Review Article

Analgesia for enhanced recovery after surgery in laparoscopic surgery

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Abstract: Effectual analgesia is one of the essential cornerstones of enhanced recovery after surgery (ERAS) programmes and indeed all anaesthetic care. It is a vital element in reducing the surgical stress response, encouraging a return to normal functions—breathing, eating, sleeping—early mobilisation and for basic humane reasons. Opioid usage is associated with side effects including postoperative nausea and vomiting, constipation, ileus, pruritis, delirium, urinary retention and respiratory depression along with a potential to cause chronic dependence. The avoidance of opioids is associated with earlier mobilisation, return of bowel function and a reduced length of stay, leading to a preference for multimodal analgesia. While laparoscopic surgical techniques have been shown to reduce the intensity of postoperative pain when compared to open surgery, pain after laparoscopic surgery can be due to a myriad of factors. This article will give an overview of the best practice choices available. Multimodal analgesia aims to reduce the side effects of individual analgesics whilst still providing adequate analgesia by using a combination of pharmacological mechanisms. Basic analgesics include paracetamol and non-steroidal anti-inflammatory drugs (NSAIDs) with other non-opioid systemic agents include lidocaine, alpha-2-agonists (dexmedetomidine and clonidine), ketamine, magnesium, gabapentinoids and dexamethasone. Local anaesthetic administration can provide analgesia in a variety of ways. This includes neuraxial blockade (spinal or epidural), regional nerve blocks [including transversus abdominis plane (TAP) blocks], wound catheter local anaesthetic infusions as well as direct local infiltration. Spinal anaesthetics are a superior alternative to epidurals for laparoscopic surgery given the good analgesia, quick delivery, limited duration and moderate attenuation of the stress response alongside lower complication rate. Analgesia is one of the cornerstones of ERAS pathways and anaesthetic practice in general. The general consensus is that a multimodal approach is best, to ensure sparing of opioids. This can involve the use of both systemic analgesia and local anaesthetics.

Keywords: Analgesia; enhanced recovery after surgery (ERAS); multimodal; local; opioid

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Introduction

Effectual analgesia is one of the essential cornerstones of enhanced recovery after surgery (ERAS) programmes and indeed all anaesthetic care. It is a vital element in reducing the surgical stress response, encouraging a return to normal functions—breathing, eating, sleeping—early mobilisation and for basic humane reasons (1). It may also help towards reduced organ dysfunction and earlier hospital discharge (2). One of the cornerstones of analgesic practice is multimodal analgesia in order to reduce the requirement for opioids peri-operatively. Opioid usage is associated with a variety

of acute side effects including postoperative nausea and vomiting, constipation, ileus, pruritis, delirium, urinary retention and respiratory depression (3). Postoperative opioid usage is also associated with chronic dependence (4) and opioid overdose has become the leading cause of accidental death in the USA (3). While different surgeries can vary in their technique and trauma, the avoidance of opioids is associated with earlier mobilisation, return of bowel function and a reduced length of stay and so a multimodal analgesia regime is favored (5-8).

Minimally-invasive and laparoscopic surgical techniques have been shown to reduce the intensity of postoperative pain when compared to open surgery and, in turn, have reduced analgesic requirements (9,10). Pain after laparoscopic surgery can be due to a myriad of factors, all of which should be considered. Incisions for operative ports will be associated with localised scar pain (11). Abdominal pain may itself be variable and associated with the degree of surgery and manipulation (11). Insufflated gas trapped in the peritoneal cavity may cause upper abdominal, shoulder tip or back pain (11).

This article aims to give an overview of the various analgesic modalities available followed by case examples of best practice with reference to how analgesia is incorporated into ERAS programmes.

Multimodal analgesia

Multimodal analgesia is a technique intended to reduce the side effects of individual analgesics whilst still providing adequate analgesia by using a combination of pharmacological mechanisms. The combination of modes of action may be additive or synergistic (12,13). As mentioned, a key concept is to reduce opioid consumption and with that their notable side effects.

