Postoperative pain relief in general surgery – recommendations of the Association of Polish Surgeons, Polish Society of Anaesthesiology and Intensive Therapy, Polish Association for the Study of Pain and Polish Association of Regional Anaesthesia and Pain Treatment

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ABSTRACT: It is estimated that there are over 310 million surgeries performed in the world every year. Appropriate analgesic management in the perioperative period constitutes a fundamental right of every patient, significantly reducing the number of postoperative complications and the time and costs of hospitalization, particularly in the high-risk group of patients (ASA III-V) subject to extensive surgical procedures and hospitalized in intensive care units. Despite such significant arguments speaking for the conduct of effective analgesia in the perioperative period, nearly 79% of patients operated in hospitalization settings and 71% of patients operated in outpatient settings (so-called first day surgery) experienced postoperative pain of moderate, strong or extreme intensity. Hence, effective relief of postoperative pain should constitute one of the priorities of integrated, modern perioperative management, the components of which apart from adequate analgesia involve early nutrition through the alimentary canal, early patient activation and active physiotherapy. In the currently published "Guidelines", a team of authors has updated the previous "Recommendations" primarily in terms of methods for optimizing postoperative pain relief and new techniques and drugs introduced for postoperative pain therapy in recent years. The algorithms of postoperative pain management in different treatment categories were also updated.

KEYWORDS: recommendations, pain, pain treatment, pharmacotherapy, general surgery, perioperative procedures

INTRODUCTION

It is estimated that there are over 310 million surgeries performed in the world every year. Proper analgesic conduct in the perioperative period constitutes a fundamental right of every patient, significantly reducing the number of postoperative complications and the time and costs of hospitalization, particularly in the high-risk group of patients (ASA III-V) subject to extensive surgical procedures and hospitalized in intensive care units [36]. Despite such significant arguments speaking for the conduct of effective analgesia in the perioperative period, nearly 79% of patients operated in hospitalization settings and 71% of patients operated in outpatient settings (so-called first day surgery) experienced postoperative pain of moderate, strong or extreme intensity. Hence, effective relief of postoperative pain should constitute one of the priorities of integrated, modern perioperative management, the components of which apart from adequate analgesia involve early nutrition through the alimentary canal, early patient activation and active physiotherapy.

In 2012, an expert team appointed by the Association of Polish Surgeons, the Polish Association for the Study of Pain and the Polish Society of Anesthesiology and Intensive Therapy developed the document "Recommendations for perioperative pain relief in general surgery" containing key information on the proper organization of a postoperative pain management system, patient education, methods of measuring postoperative pain intensity and pharmacotherapy, and methods of regional anesthesia used in perioperative patients [23].

In the currently published "Guidelines" regarding treatment of postoperative pain, the team of authors consisting of experts from the Polish Society of Anesthesiology and Intensive Therapy, Association of Polish Surgeons, Polish Association for the Study of Pain and the Polish Society of Regional Anesthesia and Pain Therapy updated the previous "Recommendations" primarily in terms of optimization of postoperative pain relief and new methods and medications introduced to therapy in the recent years. The algorithms of post-operative pain management in different treatment categories were also

discussed. The authors of the new guidelines included conclusions from the article "Management in postoperative pain – standpoint of the Regional Anesthesia and Pain Therapy of the Polish Society of Anesthesiology and Intensive Therapy, Polish Society of Regional Anesthesia and Pain Therapy, Polish Society for the Study of Pain and the National Consultant in the field of anesthesia and intensive therapy" published in 2018, in order to create a common ground for cooperation in the field of postoperative pain relief between anesthetists and doctors of surgical disciplines [30].

GENERAL ISSUES

Postoperative pain is caused by intraoperative tissue/organ damage and its severity and range are usually proportional to the extent of surgery. It appears when the effect of intraoperative analgesia withdraws and its source is damaged superficial tissues (skin, subcutaneous tissue, mucous membranes) as well as deeper structures (muscles, fascia, ligaments, periosteum). In the case of extensive surgical trauma, in addition to deep and superficial somatic pain, there also appears a visceral component of postoperative pain, caused by smooth muscle contraction, crushing or stretching of visceral structures, as well as inflammatory lesions within the operated tissues. A significant element of postoperative pain is also its neuropathic component associated with intraoperative damage to nerve fibers, the results of which include formation of pathological sodium channels and activation of ectopic centers of stimuli (pacemakers) in the somatosensory part of the nervous system [39].

