1996;8:441–5.

[32] Kehlet H. Postoperative pain relief-what is the issue? (Editorial). Br J Anaesth 1994;72:375–8.

[33] Tverskoy M, Cozacov C, Ayache M, et al. Postoperative pain after inguinal herniorrhaphy with different types of anesthesia. Anesth Analg 1990;70:29–35.

[34] Dahl JB, Moiniche S, Kehlet H. Wound infiltration with local anesthetics for postoperative pain relief. Acta Anaesthesiol Scand 1994;38:7–14.

[35] Casey WF, Rice LJ, Hannallah RS, et al. A comparison between bupivacaine instillation versus ilioinguinal/iliohypogastric nerve block for postoperative analgesia following inguinal herniorrhaphy in children. Anesthesiology 1990;72:637–9.

[36] Spittal MJ, Hunter SJ. A comparison of bupivacaine instillation and inguinal field block for pain control after herniorrhaphy. Ann R Coll Surg Engl 1992;74:85–8.

[37] Bays RA, Barry L, Vasilenko P. The use of bupivacaine in elective inguinal herniorrhaphy as a fast and safe technique for relief of postoperative pain. Surg Gynecol Obstet 1991;173:433–7.

[38] Sinclair R, Cassuto J, Hogstrom S, et al. Topical anesthesia with lidocaine aerosol in the control of postoperative pain. Anesthesiology 1988;68:895–901.

[39] Levack ID, Holmes JD, Robertson GS. Abdominal wound perfusion for the relief of postoperative pain. Br J Anaesth 1986;58:615–9.

[40] Gibbs P, Purushotam A, Auld C, et al. Continuous wound perfusion with bupivacaine for postoperative wound pain. Br J Surg 1988;75:923–4.

[41] Yndgaard S, Holst P, Bjerre-Jepsen K, et al. Subcutaneously versus subfascially administered lidocaine in pain treatment after inguinal herniotomy. Anesth Analg 1994;79:324–7.

[42] Alexander DJ, Ngoi SS, Lee L, et al. Randomized trial of periportal peritoneal bupivacaine for pain relief after laparoscopic cholecystectomy. Br J Surg 1996;83:1223–5.

[43] Tool AL, Kammerer-Doak DN, Nguyen CM, et al. Postoperative pain relief following laparoscopic tubal sterilization with silastic bands. Obstet Gynecol 1997;90:731–44.

[44] Van Ee R, Hemrika DJ, De Blok S, et al. Effects of ketoprofen and mesosalpinx infiltration on postoperative pain after laparoscopic sterilization. Obstet Gynecol 1996;88:568–72.

[45] Barclay K, Calvert JP, Catling SJ, et al. Analgesia after laparoscopic sterilisation. Effect of 2% lignocaine gel applied to Filshie clips. Anaesthesia 1994;49:68–70.

[46] Pasqualucci A, de Angelis V, Contardo R, et al. Preemptive analgesia: intraperitoneal local anesthetic in laparoscopic cholecystectomy. A randomized, double-blind, placebo-controlled study. Anesthesiology 1996;85:11–20.

[47] Mraovic B, Jurisic T, Kogler-Majeric V, et al. Intraperitoneal bupivacaine for analgesia after laparoscopic cholecystectomy. Acta Anaesthesiol Scand 1997;41:193–6.

[48] Smith I, Van Hemelrijck J, White PF, et al. Effects of local anesthesia on recovery after outpatient arthroscopy. Anesth Analg 1991;73:536–9.

[49] Katz JA, Keading CS, Hill JR, et al. The pharmacokinetics of bupivacaine when injected intra-articularly after knee arthroscopy. Anesth Analg 1988;67:871–5.

[50] Solanki DR, Enneking FK, Ivey FM, et al. Serum bupivacaine concentrations after intraarticular injection for pain relief after knee arthroscopy. Arthroscopy 1992;8:44–7.

[51] Butterworth JF, Carnes RS, Samuel MP, et al. Effect of adrenaline on plasma concentrations of bupivacaine following intra-articular injection of bupivacaine for knee arthroscopy. Br J Anaesth 1990;65:537–9.

[52] Kalso E, Tramer MR, Carroll D, et al. Pain relief from intra-articular morphine after knee surgery: a qualitative systematic review. Pain 1997;71:127–34.

[53] Joshi GP, McCarroll SM, O'Brien TM, et al. Intraarticular analgesia following knee arthroscopy. Anesth Analg 1993;76:333–6.

[54] Stein C, Comisel K, Haimeri E, et al. Analgesic effect of intraarticular morphine after arthroscopic knee surgery. New Engl J Med 1991;325:1123–6.

[55] Joshi GP, McCarroll SM, Cooney CM, et al. Intra-articular morphine for pain relief after knee arthroscopy. J Bone Joint Surg 1992;74B:749–51.

[56] Callesen T, Kehlet H. Postherniorrhaphy pain. Anesthesiology 1997;87:1219–30.

