Optimal Analgesia During Major Open and Laparoscopic Abdominal Surgery

William J. Fawcett, MB BS, FRCA, FFPMRCA[a,b,*],
Gabriele Baldini, MD, MSc[c]

KEYWORDS

- Analgesia • Opioids • Local anesthetic • Acetaminophen
- Antiinflammatory agents • Alpha-2 agonists • Anticonvulsants
- *N*-Methyl-D-aspartate (NMDA) receptor antagonist

KEY POINTS

- Analgesia is a key element of enhanced recovery after surgery (ERAS) programs, particularly following abdominal surgery.
- Multimodal opioid-sparing analgesia is a cornerstone of all analgesic regimens, especially with the use of regular acetaminophen and antiinflammatories.
- Thoracic epidural analgesia is the principal technique for open surgery, but not for laparoscopic surgery, in which intrathecal or more peripherally placed local anesthetic (trunk blocks or wound blocks) is used.
- Several other adjuvants are described but evidence is less strong.
- Interest is growing in the potential for analgesic regimens affecting not only short-term benefits but also longer-term benefits, including rates of cancer recurrence.

INTRODUCTION

Analgesia plays a pivotal role in the management of patients undergoing open or laparoscopic abdominal surgery. Although the relief of pain is one of the most fundamental humanitarian roles for all health care professionals treating patients undergoing surgery, there is now a greater understanding of how this interacts with patient recovery. It has long been recognized that a good analgesic regimen permits not only patient comfort but also facilitates other benefits such as early mobilization and enteral feeding. In the last 20 years, fast-track surgery has evolved into the enhanced recovery after

[a] Department of Anaesthesia, Royal Surrey County Hospital, Egerton Road, Guildford GU2 7XX, UK; [b] Faculty of Health and Medical Sciences, Duke of Kent Building, University of Surrey, Guildford GU2 7TE, UK; [c] Department of Anesthesia, McGill University Health Centre, Montreal General Hospital, 1650 Avenue Cedar, Montreal, Quebec H3G 1A4, Canada
* Corresponding author. Department of Anaesthesia, Royal Surrey County Hospital, Egerton Road, Guildford GU2 7XX, UK.
E-mail address: wfawcett@nhs.net

Anesthesiology Clin 33 (2015) 65–78
http://dx.doi.org/10.1016/j.anclin.2014.11.005 **anesthesiology.theclinics.com**
1932-2275/15/$ – see front matter

surgery (ERAS) program. Pivotal in the philosophy of ERAS is a reduction in the physiologic stress response to surgery and the associated catabolic response. In addition, there is growing evidence to suggest that patients on ERAS have reduced complications following surgery, which affects not only immediate survival but also long-term survival.[1] Although there are many elements to ERAS,[2] analgesic technique plays a large part. In addition, there is interest currently in how anesthetic technique in general, and analgesic technique in particular, may directly affect cancer outcome[3] by modulating immune function. This effect has been shown for breast and prostate surgery[4] but not so far for colorectal surgery.[5] This possibility is particularly relevant for this group of patients, many of whom are undergoing surgery for cancer.

Thus pain medicine has come a long way: correctly administered, it may not only give great relief to patients but may permit rapid return to normal activities and perhaps improve patients' long-term survival through reduction in early postoperative complications.[1,6]

More than 20 years ago, Kehlet and Dahl[7] described multimodal opioid-sparing analgesia, which is the cornerstone of the management of patients undergoing abdominal surgery. Using analgesic techniques acting via different mechanisms, side effects may be minimized and opioid consumption may be reduced. Although some opioid usage may be unavoidable, excess usage leads to a host of undesirable adverse effects: respiratory and cough suppression, postoperative nausea and vomiting (PONV), urinary retention, and delayed return of gastrointestinal (GI) function (**Box 1**). Following major abdominal surgery, the combination of these effects impairs the achievement of important ERAS milestones (**Fig. 1**) and can even be catastrophic; for example, hypoventilation, obtunded respiratory reflexes, and gastric stasis can predispose to passive regurgitation and pulmonary aspiration.

The most significant advance for patients undergoing GI surgery in the last 10 years has been the shift from open to laparoscopic surgery. There is a good evidence base for analgesia for the former, but the optimum analgesic modality for the latter is still debated.[8]

In addition, providing the best and safest analgesia requires more than a prescription. It is essential that regular postoperative input occurs from staff (usually specialist pain nurses) who assess the patients, monitor pain scores, and take appropriate action to relieve pain and treat any ensuing complications (such as hypotension).

