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New trends in the treatment of post-operative pain in general and gastrointestinal surgery

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A B S T R A C T

The correct application of multimodal analgesia appropriate to the pain intensity, the characteristics of the surgery, and the hospitalisation scheme provide the key to improving the management of postoperative pain, which is currently still under treated. In highly complex surgeries the best benefit is obtained by combining systemic analgesic drugs with regional analgesia techniques. Epidural analgesia, not only provides an excellent quality of analgesia, but can prevent complications and reduce postoperative morbidity. Recently, peripheral blocks and parietal infiltration techniques, with or without catheter, have gained prominence in the postoperative analgesia of haemorrhoids and hernia repair. All these analgesic techniques are integrated into the concept of early postoperative rehabilitation and pursue the objective of minimising the side effects associated with the treatment and facilitate the functional recovery of the patient. In addition, proper postoperative pain management not only increases the quality of in-patient care but is also a factor to consider in the development of chronic post-surgical pain, where the impact is significant and impairs the quality of life of the patients.

Nuevas tendencias en el tratamiento del dolor postoperatorio en cirugía general y digestiva

Palabras clave:
Dolor postoperatorio
Analgesia multimodal
Analgesia regional
Analgesia sistémica
Opioides

R E S U M E N

Una correcta aplicación de la analgesia multimodal que resulte adecuada a la intensidad del dolor, a las características de la cirugía y al régimen de hospitalización planteado aportará la clave para mejorar el manejo del dolor postoperatorio, actualmente infratratado. En las cirugías de alta complejidad el mejor beneficio se obtiene al asociar los analgésicos a las técnicas de anestesia locorregional. La analgesia epidural no sólo proporciona una excelente calidad analgésica, sino que puede prevenir complicaciones y reducir la morbimortalidad postoperatoria. Últimamente, los bloqueos periféricos y las técnicas de infiltración, parietal con o sin catéter, han adquirido mayor protagonismo en la analgesia postoperatoria de

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cirugías como hemorroides o herniorrafias. Todas estas técnicas analgésicas se integran en el concepto de rehabilitación postoperatoria precoz y persiguen como objetivo minimizar los efectos secundarios asociados al tratamiento y facilitar la recuperación funcional del paciente. Además, el correcto manejo del dolor postoperatorio no sólo aumenta la calidad asistencial intrahospitalaria, sino que es un factor que se debe considerar en el desarrollo del dolor crónico posquirúgico, cuya incidencia es significativa y deteriora la calidad de vida de los paciente

Introduction

Postoperative pain is the main feature of acute pain and is defined as a recently initiated pain, probably of limited duration and that appears as a consequence of nociceptive stimulation of a surgical intervention on different organs and tissue. The most outstanding feature of postoperative pain is that its intensity is at its maximum in the first 24 hours and then progressively decreases.

Although there are more and more advances in the neurobiological knowledge base of nociception and the physiology of analgesic drugs and techniques, postoperative pain remains under treated.

The aims of correct acute postoperative pain treatment are (Figure 1):

- Minimise patient discomfort ease postoperative recovery avoid deleterious complications related with the pain (Table 1[1-4])
- Allow for early active and passive mobilisation to achieve full functional recovery
- Effectively eliminate or control the side effects associated with the treatment
- Avoid chronification of the pain

Several therapeutic measures are applied to reach these objectives:

- Non-opioid analgesics
- Opioid analgesics
- Special analgesic techniques:
  - regional analgesia,
  - patient controlled analgesia (PCA)

The use of one or other analgesic technique depends to a great degree on the intensity of the postoperative pain[5] (Figure 2). In the presence of light pain, the best drugs are