[57] Vloka JD, Hadzic A, Mulcare R, et al. Femoral and genitofemoral nerve blocks versus spinal anesthesia for outpatients undergoing long saphenous vein stripping surgery. Anesth Analg 1997;84:749–52.

[58] Brown AR, Weiss R, Greenberg C, et al. Interscalene block for shoulder arthroscopy: comparison with general anesthesia. Arthroscopy 1993;9:295–300.

[59] Brown DE. Pain relief by suprascapular nerve block in glenohumeral arthritis. Scand J Rheumatol 1988;17:411–5.

[60] Wassef MR. Suprascapular nerve block: a new approach for the management of frozen shoulder. Anaesthesia 1992;47:120–4.

[61] Ritchie ED, Tong D, Chung F, et al. Suprascapular nerve block for postoperative pain relief in arthroscopic shoulder surgery: a new modality? Anesth Analg 1997;84:1306–12.

[62] Ejlersen E, Andersen HB, Eliasen K. A comparison between preincisional and postincisional lidocaine infiltration and postoperative pain. Anesth Analg 1992;74:495–8.

[63] Dierking G, Dahl J, Kanstrup J, et al. Effect of pre- versus postoperative inguinal field block on postoperative pain after herniorrhaphy. Br J Anaesth 1992;68:334–48.

[64] Eriksson H, Tenhunen A, Korttila K. Balanced analgesia improves recovery and outcome after outpatient tubal ligation. Acta Anaesthesiol Scand 1996;40:151–5.

[65] Michaloliakou C, Chung F, Sharma S. Preoperative multimodal analgesia facilitates recovery after ambulatory laparoscopic cholecystectomy. Anesth Analg 1996;82:44–51.

[66] Nehra D, Gemmell L, Pye JK. Pain relief after inguinal hernia repair: a randomized double-blind study (see comments). Br J Surg 1995;82:1245–7.

[67] Erichsen CJ, Vibits H, Dahl JB, et al. Wound infiltration with ropivacaine and bupivacaine for pain after inguinal herniotomy. Acta Anaesthesiol Scand 1995;39:67–70.

[68] Grant GJ, Vermeulen K, Zakowski MI, et al. Prolonged analgesia and decreased toxicity with liposomal morphine in a mouse model. Anesth Analg 1994;79:706–9.

[69] Curley J, Castillo J, Hotz J, et al. Prolonged regional nerve blockade. Injectable biodegradable bupivacaine/polyester microspheres. Anesthesiology 1996;84:1401–10.

[70] McCormack K, Brune K. Dissociation between the antinociceptive and inflammatory effects of the non-steroidal anti-inflammatory drugs. Drugs 1991;41:533–47.

[71] Jurna I, Brune K. Central effect of the non-steroid anti-inflammatory agents, indomethacin, ibuprofen, and diclofenac, determined in C fibre-evoked activity in single neurons of the rat thalamus. Pain 1990;41:71–80.

[72] Souter AJ, Fredman B, White PF. Controversies in the perioperative use of nonsteroidal anti-inflammatory drugs. Anesth Analg 1994;79:1178–90.

[73] Dueholm S, Forrest M, Hjortso E, et al. Pain relief following herniotomy: a double-blind randomized comparison between naproxen and placebo. Acta Anaesthesiol Scand 1989;33:391–4.

[74] McLoughlin C, McKinney MS, Fee JP, et al. Diclofenac for day-care arthroscopy surgery: comparison with a standard opioid therapy. Br J Anaesth 1990;65:620–3.

[75] Wong HY, Carpenter RL, Kopacz DJ, et al. A randomized, double-blind evaluation of ketorolac tromethamine for postoperative analgesia in ambulatory surgery patients (see comments). Anesthesiology 1993;78:6–14.

[76] O'Hara DA, Fragen RJ, Kinzer M, et al. Ketorolac tromethamine as compared with morphine sulphate for the treatment of postoperative pain. Clin Pharm Ther 1987;41:556–61.

[77] White PF, Joshi GP, Carpenter RL, et al. A comparison of oral ketorolac and hydrocodone–acetaminophen for analgesia after ambulatory surgery: arthroscopy versus laparoscopic tubal ligation. Anesth Analg 1997;85:37–43.

[78] Ben-David B, Baune-Goldstein U, Goldik Z, et al. Is preoperative ketorolac a useful adjunct to regional anesthesia for inguinal herniorrhaphy? Acta Anaesthesiol Scand 1996;40:358–63.

[79] Kehlet H, Mather LE. The value of non-steroidal antiinflammatory drugs in postoperative pain. Drugs 1992;44:1–63.

[80] Kehlet H, Dahl JB. Are perioperative nonsteroidal anti-inflammatory drugs ulcerogenic in the short term? Drugs 1992;44(Suppl 5):38–41.