OPIOID ANALGESIA

The use of morphine is not viewed as the gold standard for analgesia but has still become the gold standard for comparisons of effectiveness for practically all other

Box 1
Side effects of morphine

- Reduced gastrointestinal motility, leading to ileus
- Nausea and vomiting
- Cough suppression
- Respiratory depression with reduced sensitivity to $Paco_2$
- Urinary retention
- Euphoria, dysphoria, hallucination
- Histamine release (may cause itching, hypotension, and bronchospasm)
- Bradycardia
- Tolerance (over time)

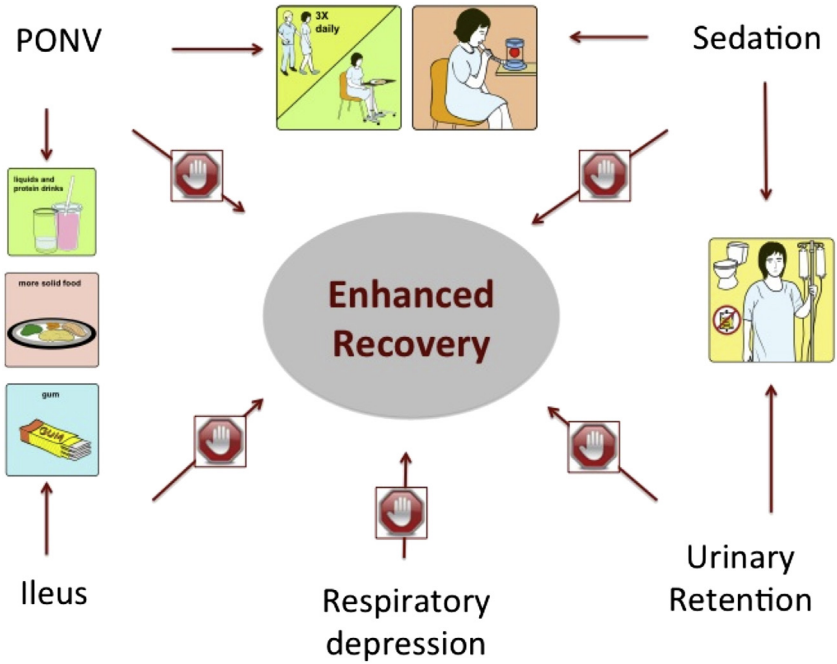

Fig. 1. Avoidance of complications to achieve ERAS.

methods of analgesia. However, for abdominal surgery, the mere mention of parenteral opioids such as morphine can produce an irrational fear. Whilst minimizing their use is desirable, that does not mean that their use has to be avoided. Leaving patients in unrelieved pain is not acceptable and opioids should be available as rescue analgesia if other methods fail. Moreover, early and limited use of morphine has little effect on outcome.[9] The use of short-acting opioids such as fentanyl in neuraxial block is discussed later. In addition because of its constipating effects, many providers avoid the use of oral moderate opioids, such as codeine, although drugs such as tramadol acting via opioid and other mechanisms (such as inhibition of reuptake of serotonin and norepinephrine) are used. In addition, in the last 5 years there has been an increasing debate about the relevance of opioid-induced hyperalgesia (OIH), in which there is a paradoxic effect from high-potency opioids (eg, perioperative remifentanil), and further opioid administration increases rather than reduces pain perception. OIH is a complex area and seems to be multifactorial, including both central and peripheral changes in nociceptive processing, the former involving *N*-methyl-D-aspartate (NMDA) receptors (discussed later), as well as genetic influences. The magnitude of the problem, including the patient's susceptibility, and potential treatments await further studies.[10,11]

If morphine is used it is often because other methods have failed. It is probably best administered intravenously as patient-controlled analgesia (PCA), permitting good control of pain in the early postoperative period, but with good knowledge of its side effects.

LOCAL ANESTHETIC TECHNIQUES

Epidural Analgesia

The mainstay of analgesia for GI surgery has been the thoracic epidural. There are several well-documented advantages (**Box 2**) but more recently its problems have

Box 2
Advantages of epidurals

- Attenuation of some aspects of the stress response
  - Neuroendocrine (sympathetic and pituitary activation)
  - Metabolic (eg, hyperglycemia, protein breakdown)
  - But no effect on inflammatory changes mediated by cytokines
- Improvement in pulmonary function
  - Reduced incidence of postoperative hypoxia
  - Reduced incidence of atelectasis and infection
- GI
  - Reduced ileus
  - Earlier return to diet
- Reduction in pulmonary thromboembolism
- Reduction in blood loss
- Some studies have shown reduction in myocardial infarction, renal failure, and mortality

been highlighted (**Box 3**). It is still considered the gold standard for open surgery, but for laparoscopic surgery there is less evidence to support its use and many clinicians have moved on to less invasive methods.

For open surgery, the placement of an epidural catheter for postoperative infusion is a straightforward theoretic concept and, when functioning optimally, provides superlative segmental analgesia for the first 48 to 72 hours. However, there are several areas that need to be addressed in this process:

Box 3
Disadvantages of epidurals

- Epidural failure
  - Wrong site (eg, lumbar and not thoracic)
  - Catheter not in epidural space (or migrated)
  - Inadequate drug dosages
- Hypotension
- Poor mobility
  - Motor block (especially with lumbar epidurals)
  - Sensory block
  - Hypotension
- Neurologic damage (temporary or permanent)
  - Space-occupying lesion of vertebral canal
  - Wrong drug injected
  - Direct trauma at insertion
- Dural puncture