Postoperative pain is self-limiting, the greatest intensity falls on the first and second postoperative day, with much smaller intensity during the 3rd and 4th postoperative days. Pain is usually the most burdensome in patients after thoracotomy and upper abdominal surgeries. The location of the operated area, its extent, degree of tissue traumatization, direction of skin incision and use of specific analgesia methods and techniques in the perioperative period significantly influence the degree of pain perception. The primary goals of pain management in patients after surgical procedures include eliminating unnecessary suffering, providing comfort, facilitating recovery and inhibiting the development of the whole cascade of unfavorable processes in the body induced by surgical trauma. Therefore, perioperative analgesia should consist of multidirectional activities constituting a determinant in obtaining the proper quality of analgesia, such as [23, 36]:

- informing patients before the surgical procedure about the possibilities and methods for post-operative pain relief,
- assessment of pain severity in all operated patients, at least 4 times per hour,
- keeping documentation comprising severity of pain and the applied management in accordance with the pain treatment guidelines,
- monitoring possible adverse events of the applied treatment on a special adverse drug reaction and medication error report form.

Patients' proper education constitutes an extremely important element of perioperative analgesia. It involves the transmission of oral and written information regarding postoperative pain and methods of treatment. This information should contain the most important data regarding:

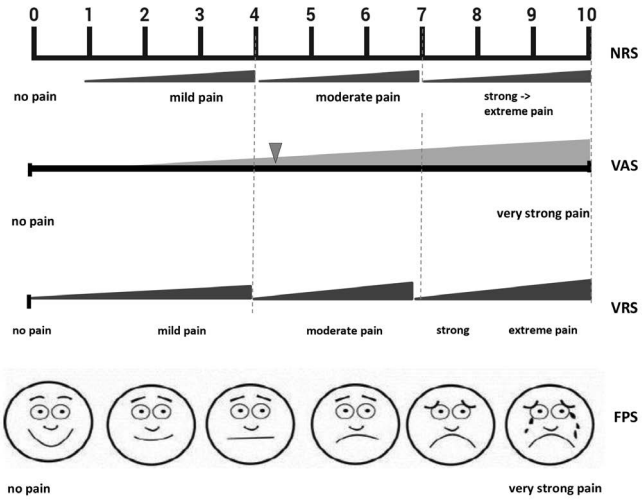


Fig. 1. Pain Assessment Scales.

- measurement methods of pain severity,
- postoperative pain relief methods,
- the importance of relieving postoperative pain for the healing process.

Preoperative conversation with the patient, with his legal guardians or relatives should concentrate on [23]:

- obtaining information on previous pain experiences and preferences in the field of analgesic management,
- discussing with the patient the tools for measurement of pain severity and teaching the patient how to use those tools, determining the level of pain severity, at which analgesia will be implemented,
- discussing with the patient the pain management plan which will be implemented in this case.

ASSESSMENT OF PAIN SEVERITY

An important element of effective pain relief is the measurement of its severity, which should be carried out both at rest and in dynamic conditions, with movements, coughing and deep breathing at a frequency of every 4 to 8 hours.

The NRS (Numerical Rating Scale) numeric scale is the most recommended tool for assessing pain severity, in which 0 means no pain, and 10 stands for the strongest pain imaginable. Usually the result of 1–3 (to 4) means mild pain, 4–6 moderate pain, 7–8 strong pain, and 9–10 very strong and extreme pain. When assessing pain intensity on the NRS scale, the patient is asked to determine the severity of the currently experienced pain, indicating the appropriate number, with "0" responding "I do not feel pain at all" and "10" to "feeling the worst pain I can imagine". At present, this scale is a standard tool for assessing the severity of pain and monitoring the effectiveness of pain management. Postoperative pain is considered to be relieved if the severity of pain measured by the NRS is ≤4. The second scale frequently used to assess pain severity is the Visual Analogue Scale (VAS). The patient is shown a ruler, one end of which determines the absence of pain, and the other, on the contrary, means extreme pain. The patient's task is to place the slider or to indicate the place which best reflects the severity of the pain experienced at the given moment on the scale.

Tab. I. T-max of selected analgesics administered orally.