The basic pharmacological agents include paracetamol (acetaminophen) and (where suitable) non-steroidal anti-inflammatory drugs (NSAIDs). Paracetamol is a cyclo-oxygenase (COX) inhibitor and, when given at a suitable dose based upon weight and hepatic sufficiency, has an excellent safety record and can be administered via a number of methods including intravenously. NSAID treatment is somewhat variable owing to the array of drugs which fall into this class. There are concerns as to the safety profile of this class of drug as there are strong associations with cardiovascular complications, bleeding, renal dysfunction impaired wound healing and anastomotic breakdown (14,15) with the more selective NSAIDs (for example parecoxib and celecoxib) thought to have a reduced adverse effect profile when compared to their non-selective counterparts (for example diclofenac), including the risk of anastomotic breakdown (16). Other non-opioid systemic agents include lidocaine, alpha-2-agonists (dexmedetomidine and clonidine), ketamine, magnesium, gabapentinoids and dexamethasone.

Lidocaine is an amide local anaesthetic that works by blocking sodium channels and therefore reducing neuronal transmission. When given as a systemic infusion, it has been shown to provide analgesia, reduce opioid consumption whilst reducing nausea and vomiting and ileus risk (17,18). The infusion usually starts after a pre-incision bolus and plasma concentrations tend to be similar to that of an epidural local anaesthetic infusion (1). An analgesic benefit has been particularly observed in laparoscopic colorectal surgery and the benefit continues after the infusion has stopped (19). It has also been shown to have a similar impact on improving postoperative bowel function when compared to thoracic epidural (20) and an intraoperative infusion can decrease opioid consumption and hospital length of stay in procedures such as gastrectomy (21). However, the effect may be less significant in surgeries requiring small incisions when compared to major open surgery (22).

Ketamine acts as a N-methyl D-aspartate (NMDA)-antagonist and has a synergistic effect to morphine. Used in analgesic doses it may help in the reduction of chronic pain syndrome. In major abdominal surgery it has been shown to half morphine consumption but can cause more psychiatric complications such as nightmares and hallucinations (23). Where suitable ketamine can also be used in combination with morphine for patient-controlled analgesia (PCA). Magnesium also has a NMDA-antagonistic effect making another useful analgesic adjunct. It has also been shown to reduce the risk of ileus but should be noted that it can prolong neuromuscular blockade thus appropriate dosing and monitoring must be used.

Gabapentinoids (pregabalin and gabapentin), initially developed as anticonvulsants, were found to be effective in neuropathic and postoperative pain (24). They can reduce postoperative pain and be opioid sparing but can cause visual disturbances (more prevalent with pregabalin) (25,26). They have been successfully used in laparoscopic cholecystectomy and can help provide pain relief as a single preoperative dose as part of a multimodal regime (27). Higher doses can have sedative effects which have the potential to interfere with a successful ERAS programme.

Alpha-2-agonists have an analgesic effect through

Table 1 Analgesic recommendations in laparoscopic colorectal surgery (35)

Recommendation	Quality of evidence	Recommendation grade
Multimodal analgesia avoiding opioids	Moderate	Strong
Avoiding thoracic epidural for analgesia	Moderate	Strong
Spinal with low dose opioids as an adjunct to GA	Moderate	Strong
Lidocaine infusions to reduce opioid usage	High	Strong
TAP blocks to reduce opioids and improve recovery	Moderate	Strong

GA, general anaesthesia; TAP, transversus abdominis plane.

reduction of sympathetic outflow and noradrenaline release within the central and peripheral nervous systems thus interrupting pain pathways, including the release of the substance P. Clonidine can be used as part of a nerve block or intrathecal preparation for its analgesic effect, however, its adverse effect profile (sedation, hypotension, bradycardias) make it otherwise less popular, particularly as part of an ERAS programme.

Glucocorticoids can also be considered as an analgesic adjunct as they have an opioid-sparing effect as well as reducing post-operative nausea and vomiting (PONV), hospital length of stay and modifying the surgical stress response (28).

Local anaesthetic administration can provide analgesia in a variety of ways from neuraxial blockade to regional nerve blocks as well as direct local infiltration.