1. Epidural positioning: the epidural needs to be placed appropriately for the type of surgery. Lumbar epidurals much less desirable because of their higher incidence of leg weakness.
2. The insertion technique used is important: the paramedian has been described as having advantages compared with the midline in terms of ease of identification of the epidural space and placement of the catheter with less paresthesia, but personal preference plays a large part in the technique used.
3. The drugs used. Local anesthetic alone was classically used, but in order to reduce excessive sympathetic and motor blockade and improve the quality of analgesia various other drugs have been added to the local anesthetic. These drugs include opioids (most commonly[12]) but also other adjuvants such as epinephrine or alpha-2 agonists (discussed later).
4. The postoperative management is fundamental in terms of titrating the epidural infusion and dealing with side effects, in particular hypotension and leg weakness (discussed later).
5. Contraindications to the insertion of an epidural catheter most commonly involve abnormalities of coagulation; historically thrombocytopenia and an increased International Normalized Ratio (INR) resulting from warfarin. Although there are no absolute agreed figures, many clinicians are reluctant to site an epidural with a platelet count of less than 75×10^9/L or an INR of greater than 1.4. However, many coagulation-modifying drugs are used, including heparin (both unfractionated heparin and low-molecular-weight heparin), antiplatelet drugs (aspirin, thienopyridines, and glycoprotein IIb/IIIa receptor inhibitors), and the new oral anticoagulants (such as rivaroxaban and dabigatran) and thrombolytic drugs. Many of these drugs have no accepted laboratory test to confirm return of normal coagulation, have no antidote, and require knowledge of when the last dose was administered and in some cases (eg, rivaroxaban and dabigatran) renal function as well. However, there is no absolute evidence based on large studies confirming when it is safe to insert epidurals (vertebral canal hematomas are rare). Based on international guidelines and recommendations,[13,14] a suggested protocol is given in **Table 1**.

Poorly managed epidurals have potential to cause great harm and the management of their side effects and complications is paramount.

1. Poorly working or nonworking epidurals are common (up to 50% in some studies) and have recently been reviewed.[15] Patients are often denied other forms of analgesia (eg, systemic opioids) because of concern of causing respiratory depression and compounding the situation. Early identification of a nonworking epidural (primary failure) is essential to avoid returning patients to the ward with an ineffective analgesic modality. Effectiveness of epidural analgesia must be verified soon after the epidural catheter is placed, and ideally before the beginning of surgery or in the postanesthesia care unit. The problem then needs to be swiftly addressed by increasing the epidural rate, adding an adjuvant drug (eg, an epidural opioid), reinserting the epidural, or removing it and instituting an alternative analgesic regime, such as PCA morphine (**Fig. 2**).
2. Hypotension may commonly occur, caused by vasodilatation from sympathectomy, fluid depletion, or a combination of the two. Although the treatment of the fluid depletion is carefully titrated fluid management, the sympathectomy is more difficult to treat. There may be an early response to intravenous fluids but the effect may be transient and can result in excessive fluid administration, predisposing to edema, which is highly undesirable in both the lungs and any bowel anastomosis,

Table 1
Insertion of epidurals in patients receiving coagulation-modifying therapy

Drug Class	Safe to Insert Once Stopped	Comments
Heparin (unfractionated) prophylaxis dose	>4 h	Can confirm with normal APTT too
Heparin (fractionated) prophylaxis dose	>12 h	—
Heparin (fractionated) treatment dose	>24 h	—
Aspirin/dipyridamole	No precautions required	Irreversible platelet inhibition
Thienopyridines* (eg, clopidogrel)	1 wk	Irreversible platelet inhibition
Glycoprotein IIb/IIIa* inhibitors (eg, abciximab)	48 h	—
Warfarin	4–5 d	Check INR <1.4
Factor Xa inhibitors* (eg, rivaroxaban)	At least 24–48 h	Longer in elderly and/or reduced renal function
Thrombolytic drugs (eg, streptokinase)	10 d	—

Abbreviation: APTT, activated partial thromboplastin time.
* The times quoted are for the specific drugs mentioned. Other drugs in that drug class may have different durations of action.

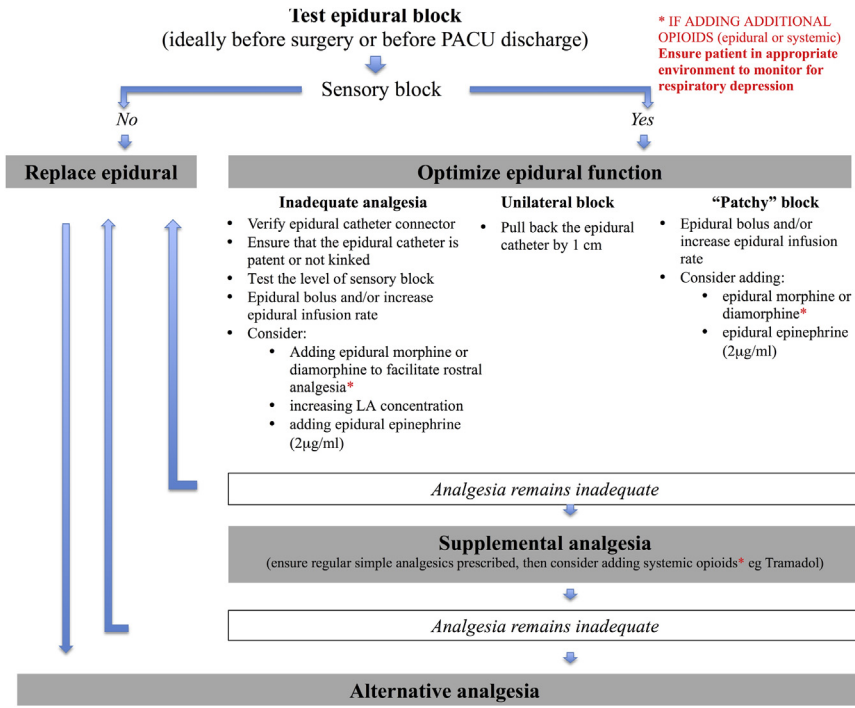

Fig. 2. Epidural analgesia: troubleshooting. PACU, postanesthesia care unit.

particularly if the epidural (and sympathectomy) is then stopped and there is further relative fluid overload as vascular tone begins to increase while the intravascular volume remains unchanged. A more logical approach is the use of vasoactive drugs to maintain perfusion pressure to the anastomosis,[16] but this requires the patient to be nursed in a more intensive environment (eg, critical care or high-dependency unit).