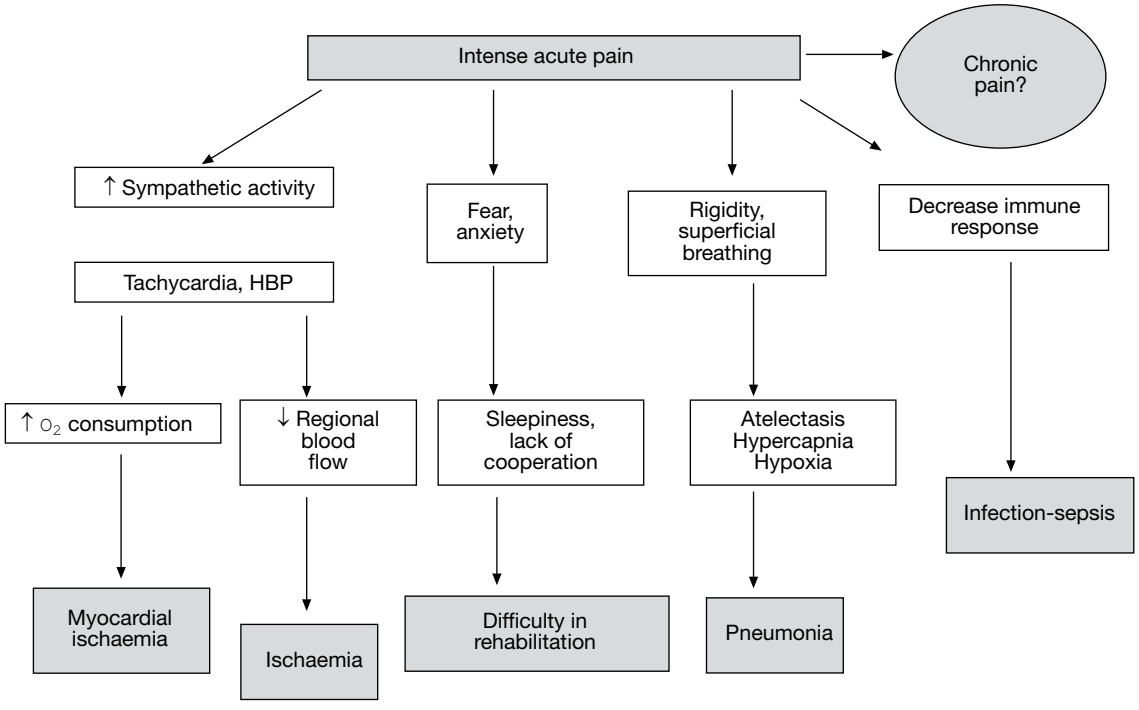

Figure 1 – Consequences of pain infiltration.

non-opioid analgesics which, associated to weak opioids are able to moderately control pain. The strong opioids, as well as the nervous block techniques (central or peripheral) y local or opioid anaesthetics are set aside for highly intense pain.

However, the best therapeutic option is one of "balanced or multimodal analgesia."[6] Based on the combination of different drugs or analgesic techniques with differing action mechanisms and in lower doses to those applied in monotherapy. The aim is to obtain greater analgesic potency with fewer side effects. Many studies have been carried out that endorse this concept of multimodal analgesia: epidural analgesia with opioids or non-steroidal anti-inflammatory drugs (NSAIDs), PCA with opioids combined with non-opioid drugs.[7,8] Along these lines, scientific evidence shows that, in high complex surgery, the greatest benefit is obtained from the association of analgesics to locoregional anaesthesia techniques.

Table 2 describes the conclusions of the comparison of methods used to con control postoperative pain by experts in perioperative medicine, with the available scientific evidence.[9]

Analgesic techniques

Systemic analgesia

Non-opioid analgesics

Non-opioid analgesics include a vast group of drugs characterised by producing light analgesia and having a ceiling effect, which means that the benefit does not increase with the dose. They are classified according to the place of action:

Table 1 – Complications related to postoperative pain

Respiratory complications	Basically after thoracic and upper abdominal surgery
	Incidence of 10% in elective abdominal surgery Multifactorial pathophysiology: Interruption of normal activity of the respiratory muscles Reflex inhibition of the diaphragmatic function Voluntary inhibition of the dynamics of breathing due to pain
	All of this leads to a decrease in pulmonary volume and to the development of atelectasis and pneumonia
Cardiovascular complications	Incidence of 5% in surgical patients
	Sympathetic hyperactivity that leads to an increase in cardiac frequency, average blood pressure, heart rate, and myocardial consumption of oxygen Hypercoagulability and hypofibrinolysis that stimulate thrombotic processes
Digestive complications	Abdominal distension, nausea, vomits and inhibition of gastrointestinal motility
	High incidence of paralytic ileus (>90%) after abdominal surgery Multifactorial pathophysiology (neurogenic, inflammatory ,and pharmacological mechanisms)
Metabolic complications	Postoperative pain increases neuroendocrine response against surgical intensity by inducing a state of sympathetic and hypothalamic hyperactivity, which results in: hyperglycaemia, glucosuria, sodium and water retention, stimulation of the rennin-angiotensin system, oliguria, lipolysis and proteinic hypercatabolism
Psychological complications	Distress, fear, or apprehension

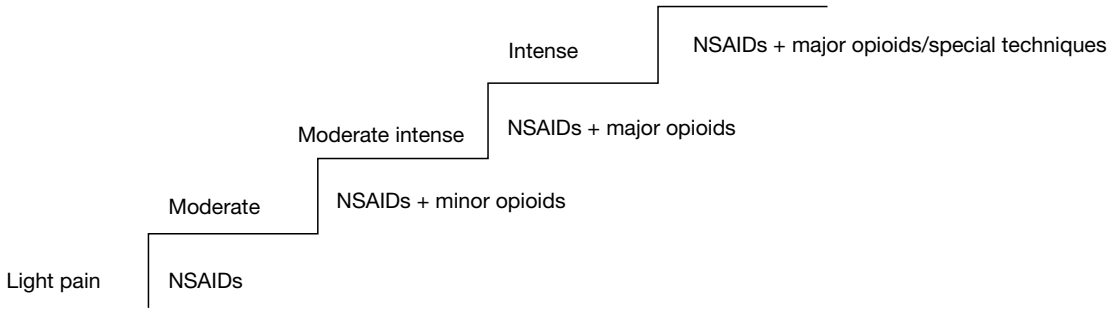

Figure 2 – Acute pain treatment scale.

Table 2 – Scientific evidence in postoperative pain (PP)[9]

Results	EL[a]	SL[b]
Intravenous PCA provides better analgesia compared with the administration of parenteral opioids in the infirmary	Ia	C
Ongoing technique of regional peripheral analgesia provide better analgesia compared with the administration of systemic opioids	Ia	A
Multimodal analgesia (NSAID, COX-1 inhibitors or paracetamol plus intravenous PCA with opioids) improve PPa and reduce the adverse effects related to analgesiab (basically those secondary to opioids)	Ia	[a]A (infusion and NSAID multidose and COX-2 inhibitors) [a]E (single dose NSAID and paracetamol) [b]E (paracetamol, COX-2 inhibitors) [b]B (unspecific NSAIDs)
Technical problems limit effectiveness and safety of the intravenous and epidural PCA	III	B
New emergent treatments (fentanyl iontophoretic transdermal device and delayed release epidural morphine) for the treatment of PP offer certain advantages over existing analgesic options	Ib	C
The creation and disclosure of clinical practice guides in the treatment of acute pain have improved the handling of PP	Ib	C
The poor control of PP increases the probability of developing post-surgical chronic pain	II	A
Epidural analgesia continues to be the most beneficial (less morbidity, pain control, intestinal motility and mobility)	Ia	A (benefits of epidural analgesia in heart and lung function) E (improvement in severe morbid-mortality) D (cardiac morbidity)
Non-opioid analgesia regimes result in faster recovery of intestinal function after major abdominal surgery	Ib	C
PP should be effectively controlled in patients with opioid tolerance	III	C

COX-2 indicates cyclooxygenase-2; EL, evidence level; NSAIDs, nonsteroidal anti-inflammatory drugs; PCA, patient controlled analgesia (PCA); PP, postoperative pain; SL, support level.
[a]Levels of scientific evidence: Ia: evidence obtained from meta-analysis, included in at least one controlled and randomised study with a large number of cases; Ib: evidence obtained from meta-analysis, included in at least one controlled and randomised study with a lower number of cases; II: evidence obtained from panel studies or well-designed cases and controls; III: evidence obtained from non-experimental well-designed descriptive studies, with comparative studies, of correlation or cases and controls; IV: evidence obtained from expert opinions based on clinical experiences, descriptive studies or committees; V: insufficient evidence to form an opinion. [b]Support levels: A: strong recommendation, always applied and accepted; B: recommendation in which intervention could be of use; C: recommendation in which intervention could be considered; D: recommendation in which a procedure would not be of use; E: insufficient proof for a recommendation.