Spinal anaesthesia is a commonly performed regional analgesic technique and has been shown to help reduce opioid usage and improve speed of recovery (29). It is a superior alternative to epidurals for laparoscopic surgery given the good analgesia, quick delivery, limited duration and moderate attenuation of the stress response alongside lower complication rate (30). Usually, the spinal will contain a mixture of local anaesthetic (for example hyperbaric 0.5% bupivacaine/levobupivacaine) along with an opiate suitable for neuraxial injection (for example diamorphine) totalling a dose suitable for analgesic cover but avoiding too widespread a block. Mobilisation is possible once the motor block has resolved and when compared to epidural the patient can likely be mobilised sooner (30). The intrathecal opioid helps to provide a six-fold reduction in postoperative opioid requirements (31). Another benefit is that there is a reduction in the surgical stress response (32). When compared to continuous epidural usage there is also a reduced risk of postoperative fluid overload due to treatment for hypotension (30). Several contraindications remain when considering intrathecal injection. Coagulopathies of the ongoing use of anticoagulants should be considered on an individual patient basis. Patients with septicaemia are considered not suitable for neuraxial blockade owing to the increased risk of abscess around the injection site and CSF infection. Patient refusal and certain cardiac conditions (most notably severe aortic stenosis) are also important contraindications.

Epidural anaesthesia is an established method to both reduce the surgical stress response and is considered the gold standard to provide adequate analgesia in open colorectal surgery (33,34). ERAS guidelines strongly recommend thoracic epidural usage in open colorectal surgery to minimise the surgical stress response and for analgesia postoperatively (*Table 1*) (35). However, these benefits are not translated to laparoscopic colorectal surgery and in fact, RCT results suggest many outcomes were significantly worse than spinal or opioid-based PCA (30,31). Levy *et al.*, showed the possibility of an enhanced recovery assisted 23 hours stay laparoscopic colectomy in 2009 (29). Analgesia was provided using a spinal and low dose opioid along with post-operative paracetamol and diclofenac or tramadol. Only one of the 10 successful 23 hour stay patients required breakthrough morphine and only three required breakthrough analgesia. There is evidence to suggest that epidurals may increase the length of stay in laparoscopic colorectal surgery (30,36,37). Recent meta-analyses of RCTs of patients having laparoscopic colorectal surgery did not show any additional clinical benefits (36). Potential issues of epidurals include hypotension, urinary retention and residual motor blockade, which may all contribute to the increased length of stay in these patients (30,38).

Local anaesthetic abdominal wall nerve blocks include transversus abdominis plane (TAP) blocks and rectus sheath blocks. TAP blocks are well established and include provision by landmark, ultrasound or laparoscopic assisted (1).

They can be one-shot injections or continuous via placement of an infusion catheter. They have been shown to allow for opioid sparing in colorectal surgery and faster return of bowel function (39,40). It is important to note that TAP blocks will only be able to provide sufficient analgesia for incisions below the T10 dermatome. Meta-analyses data supports its use in laparoscopic colorectal surgery for systemic analgesia (41,42). Rectus sheath blocks can also be delivered as one-shot injections or via infusion catheters. Some evidence suggests opioid-sparing, avoidance of hypotension and mobility issues associated with epidurals and superiority over wound catheters (43,44).

Wound catheter local anaesthetic usage shows varying results but include reduced opioid usage and some reduced length of stay and faster return of bowel function (45).

Specific cases

Colo-rectal

The mainstay of treatment uses a multimodal principal and this is associated with early mobilisation, faster return of bowel function and a reduction in complications (*Table 1*) (35). The 2018 ERAS guidelines advocate avoidance of opioids and combination of multimodal analgesia with spinal or TAP blocks. Epidurals were not recommended for laparoscopic surgery given the alternatives of spinal with low dose opioid or TAP blocks, the former associated with a stress reduction along with good analgesic effects. Lidocaine infusions were shown to reduce opiate usage post-operatively. TAP blocks also showed a reduction in opioid usage, however, optimal pain relief was dependent on spread and technique dependent (*Table 1*) (35).

Many studies do not distinguish between colonic and rectal surgery but there can be more extensive tissue dissection in rectal surgery (5). Epidural is shown to be superior to intravenous opioids in open procedures, but in laparoscopic procedures in an ERAS programme epidural or lidocaine infusions have shown adequate analgesia in the first 24 hours and a similar time for bowel function return (20). TAP blocks and local anaesthetic infusions provide satisfactory analgesia but the latter has not been shown in ERAS programmes yet. A multimodal pharmacological approach is once again used to spare opioid use.