3. A catastrophic complication is vertebral canal and spinal cord compression from hematoma or abscess and its early recognition and management is of paramount importance. This condition usually presents with leg weakness and back pain. The epidural needs to be stopped immediately and, if there is no resolution of leg weakness, urgent imaging of the spine is required, with urgent spinal decompression required to prevent neurologic injury. It is paramount that good training and monitoring for this complication is in place.[17]
4. Accidental dural puncture should be a rare occurrence (0.5%) with appropriate training and skill. It can cause a severe postdural puncture headache and, rarely, more serious complications, including subdural hematoma. Severe postdural puncture headache is usually treated by autologous blood patching; commonly required in obstetric patients but much rarer in older patients undergoing major abdominal surgery.

Epidural analgesia has a considerable evidence base to support its use for open surgery. There is little to support its use on laparoscopic surgery,[8] for which it is regarded as unnecessary and even prolonging length of hospital stay (LOS),[9] although we consider the use of a thoracic epidural for patients having laparoscopic surgery who are at high risk for pulmonary complications, because epidurals may have a place in reducing these complications.[18] Another difficult issue from a practical standpoint is the unexpected prolonged laparoscopic cases or conversion to open surgery, for which an epidural may need to be sited postoperatively, with perhaps extra risks and/or issues with consent.

Intrathecal Analgesia

Intrathecal or spinal analgesia has functional similarities to epidural analgesia, but because it invariably involves a single-shot injection into the cerebrospinal fluid (rather than catheter placement) its duration of action is limited and its use is thus generally unsuitable for major open abdominal surgery. It is more logical for laparoscopic surgery, for which wound pain relief requirements are more modest, with many anesthesiologists having gained experience in intrathecal analgesia from other types of surgery (eg, cesarean sections). It also has a rapid onset of action, particularly the sympathetic blockade, which can be profound in the elderly, in the presence of hypovolemia, or with positioning the patient head down.

As with epidurals, a combination of local anesthetic (either hypobaric plain bupivacaine or hyperbaric bupivacaine) with an opioid (such as fentanyl, diamorphine, or morphine) is traditionally used. Some clinicians have tried shorter-acting local anesthetics (such as prilocaine) or adjuvants such as clonidine to enhance the quality of block and minimize side effects. In addition, similar contraindications for intrathecal analgesia and epidural analgesia exist, although given that spinals are more than 2.5 times as safe as epidurals for serious sequelae[17] (perhaps related to the smaller size of a spinal needle and the absence of passing a catheter) there is a more relaxed view of intrathecal analgesia compared with epidural analgesia in the presence of a coagulopathy.

The major side effect is hypotension, which can be rapid in onset and at times profound, and many clinicians choose to use intraoperative arterial access with invasive

blood pressure transducing perioperatively. Vasopressors and/or sympathomimetics should always be at hand.

Outcomes

Evidence for spinal anesthesia in laparoscopic surgery over the last 5 years has increased. There are several studies confirming its safety efficacy both for 23-hour-stay surgery[19] and also its superiority compared with epidural analgesia, with a marked opioid-sparing effect and rapid return to GI function and reduced LOS.[9] Other clinicians have found less consistent results, albeit with better analgesia and reduced LOS, with either no effect on return to gut function and PONV[20] or with excessive respiratory depression with spinal morphine in the elderly.[21] There is little to support its use following prolonged laparoscopic or open surgery because the analgesia may have started to subside before the end of surgery. However, although it is regarded as a safer technique than epidural analgesia, it has risks and many clinicians think that even spinal analgesia may not be warranted in the future for laparoscopic surgery.

LOCAL ANESTHETIC DRUGS ADMINISTERED PERIPHERALLY

Although the use of local anesthetics administered centrally (eg, epidural or intrathecal) is effective, hypotension and reduced mobility are common and the potential for harm is great. Administering local anesthetics more peripherally on the pain pathway, such as with transversus abdominis plane (TAP) blocks, rectus sheath blocks, intraperitoneal instillation, and wound catheters, is considered safer in this regard. However, some of the techniques use large amounts of local anesthetic and the risk of high plasma levels of local anesthetic and the concomitant cardiac toxicity and neurotoxicity should not be underestimated. The location of lipid emulsion in clinical areas and knowledge of its administration to treat local anesthetic toxicity should be readily to hand.