- Cyclooxygenase (COX) inhibitors in the central region (central nervous system and in the descending inhibitory pain channels by activation of the descending antinociceptive serotonergic system[10,11]): paracetamol
- COX inhibitors in the peripheral region: NSAID

There is a current tendency to associate minor analgesics that act in both in the peripheral and the central regions, aimed at obtaining more effective analgesia.

Opioid analgesics

Opioids are the optimum postoperative analgesic drugs, above all when the intensity of the pain cannot be controlled by minor analgesics or when these have been contraindicated.

For correct pain control with these drugs, a few frequent mistakes should be avoided, such as infradosing, over excessively long or inappropriate periods of time between doses, lack of knowledge of the administration routes and treatment standardisation without assessing differences between individuals. Also, lack of guidelines and "on demand" prescribing should also be avoided. Although it is well known that opioids can cause respiratory depression, the most frequent problems that can arise in daily practice are sleepiness, nausea, vomiting, water retention or prolongation of paralytic ileus. The advantage of adding a systemic non-opioid analgesic rests not only on the increase in analgesic effectiveness, but since it allows a decrease in the dose of opioids needed, the incidence of related side effects is reduced.

In the last few years, intravenous administration has been propagated as the main method for opioids in the immediate postoperative, just as the diffusion of others has decreases, such as the intramuscular, subcutaneous or rectal methods. These tendencies are due not only to the inherent inconveniences of these methods (pain from the injection, erratic absorption), but to the surge in PCA techniques, suitable for intravenous or spinal routes. Intravenous PCA can be currently considered as the standard for the handling of postoperative pain.[5] However, there are also limitations in this modality, such as the technical and instrumental difficulties, which has initiated the study and development of non-traditional methods (oral and nasal transmucosal) and new techniques with non-invasive PCA systems (PCA with intra-nasal fentanyl, PCA with transdermal fentanyl via iontophoresis.[5]

Regional analgesia

The different techniques and analgesic agents available provide not only analgesic benefits, but they can prevent postoperative complications and as a consequence, derive in differences in perioperative morbid-mortality. In general, the regional techniques provide greater analgesic quality and are associated to a lower incidence of nausea, vomiting and sedation than the systemic with opioids.[7,9,12-14] It has even been suggested that postoperative epidural analgesia can be associated to a lower risk of death in high risk procedures, such as pulmonary resection, colectomy, etc.[15]

The current debate centres on the possibility of reducing side effects and postoperative morbidity according to the analgesic therapy chosen.

Epidural analgesia

The efficiency of epidural analgesia depends on the specific handling of the technique. The influencing factors are the type of analgesic used (opioids provide analgesia, but the physiological effects are more advantageous for local anaesthetics), the agreement of the catheter localisation with the surgical incision dermatome, the epidural analgesia duration (premature removal of the catheter decreases many of its beneficial effects) and the use of epidural analgesia as part of a multimodal technique.

Several studies have brought the role of epidural analgesia into relief in the reduction of the incidence rate and severity of the physiological disorders that cause acute pain.

Effects on pulmonary function. Postoperative epidural analgesia with local anaesthetics reduces pulmonary morbidity[2-4,9] by providing an analgesic improvement, limiting the degree of diaphragmatic dysfunction, improving elasticity in the thoracic and abdominal walls and reducing the incidence and severity of postoperative hypoxaemia. By contrast, these benefits have not been observed with epidural opioids, intercostal blocks or intra-pleural analgesia.[4]

Effects on cardiovascular function. The epidural administration of local and opioid anaesthetics, by providing better analgesia, decreases surgical response to stress and reduces the incidence of myocardial ischaemia and arrhythmia when compared with the systemic administration of opioids.[2,3,9]