Gynae-oncology

A multimodal analgesic, opioid sparing method is preferred and shown to be effective. ERAS guidelines recommend a pharmacological regime including paracetamol, celecoxib and gabapentin (46). Thoracic epidurals are commonly used in major open gynaecology surgery and effectively reduce postoperative pain and stress (47) but intrathecal injections are still preferred for laparoscopic surgery. Incisional local anaesthetic (such as bupivacaine) infiltration should also be incorporated (12). Transverse abdominis plane blocks can also be used and have been shown to reduce pain scores at discharge in laparoscopic hysterectomy patients (48) but some studies did not show any reduction in opioid usage (49). Another study was not able to show any significant clinical benefit of TAP blocks over incisional site bupivacaine infiltration (50).

Prostatectomy/cystectomy

One of the most important aspects of analgesia for these patients is the use of neuraxial anaesthesia, specifically intrathecal blockade, especially in those with cardiovascular and respiratory disease (51). Neuraxial block is associated with reduced blood loss, early return of bowel function and pain control (52,53). There is also evidence showing the benefits of rectus sheath catheters in cystectomies on ERAS programmes, with benefits including safety in patients on anti-platelets, reliability postoperatively and ease of insertion (54,55)

Oesophagectomy

The choice of analgesia depends on surgical approach and while thoracic epidural is the gold standard and tends to be first line, it is worth considering other methods especially if any parts of the procedure are performed using minimally-invasive techniques rather than open. A paravertebral block can reduce postoperative hypotension and the reduced mobility associated with epidural usage (1). Analgesia from this has been shown to be as effective as epidural for thoracotomy (56-58). Multimodal analgesia is useful for the general reasons as listed above but consideration should be made for intravenous therapy when the enteral route may be difficult postoperatively. Regular paracetamol is useful also for anti-inflammatory and anti-pyretic effects. NSAIDs, whilst being useful for analgesia and anti-inflammatory, should be used with caution in individual cases and close attention be paid to postoperative renal dysfunction which may be more frequent after oesophagectomy (1). Gabapentinoids may be useful to reduce chronic thoracic

pain and should be introduced pre-operatively (59). Ketamine may improve analgesic effect as well as reducing chronic pain (60). Magnesium may also improve postoperative pain and will have added benefits including improving electrolyte deficiency (61). Lidocaine infusions have limited data in oesophagectomy but may have a role in providing analgesia along with improved bowel function as they have in abdominal surgery (1).

Hepatic

Once again, the same principals of multimodal analgesia apply. Much of the evidence available relates to open liver surgery and there are current concerns that thoracic epidural may cause postoperative renal dysfunction (62) and epidural catheter removal may be delayed due to a prolonged prothrombin time (63). This in turn can impact upon postoperative mobilisation. Intrathecal opiates or local anaesthetic wound catheter with PCA may provide a suitable alternative (64,65) and in open surgery a meta-analysis showed similar outcomes with wound catheters but a higher complication rate in epidurals (66).

Bariatric

The reduction of opioid usage is even more important in this patient population with the increased risk of postoperative respiratory depression especially in those with obstructive sleep apnoea (67). A multimodal strategy is employed, and dosage should be adapted according to ideal body weight (68). If opioids are to be used, an increased refractory period between PCA boluses and an early switch to the enteral route is recommended (67). Whilst no specific studies exist in bariatrics, the use of local anaesthetics for laparoscopic surgery can be extrapolated from colorectal surgery. Evidence also suggests efficacy of intraperitoneal aerosolisation of local anaesthetics in bariatric surgery with levobupivacaine being more effective than lidocaine (69) and ultrasound TAP blocks safe and feasible (70). Whilst epidurals can be used for bariatric laparotomies, there is no strong evidence to back their use in laparoscopic surgery (31).

Summary

Analgesia is a vital principal of ERAS pathways and anaesthetic practice in general. The general consensus is that a multimodal approach is best, to ensure sparing of opioids. This can involve the use of both systemic analgesia and local anaesthetics. Whilst the majority of evidence is for colorectal laparoscopic work, there is growing evidence of specialty and procedure specific analgesia.

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