TAP blocks were popularized nearly 10 years ago and have a growing evidence base to support their use. Local anesthetic is instilled between internal oblique and transversus abdominis muscles, preferably using ultrasonography. A blind technique was originally used, using a double-pop technique as a blunted needle passes through the external and internal oblique muscles. The needle is inserted in the lumbar triangle of Petit, the borders of which are the external oblique muscle anteriorly, the latissimus dorsi muscle posteriorly, and the iliac crest inferiorly. A large volume (20 mL) of local anesthetic provides block of the T10 to L1 dermatomes, and covers incision for specimen and some port sites. TAP blocks have been used in open and laparoscopic surgery, for which reductions in pain scores and morphine use (in the first 24 hours), time to tolerating diet, PONV, and LOS have been described.[22–24] Results from recent meta-analysis showed that preoperative TAP blocks provide greater analgesia than postoperative TAP blocks.[25] It is generally safe, although liver trauma has been described with inexpert clinicians.[26] Laparoscopy-guided TAP block has also been successfully used recently.[25,27,28] Subcostal TAP blocks are performed to provide analgesia in the upper quadrants of the abdominal wall.[29,30] The analgesic efficacy of TAP blocks can be prolonged by intermittent boluses or continuous infusion of local anesthetic through multihole catheters placed between the internal oblique and transversus abdominis muscle.[31–33]

Rectus sheath blocks have also used but the evidence base is mainly for gynecologic and urologic surgery and pediatric hernias. Like TAP blocks, they can be inserted by a loss of resistance or ultrasonography, although the surgeon can also insert them

under direct vision. A catheter is commonly left in situ and local anesthetic can be administered either by bolus dosing or via infusion.

Wound catheters or surgical site analgesia have also been described for open surgery. These devices are multihole catheters placed in the preperitoneal space during layered closure, following which local anesthetic is administered via bolus or preferably by infusion for 48 hours or so.

The analgesic efficacy of these techniques has been compared with patients receiving systemic opioids, and recently with patients receiving thoracic epidural analgesia.[34,35] Results are varied, with Bertoglio and colleagues[34] reporting similar pain scores but less PONV and accelerated return of bowel function and reduced LOS compared with the epidural group, although these findings were not repeated in a later study by Jouve and colleagues.[35] Concerns of an increased wound infection rate seem to be unsubstantiated.

Intraperitoneal Local Anesthetic

Administering local anesthetic directly into the peritoneum was first described for open procedures more than 60 years ago but interest in this technique has been rekindled more recently for laparoscopic procedures such as gastric surgery, cholecystectomy, colonic resection, and gynecologic procedures. It is a promising technique, using 20 mL of 0.5% bupivacaine, and reductions in pain, morphine consumption, shoulder pain, and stress response activation have been described.[36,37]

SYSTEMIC ANALGESICS

In the quest to reduce systemic morphine consumption, several drugs with little or no opioid action have been successfully used.

Acetaminophen (Paracetamol)

Acetaminophen has been used for more than 125 years and is used worldwide with an excellent safety record, although hepatotoxicity, resulting from altered metabolism or prescription errors, has been recorded. Issues relating to variable bioavailability (particularly when administered rectally) have been solved with widespread use of an intravenous preparation, particularly valuable for GI patients who are unable to take medication orally. It is commonly used regularly for both open and laparoscopic surgery for 48 hours and has a good opioid-sparing effect. The maximum dose is 1 g 4 times per day for patients weighing more than 50 kg. There is some evidence to support a 2-g loading dose, with better pain relief and no increase in toxicity.

Antiinflammatory Drugs

The cyclooxygenase (COX) inhibitors are usually subdivided according to whether they are nonselective (ie, inhibit both the constitutive COX-1 isoform and the inducible COX-2 isoforms) or whether they inhibit principally the COX-2 isoform. Both drugs are commonly used, although care is required in the use of these drugs in patients with cardiac and cerebrovascular disease because of increased risk of thrombotic events. A more specific concern for GI patients is the increased risk of anastomotic leakage reported with both nonselective COX inhibitors (eg, diclofenac)[38] and COX-2 inhibitors after colonic surgery,[39] with a recent study suggesting that nonselective COX inhibitors were more likely to be implicated.[40] However, these drugs are still widely used, but their potential detrimental effects on healing, both in GI surgery and in other surgery (orthopedics), has led to reluctance by some clinicians to use these agents.

Intravenous Lidocaine

Intravenous lidocaine as an analgesic was described more than 50 years ago and has recently been reintroduced. A dose of 1.5 to 2 mg/kg is typically given before the surgical incision and then 1.5 to 2 mg/kg for up to 24 hours postoperatively, usually in a critical care or high-dependency environment. It has several beneficial effects apart from reducing opioid requirements (by up to two-thirds): there is a reduced duration of PONV, ileus, and hospital stay.[41,42] In addition, there are other systemic effects, such as reduced stress response as measured by total leukocyte count, C-reactive protein, and interleukin-6 (IL-6),[43] and possibly an anticancer effect too.[44] Many of these effects seem to be more marked for open surgery. There is good evidence to support its use, particularly as a second-line drug, and it is perhaps surprising that it is not more commonly used, although caution is urged concerning its safety given that some studies have observed toxic levels and others did not look for signs of toxicity.[41] Furthermore, its use in the postoperative period is limited because continuous cardiovascular monitoring is required.