Effects on gastrointestinal function. Analgesic drugs affect gastrointestinal motility in a different way and, therefore, cause different degrees of paralytic ileus. The administration of opioids, especially through intravenous PCA, can cause a significant delay in intestinal transit recovery,[9] delay the start of ingestion and, therefore, discharge. A systematic review indicates that epidural analgesia based solely on local anaesthetics provides a faster recovery of the postoperative ileus.[16] Several factors inherent to the technique, such as good pain control, systemic absorption of the local anaesthesia (which stimulates colon motility), sympathetic innervation block in the intestine and reduction in the need for systemic opioids, allow for advance in the recovery of the superior ileus to 24 h. Furthermore, the metameric localisation of the catheter near the surgical incision also benefits normalisation of the gastrointestinal function.[17] A recent study shows an increase in splanchnic perfusion and hepatic flow after major abdominal surgery in patients under anaesthesia and thoracic epidural analgesia. However, the same technique applied to the lumbar region does not achieve these effects.[18]

Peripheral blocks and infiltrations

Infiltration techniques in the abdominal wall have become a part of the multimodal strategy of postoperative pain treatment, basically due to its easy execution. They enable the delay of the first intake of analgesics by decreasing o even avoiding the consumption of opioids, which enables the reduction of side effects. They are also integrated in the concept of early postoperative rehabilitation since they do not cause paralytic ileus and enable early discharge. Its limitations stem from the pharmacology of the local anaesthetics, especially the duration and toxicity, and from the inability to reach complete analgesia according to the extension of the surgical field in the intervention. There is no cross-referenced scientific evidence of the deleterious effect that could take place on the delay of wound healing.

The choice of the local anaesthetic should be oriented towards those with long-lasting effects, such as bupivacaine. Ropivacaine and levobupivacaine have clinical profiles similar to bupivacaine, but less toxicity, making them the drugs of choice used in high doses or when the risk of intravascular absorption is high.[19]

Abdominal wall blocks. Although all blocks can be used as sole techniques for the anaesthesia, many of them are used for postoperative analgesia or both. The most used blocks and their main applications are specified in Table 3.

Haemorrhoidal block. There are 3 possibilities in proctology: "pudendum infiltration" isolated with a minimum volume of 10 mL of local anaesthetic per side; "block of the pudendum nerve with neurostimulation" and "deep perineal infiltration" per infiltration in multiple points. This technique manages to decrease the analgesic requirements, both in the intraoperative stage as well as the first postoperative day.[20]

Table 3 – Applications of abdominal wall blocks in digestive surgery

Block	Applications
Paraumbilical	Anaesthesia[a]: umbilical hernias Postoperative analgesia: umbilical hernias, digestive laparoscopy
Rectus abdominis sheath	Postoperative analgesia: linea alba hernias, midline or transverse laparotomy in digestive surgery
Ilioinguinal and iliohypogastric	Anaesthesia[a]: inguinal hernias Postoperative analgesia: inguinal hernias Chronic pain after herniorrhaphies

[a]Blocks used as a single anaesthetic technique mainly in outpatient surgery.

Parietal infiltration of the scar. It is a simple technique that can be performed in any laparotomy or in the laparoscopic surgery trocar insertion orifices. There is currently a new-found interest in its postoperative use to accelerate patient mobility and discharge. Although in general it is a technique that enables good pain control over several hours, there is large variability in the effectiveness of the analgesia according to the published results.[21,22]

A study which evaluates the anaesthetic efficiency of 20 mL of levobupivacaine in the infiltration of a wound in herniorrhaphy displays good resting pain control, but a considerable number of patients experienced moderate to intense pain with movement.[23]

Continued parietal catheter infiltration. The placement of a subcutaneous catheter over the muscular fascia enables the administration of a local anaesthetic for 2 or 3 days, exceeding the limitation of the analgesic effect that a single dose causes. At the same time, it enables outpatient pain treatment in certain pathologies and in selected patients. It is effective in the repair of inguinal hernias and haemorrhoids, allowing prolonged analgesia, but, in return, it is insufficient in complex digestive surgery.