[81] Kenny GNC. Potential renal, haematological and allergic adverse effects associated with nonsteroidal anti-inflammatory drugs. Drugs 1992;44(Suppl 5):31–7.

[82] Feldman HI, Kinman JL, Berlin JA, et al. Parenteral ketorolac: the risk for acute renal failure. Ann Intern Med 1997;126:193–9.

[83] Strom BL, Berlin JA, Kinman JL, et al. Parenteral ketorolac and risk of gastrointestinal and operative site bleeding. J Am Med Assoc 1996;275:376–82.

[84] Camu F, Lersberghe CV, Lauwers MH. Cardiovascular risks and benefits of perioperative nonsteroidal anti-inflammatory drug treatment. Drugs 1992;44(Suppl 5):42–51.

[85] Claxton AR, McGuire G, Chung F, et al. Evaluation of morphine versus fentanyl for postoperative analgesia after ambulatory surgical procedures. Anesth Analg 1997;84:509–14.

[86] Litman RS, Shapiro BS. Oral patient-controlled analgesia in adolescents. J Pain Symp Manag 1992;7:78–81.

[87] Sunshine A, Olson NZ, Rivera J, et al. Analgesic efficacy of controlled-release oxycodone in postoperative pain. J Clin Pharmacol 1996;36:595–603.

[88] Koffer H, Hilderbrand JRI, Connell ML. Potential for nonnarcotic analgesics to save personnel costs associated with controlling injectable morphine and meperidine. Am J Hosp Pharm 1990;47:1084–8.

[89] Ashburn MA, Lind GH, Gillie MH, et al. Oral transmucosal fentanyl citrate (OTFC) for the treatment of postoperative pain. Anesth Analg 1993;76:377–81.

[90] Vercauteren M, Boeckx E, Hanegreefs G, et al. Intranasal sufentanil for preoperative sedation. Anaesthesia 1988;43:270–3.

[91] Striebel WH, Malewicz J, Hermanns K, et al. Intranasal meperidine titration for postoperative pain relief. Anesth Analg 1993;76:1047–51.

[92] Striebel HW, Pommerening J, Rieger A. Intranasal fentanyl titration for postoperative pain management in an unselected population. Anaesthesia 1993;48:753–7.

[93] Holley FO, van Steennis C. Postoperative analgesia with fentanyl: pharmacokinetics and pharmacodynamics of constant-rate i.v. and transdermal delivery. Br J Anaesth 1988;60:608–13.

[94] Sebel PS, Barrett CW, Kirk CJC, et al. Transdermal absorption of fentanyl and sufentanil in man. Eur J Clin Pharmacol 1987;32:529–31.

[95] Ashburn MA, Stephen RL, Ackerman E, et al. Controlled iontophoretic delivery of morphine HCL for postoperative pain relief. J Pain Symp Manag 1992;7:27–33.

[96] Striebel HW, Oelmann T, Spies C, et al. Patient-controlled intranasal analgesia: a method for noninvasive postoperative pain management. Anesth Analg 1996;83:548–51.

[97] Segerdahl M, Ekblom A, Sandelin K, et al. Peroperative adenosine infusion reduces the requirements for isoflurane and postoperative analgesics. Anesth Analg 1995;80:1145–9.

[98] Reuben SS, Connelly NR. Postoperative analgesia for outpatient arthroscopic knee surgery with intraarticular bupivacaine and ketorolac. Anesth Analg 1995;80:1154–7.

[99] Cook TM, Tuckey JP, Nolan JP. Analgesia after day-case knee arthroscopy: double-blind study of intra-articular tenoxicam, intra-articular bupivacaine and placebo. Br J Anaesth 1997;78:163–8.

[100] Brandt KD, Slowman-Kovacs S. Nonsteroidal antiinflammatory drugs in treatment of osteoarthritis. Clin Orthop 1986;213:84–91.

[101] Yang LC, Chen L-M, Wang C-J, et al. Postoperative analgesia by intraarticular neostigmine in patients undergoing knee arthroscopy. Anesthesiology 1998;88:334–9.

[102] White PF. Subcutaneous-PCA: an alternative to IV PCA for postoperative pain management. Clin J Pain 1990;6:297–300.

[103] Goldstein ET, Williamson PR, Larach SW. Subcutaneous morphine pump for postoperative hemorrhoidectomy pain management. Dis Colon Rectum 1993;36:439–46.

[104] Rawal N, Axelsson K, Hylander J, et al. Postoperative patient-controlled local anesthetic administration at home. Anesth Analg 1998;86:86–9.

[105] Carapeti EA, Kamm MA, McDonald PJ, et al. Double-blind randomised controlled trial of effect of metronidazole on pain after day-case haemorrhoidectomy. Lancet 1998;351:169–72.

[106] Guard BC, Wiltshire SJ. The effect of glycopyrrolate on postoperative pain and analgesic requirements following laparoscopic sterilisation. Anaesthesia 1996;51:1173–5.