Gabapentinoids (Gabapentin and Pregabalin)

These agents, which are familiar to chronic pain physicians, are now increasingly used for postoperative pain, with patients benefiting from reduced pain, opioid sparing, and a reduction in PONV. There is more evidence to support gabapentin because it is an older drug, but pregabalin has a better pharmacokinetic profile. There are many areas of debate, such as the dose and duration perioperatively, and perhaps most importantly how they affect the incidence of the progression to chronic pain syndromes. Common side effects include sedation and dizziness, and visual disturbances in the case of pregabalin, and these will probably limit their widespread clinical usefulness. A single dose of pregabalin 150 to 300 mg preoperatively is commonly used, but side effects are more common at the higher dose.[45,46]

N-Methyl-d-Aspartate Receptor Antagonists (Ketamine and Magnesium)

NMDA glutamate receptor activation is involved in several aspects of acute pain, including acute tolerance and hyperalgesia with central sensitization. Several drugs are antagonists at these excitatory receptors, including ketamine and magnesium, and both have been used to provide analgesia. Many anesthesiologists are more familiar with ketamine and its analgesic actions. NMDA glutamate receptor activation has been used to provide postoperative pain in several ways: mixed with morphine PCA (which has a more beneficial action for chest rather than abdominal surgery),[47] and also given intraoperatively, both as a bolus and infusion. As with the anticonvulsants agents, the optimal timing, dose, and duration is undecided, but when given at low doses (2 μg/kg/min after a 0.5-mg/kg bolus) morphine consumption was halved and the expected side effects, such as sedation, delusions, nightmares, and psychiatric disorders, were not an issue at these doses.[48] It also reduced the inflammatory response, as measured by IL-6.[49] Magnesium also has a documented place as an analgesic, but its other effects, such as potentiation of neuromuscular blockade and effects on cardiac conduction, will probably limits its use.[50]

Alpha-2 Agonists (Clonidine, Dexmedetomidine)

These agents reduce sympathetic outflow and norepinephrine release within the central and peripheral nervous systems, which has a multitude of effects including inhibiting pain pathways (and release of substance P). There are predictable side effects from their action and the Perioperative Ischemic Evaluation-2 trial highlighted

these,[51] showing that clonidine was associated with significant excess in clinically significant hypotension, bradycardia, and (nonfatal) cardiac arrest. These side effects, as well as a lack of good-quality data on these agents, are sure to limit its usefulness, with optimum dose, timing, and routes of administration remaining largely unknown.

Peripheral Opioid Antagonists

Drugs such as alvimopan (a peripherally acting μ-opioid receptor antagonist) antagonize the peripheral adverse effects of opioids (eg, constipation), with the central analgesic effects unaffected. A few trials have shown benefit in open surgery, with reductions in time taken for return of GI function and LOS, but further work is needed to determine the usefulness of this approach, including its impact in laparoscopic surgery and cost-benefit analyses.[52]

Glucocorticoids

These agents, which are often used as perioperative antiemetics, have other actions too, including mild opioid-sparing effects,[53] reductions in length of stay, and modifications of the stress response, apparently without increasing complications (such as anastomotic leak). Further studies are underway to define their place within ERAS for abdominal surgery.[54]

SUMMARY

There are a multitude of analgesic techniques described and the combinations are therefore many. For open surgery, a thoracic epidural for 48 to 72 hours, with regular acetaminophen and antiinflammatories, is probably the treatment of choice provided there are no contraindications. For laparoscopic surgery, either intrathecal or local anesthesia in the wound combined with regular acetaminophen and antiinflammatory drugs is effective. If epidurals fail or are not used for open surgery, the best evidence is for intravenous lidocaine. For many of the other techniques described there is a weaker body of supporting evidence, but they are often used where local expertise has developed. Readers are directed to the PROSPECT (Procedure-specific Postoperative Pain Management) Web site at http://www.postoppain.org/ for the most recent evidence-based recommendations. Analgesia has come a long way from the immediate relief of postoperative pain: clinicians are now starting to determine how it may not only affect short-term outcome but may have a variety of effects on long-term outcome, including survival after major cancer surgery.[6]

REFERENCES

1. Khuri SF, Henderson WG, DePalma RG, et al. Determinants of long-term survival after major surgery and the adverse effect of postoperative complications. Ann Surg 2005;242(3):326–41 [discussion: 341–3].
2. Fearon KC, Ljungqvist O, Von Meyenfeldt M, et al. Enhanced recovery after surgery: a consensus review of clinical care for patients undergoing colonic resection. Clin Nutr 2005;24(3):466–77.
3. Snyder GL, Greenberg S. Effect of anaesthetic technique and other perioperative factors on cancer recurrence. Br J Anaesth 2010;105(2):106–15.
4. Myles PS, Peyton P, Silbert B, et al. Perioperative epidural analgesia for major abdominal surgery for cancer and recurrence-free survival: randomised trial. BMJ 2011;342:d1491.