Analgesia according to the type of surgery

The difficulty involved in establishing adequate pain treatment protocols in all surgical patients has determined that, at this point in time, the guidelines tend to be elaborated according to the surgical aggressivity. For this reason, the protocols should be adapted not only to the type of surgery and patient, but also to the environment in which they are applied. The analgesic procedures are described next according to features of the surgical processes.

Analgesia in outpatient surgery

Recent studies have shown that a significant number of patients intervened in outpatient procedures experience moderate to severe pain during the first 24 to 48 h. The success of a fast recovery of the outpatient largely depends on the efficient handling of postoperative pain[24] given that poor pain control can cause rehospitalisation, with the ensuing increase in costs.

Despite the use of multimodal analgesia (paracetamol, NSAID, tramadol), the analgesia is not always sufficient. The use of perineural or incisional catheters in outpatient treatment has recently begun to gain importance. Evidence suggests that these techniques are effective, feasible and safe in selected patients provided there is an adequate support infrastructure and follow-up available.

Analgesia in laparoscopic surgery

Pain after laparoscopic surgery is caused by multiple causes (Figure 3). However, patients intervened under laparoscopic surgery present less postoperative pain, the need for analgesics is reduced and discharge is expedited.[25,26] A systematic review on laparoscopic colon surgeries shows a reduction in the assessment indexes of postoperative pain by 12.6% and in the consumption of opioids by 30.7% in comparison with open surgery.[27]

Within the framework of multimodal analgesia use in the laparoscopic surgery postoperative it is important to consider pain treatment in relation to the etiopathogenic mechanism that causes it (Table 4).

Analgesia in hernia and haemorrhoid surgery

Diverse studies comparing spinal anaesthesia with local anaesthesia such as techniques for herniorrhaphy display effectiveness of postoperative analgesia comparable or superior to local anaesthesia. Less postoperative complications were observed in this group, such as nauseas, vomiting, water retention and reduction in the time to the first intake of solids. Furthermore, local anaesthesia was proven to be a safe and advantageous method compared to other techniques because it expedited early mobility, premature discharge and decreased the rate of readmission.[28-32]

Haemorrhoid surgery is very painful. Therefore, nervous system blocks associated or not with infiltration in the most distal branches are ideal for multimodal analgesia; they provide good sphincter relaxation and reduce the incidence of water retention.[33,34]

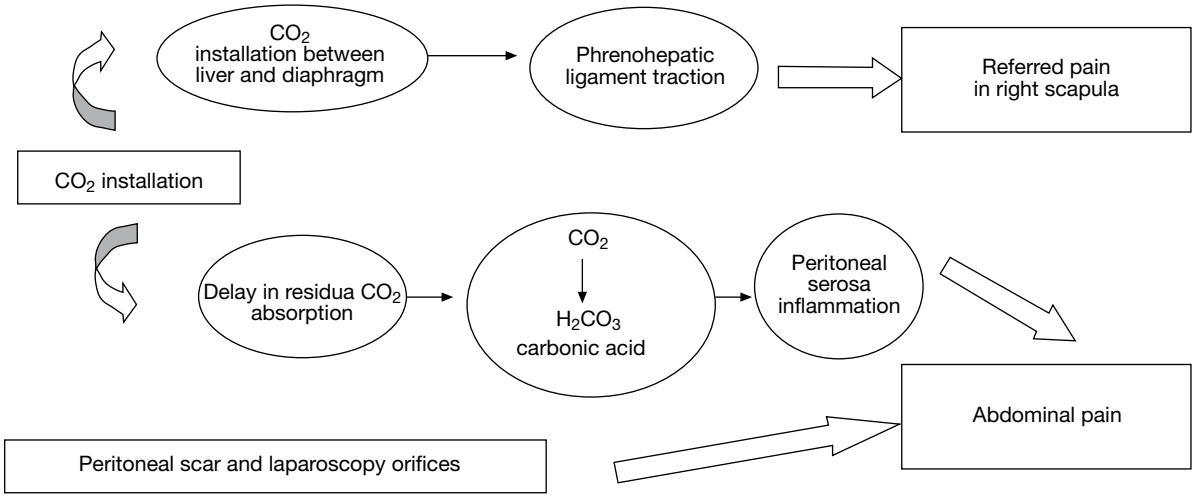

Figure 3 – Etiopathogenesis of pain in laparoscopic surgery.