5. Day A, Smith R, Jourdan I, et al. Retrospective analysis of the effect of postoperative analgesia on survival in patients after laparoscopic resection of colorectal cancer. Br J Anaesth 2012;109(2):185–90.
6. Fawcett WJ, Mythen MG, Scott MJ. Enhanced recovery: more than just reducing length of stay? Br J Anaesth 2012;109(5):671–4.
7. Kehlet H, Dahl JB. The value of "multimodal" or "balanced analgesia" in postoperative pain treatment. Anesth Analg 1993;77(5):1048–56.
8. Levy BF, Tilney HS, Dowson HM, et al. A systematic review of postoperative analgesia following laparoscopic colorectal surgery. Colorectal Dis 2010;12(1):5–15.
9. Levy BF, Scott MJ, Fawcett W, et al. Randomized clinical trial of epidural, spinal or patient-controlled analgesia for patients undergoing laparoscopic colorectal surgery. Br J Surg 2011;98(8):1068–78.
10. Colvin LA, Fallon MT. Opioid-induced hyperalgesia: a clinical challenge. Br J Anaesth 2010;104(2):125–7.
11. Zhao M, Joo DT. Enhancement of spinal N-methyl-D-aspartate receptor function by remifentanil action at delta-opioid receptors as a mechanism for acute opioid-induced hyperalgesia or tolerance. Anesthesiology 2008;109(2):308–17.
12. Finucane BT, Ganapathy S, Carli F, et al. Prolonged epidural infusions of ropivacaine (2 mg/mL) after colonic surgery: the impact of adding fentanyl. Anesth Analg 2001;92(5):1276–85.
13. Gogarten W, Vandermeulen E, Van Aken H, et al. Regional anaesthesia and antithrombotic agents: recommendations of the European Society of Anaesthesiology. Eur J Anaesthesiol 2010;27(12):999–1015.
14. Horlocker TT, Wedel DJ, Rowlingson JC, et al. Regional anesthesia in the patient receiving antithrombotic or thrombolytic therapy: American Society of Regional Anesthesia and Pain Medicine Evidence-Based Guidelines (third edition). Reg Anesth Pain Med 2010;35(1):64–101.
15. Hermanides J, Hollmann MW, Stevens MF, et al. Failed epidural: causes and management. Br J Anaesth 2012;109(2):144–54.
16. Gould TH, Grace K, Thorne G, et al. Effect of thoracic epidural anaesthesia on colonic blood flow. Br J Anaesth 2002;89(3):446–51.
17. Third National Audit Project of the Royal College of Anaesthetists (NAP3): major complications of central neuraxial block. Available at: http://www.rcoa.ac.uk/system/files/CSQ-NAP3-Full_1.pdf. Accessed December 8, 2014.
18. Popping DM, Elia N, Marret E, et al. Protective effects of epidural analgesia on pulmonary complications after abdominal and thoracic surgery: a meta-analysis. Arch Surg 2008;143(10):990–9 [discussion: 1000].
19. Levy BF, Scott MJ, Fawcett WJ, et al. 23-hour-stay laparoscopic colectomy. Dis Colon Rectum 2009;52(7):1239–43.
20. Virlos I, Clements D, Beynon J, et al. Short-term outcomes with intrathecal versus epidural analgesia in laparoscopic colorectal surgery. Br J Surg 2010;97(9):1401–6.
21. Wongyingsinn M, Baldini G, Stein B, et al. Spinal analgesia for laparoscopic colonic resection using an enhanced recovery after surgery programme: better analgesia, but no benefits on postoperative recovery: a randomized controlled trial. Br J Anaesth 2012;108(5):850–6.
22. Zafar N, Davies R, Greenslade GL, et al. The evolution of analgesia in an 'accelerated' recovery programme for resectional laparoscopic colorectal surgery with anastomosis. Colorectal Dis 2010;12(2):119–24.
23. Johns N, O'Neill S, Ventham NT, et al. Clinical effectiveness of transversus abdominis plane (TAP) block in abdominal surgery: a systematic review and meta-analysis. Colorectal Dis 2012;14(10):e635–42.