Table 4 – Pain treatment in laparoscopic surgery

Intraperitoneal CO_2 extraction, as complete as possible, at the end of surgery	Essential for pain control
Infiltration of the laparoscopy orifices with local anaesthetic	Preincisional
Intraperitoneal local anaesthetic injection in the subdiaphragmatic region	Reduces referred shoulder pain up to 48 h after surgery, but does not affect abdominal pain
Intravenous NSAIDs: dexketoprofen	Effective as analgesic and anti-inflammatory drugs by reducing irritation of the peritoneal serosa produced by carbonic acid
Intravenous opioids	In intense pain
Regional techniques: epidural analgesia	Applied in colon surgery included in fast-track functional recovery programs, morbid obesity surgery or patients with prior lung disease

Degrees of action.
CO_2 indicates carbon dioxide; NSAIDs, nonsteroidal anti-inflammatory drugs.

Analgesia in colon surgery (fast-track)

Fast-track recovery programs aim to accelerate the return to the preoperative functional and psychological state minimising the factors causing the delay, such as surgical stress, paralytic ileus or postoperative pain. Anaesthesia-analgesia plays a vital role in the patient's early global functional recovery. Thoracic epidural analgesia (metameric) with local anaesthetics and opioids enables excellent pain control and early mobility.[35]

Analgesia in peritoneal surgery

Cytoreductive surgery with hyperthermic intraperitoneal chemotherapy is an invasive procedure that involves important physiopathological alterations. Thoracic epidural analgesia performed metamerically is the main procedure used in the perioperative handling of this type of surgery. This technique minimises the use of opioids and significantly reduces the duration of postoperative mechanical ventilation.[36]

Analgesia in hepatic surgery

Traditionally, postoperative analgesia treatment after major hepatic surgery has been carried out with parenteral analgesics. The use of an epidural analgesia is object of controversy due to the changes in coagulation that can occur in the postoperative of this type of surgery. However, its application would provoke a redistribution of blood flow that involves a reduction in return via the portal vein and the central venous pressure, which would contribute to a reduction in hepatic congestion and surgical blood loss.[37]

If the appropriate conditions are respected (choice of the right puncture and catheter removal moment, personal

skill in puncturing and catheterisation and absence of liver failure or moderate liver dysfunction) there does not seem to be greater risk of spinal haematoma or neurological complications than when an epidural technique is performed in any other type of abdominal surgery .

Prevention of chronic post-surgical pain

Chronic post-surgical pain (CPSP) is pain which lasts for at least 2 months, persists after a surgical procedure and in which other possible causes have been excluded, such as a recurrence of the disease or the existence of a previous painful syndrome. From an epidemiological viewpoint, the best established risk factor is the type of surgery,[38] with a high incidence of CPSP in procedures involving major tissue and nervous structure injury, such as amputation (incidence of 30% to 81%), thoracotomy (22% to 67%), breast surgery (17% to 57%), inguinal hernia surgery (4% to 37%), and cholecystectomy surgery (6% to 56%).[39] The correct handling of postoperative pain is also a factor to consider in the development of CPSP. Likewise, studies state that the optimisation of the surgical technique could reduce the incidence of CPSP.[40] Basically, avoiding reinterventions, using minimally invasive approaches, a refined surgical technique and avoiding extensive tissue injury and nervous injury.

There is very limited evidence in medical literature on the influence of preventive analgesia techniques[40] in the reduction of CPSP incidence: epidural analgesia, above all when initiated before surgery and continued during the postoperative period, reduces the incidence of severe phantom limb pain after an amputation (evidence level I) and of chronic pain after thoracotomy and laparotomy (evidence level II).

In brief, the choice of correct postoperative analgesia appropriate to the type of surgery and the patient's environment are fundamental for the development of good and effective functional recovery of the post-operative patient. Treatment of postoperative pain is not only an ethical question for patient well-being, but it also influences greatly on the progression of the surgical lesion.

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