24. De Oliveira GS Jr, Castro-Alves LJ, Nader A, et al. Transversus abdominis plane block to ameliorate postoperative pain outcomes after laparoscopic surgery: a meta-analysis of randomized controlled trials. Anesth Analg 2014;118(2):454–63.
25. Favuzza J, Delaney CP. Outcomes of discharge after elective laparoscopic colorectal surgery with transversus abdominis plane blocks and enhanced recovery pathway. J Am Coll Surg 2013;217(3):503–6.
26. Lancaster P, Chadwick M. Liver trauma secondary to ultrasound-guided transversus abdominis plane block. Br J Anaesth 2010;104(4):509–10.
27. Favuzza J, Brady K, Delaney CP. Transversus abdominis plane blocks and enhanced recovery pathways: making the 23-h hospital stay a realistic goal after laparoscopic colorectal surgery. Surg Endosc 2013;27(7):2481–6.
28. Keller DS, Stulberg JJ, Lawrence JK, et al. Process control to measure process improvement in colorectal surgery: modifications to an established enhanced recovery pathway. Dis Colon Rectum 2014;57(2):194–200.
29. Niraj G, Kelkar A, Jeyapalan I, et al. Comparison of analgesic efficacy of subcostal transversus abdominis plane blocks with epidural analgesia following upper abdominal surgery. Anaesthesia 2011;66(6):465–71.
30. Wu Y, Liu F, Tang H, et al. The analgesic efficacy of subcostal transversus abdominis plane block compared with thoracic epidural analgesia and intravenous opioid analgesia after radical gastrectomy. Anesth Analg 2013;117(2):507–13.
31. Allcock E, Spencer E, Frazer R, et al. Continuous transversus abdominis plane (TAP) block catheters in a combat surgical environment. Pain Med 2010;11(9):1426–9.
32. Kadam VR, Moran JL. Epidural infusions versus transversus abdominis plane (TAP) block infusions: retrospective study. J Anesth 2011;25(5):786–7.
33. Niraj G, Kelkar A, Hart E, et al. Comparison of analgesic efficacy of four-quadrant transversus abdominis plane (TAP) block and continuous posterior TAP analgesia with epidural analgesia in patients undergoing laparoscopic colorectal surgery: an open-label, randomised, non-inferiority trial. Anaesthesia 2014;69(4):348–55.
34. Bertoglio S, Fabiani F, Negri PD, et al. The postoperative analgesic efficacy of preperitoneal continuous wound infusion compared to epidural continuous infusion with local anesthetics after colorectal cancer surgery: a randomized controlled multicenter study. Anesth Analg 2012;115(6):1442–50.
35. Jouve P, Bazin JE, Petit A, et al. Epidural versus continuous preperitoneal analgesia during fast-track open colorectal surgery: a randomized controlled trial. Anesthesiology 2013;118(3):622–30.
36. Kahokehr A, Sammour T, Shoshtari KZ, et al. Intraperitoneal local anesthetic improves recovery after colon resection: a double-blinded randomized controlled trial. Ann Surg 2011;254(1):28–38.
37. Kahokehr A, Sammour T, Soop M, et al. Intraperitoneal local anaesthetic in abdominal surgery - a systematic review. ANZ J Surg 2011;81(4):237–45.
38. Klein M, Andersen LP, Harvald T, et al. Increased risk of anastomotic leakage with diclofenac treatment after laparoscopic colorectal surgery. Dig Surg 2009;26(1):27–30.
39. Holte K, Andersen J, Jakobsen DH, et al. Cyclo-oxygenase 2 inhibitors and the risk of anastomotic leakage after fast-track colonic surgery. Br J Surg 2009;96(6):650–4.
40. Gorissen KJ, Benning D, Berghmans T, et al. Risk of anastomotic leakage with non-steroidal anti-inflammatory drugs in colorectal surgery. Br J Surg 2012;99(5):721–7.

41. Vigneault L, Turgeon AF, Cote D, et al. Perioperative intravenous lidocaine infusion for postoperative pain control: a meta-analysis of randomized controlled trials. Can J Anaesth 2011;58(1):22–37.
42. Sun Y, Li T, Wang N, et al. Perioperative systemic lidocaine for postoperative analgesia and recovery after abdominal surgery: a meta-analysis of randomized controlled trials. Dis Colon Rectum 2012;55(11):1183–94.
43. Sridhar P, Sistla SC, Ali SM, et al. Effect of intravenous lignocaine on perioperative stress response and post-surgical ileus in elective open abdominal surgeries: a double-blind randomized controlled trial. ANZ J Surg 2014. [Epub ahead of print].
44. Lirk P, Berger R, Hollmann MW, et al. Lidocaine time- and dose-dependently demethylates deoxyribonucleic acid in breast cancer cell lines in vitro. Br J Anaesth 2012;109(2):200–7.
45. Ramaswamy S, Wilson JA, Colvin L. Non-opioid-based adjuvant analgesia in perioperative care. Cont Educ Anaesth Crit Care Pain 2013;13:152–7.
46. Zhang J, Ho KY, Wang Y. Efficacy of pregabalin in acute postoperative pain: a meta-analysis. Br J Anaesth 2011;106(4):454–62.
47. Carstensen M, Moller AM. Adding ketamine to morphine for intravenous patient-controlled analgesia for acute postoperative pain: a qualitative review of randomized trials. Br J Anaesth 2010;104(4):401–6.
48. Zakine J, Samarcq D, Lorne E, et al. Postoperative ketamine administration decreases morphine consumption in major abdominal surgery: a prospective, randomized, double-blind, controlled study. Anesth Analg 2008;106(6):1856–61.
49. Dale O, Somogyi AA, Li Y, et al. Does intraoperative ketamine attenuate inflammatory reactivity following surgery? A systematic review and meta-analysis. Anesth Analg 2012;115(4):934–43.
50. Fawcett WJ, Haxby EJ, Male DA. Magnesium: physiology and pharmacology. Br J Anaesth 1999;83(2):302–20.
51. Devereaux PJ, Sessler DI, Leslie K, et al. Clonidine in patients undergoing noncardiac surgery. N Engl J Med 2014;370(16):1504–13.
52. Vaughan-Shaw PG, Fecher IC, Harris S, et al. A meta-analysis of the effectiveness of the opioid receptor antagonist alvimopan in reducing hospital length of stay and time to GI recovery in patients enrolled in a standardized accelerated recovery program after abdominal surgery. Dis Colon Rectum 2012;55(5):611–20.
53. Waldron NH, Jones CA, Gan TJ, et al. Impact of perioperative dexamethasone on postoperative analgesia and side-effects: systematic review and meta-analysis. Br J Anaesth 2013;110(2):191–200.
54. Srinivasa S, Kahokehr AA, Yu TC, et al. Preoperative glucocorticoid use in major abdominal surgery: systematic review and meta-analysis of randomized trials. Ann Surg 2011;254(2):183–91.