CHEMICAL SUBSTANCE	T MAX	POSSIBILITY OF USE BEFORE A MEAL
dexketoprofen (granules for oral solution)	15-20 min	YES
dexketoprofen (coated tablets)	30 min	YES
ibuprofen (soft capsules)	30 min	NO
salicylic acid	45 min	NO
paracetamol	ok.1h	YES
metamizole	1h 12 min-2h	NO
ketoprofen	1h 22min	NO
ketoprofen with lysine	no data	NO
aceclofenac	1h 15 min- 3 h	NO
ibuprofen (tablets)	1-2h	NO
dexibuprofen	1-2h	NO
nimesulide	2-3 h	NO
diclofenac	2-3 h	YES/NO
naproxen	2-4 h	NO
meloxicam	5-6 h	NO

Tab. II. Dosing of nonopioid analgesics in perioperative period [9].

DRUG	DOSAGE	MAXIMUM DAILY DOSE
metamizole	1-2.5 g i.v. every 6-12 hours	5 g
paracetamol	0.5 -1 g every 6 hours	4 g
dexketoprofen	50 mg i.v. every 8 hours 25 mg per os every 8 hours	150 mg i.v. 75 mg per os
ketoprofen	50 mg i.v. every 6 hours	200 mg
ibuprofen	400 mg per os, every 6-8 hours 5-10 mg/per kg body weight Every 6-8 hours i.v.	2400 mg
naproxen	250-500 mg per os every 8 hours	1500 mg
nimesulide	100 mg per os every 12 hours	200 mg
diclofenac	50 mg per os, per rectum Every 8 hours	150 mg
celecoxib	100-400 mg per os every 24 hours	400 mg
etoricoxib	30-120 mg per os every 12-24 hours,	120 mg

Another method of assessing pain severity is the Verbal Rating Scale (VRS). Patients are asked to describe whether they are experiencing mild, moderate, severe or extreme pain. In patients with impaired contact, the Faces Pain Scale (FPS) can be used, according to which the severity of pain is assessed based on drawings of faces with different facial expressions (calm face, grimaces of pain, etc.).

POSTOPERATIVE PAIN RELIEF

Non-opioid analgesics (metamizole, paracetamol, non-steroidal anti-inflammatory drugs) as well as opioids used in combination with regional anesthetic techniques (central blocks, plexus and peripheral nerve blocks, interfascial nerves blocks, operative wound infiltration) are used in postoperative analgesia. Intensive development of neurophysiology and neuropharmacology allowed for the optimization of postoperative analgesia and the introduction of so-called multimodal analgesia, the aim of which is to potentiate the action of analgesics and inhibit the development of the process of nociception (the phenomenon of pain) through combined use of drugs with different mechanisms of action, i.e., administration with analgesics or so-called coanalgesics: (lidocaine, NMDA receptor antagonists (ketamine, magnesium sulfate), corticosteroids, calcium channel blockers (gabapentin, pregabalin) or alpha-2 adrenergic receptor agonists (clonidine, dexmedetomidine).

PHARMACOTHERAPY OF POSTOPERATIVE PAIN

It should be emphasized that analgesics should not be administered intramuscularly or rectally in the perioperative period. One of the reasons are humanitarian grounds – pain during intramuscular administrations, patient's discomfort during rectal administration – but above all, a long-term analgesic effect and variable absorption of drugs administered through these pathways. Subcutaneous injection of analgesics is also not recommended in this period due to hypovolemia frequently coexisting in the immediate postoperative period and patients' hypothermia, which may disrupt the absorption and distribution of drugs in the body, and thus cause an analgesic effect that is difficult to predict. Therefore, in the case of systemic analgesia, analgesics after extensive procedures in the immediate postoperative period should be administered intravenously. In selected types of surgical procedures, analgesics may be administered orally.

NON-OPIOID ANALGESICS IN POSTOPERATIVE PAIN RELIEF

In patients with acute and postoperative pain does not exceed 4 on the NRS scale, non-opioid analgesics are recommended. They can be administered in monotherapy, while at higher pain intensity they should constitute components of multimodal analgesia, which allows broadening the spectrum of analgesic action and reduction of the total dose of opioid analgesics by about 25-40% (level I credibility according to EBM). Thus, the risk of adverse effects associated with the use of opioids – respiratory failure, drowsiness, nausea, vomiting, dizziness (I level credibility according to EBM) decreases [27].

Nonsteroidal anti-inflammatory drugs (NSAIDs) are effective in any type of nociceptive pain (mechanical, inflammatory, visceral). In contrast, paracetamol – due to the lack of anti-inflammatory activity – proves effective only in nociceptive pain of somatic type. Due to its pharmacokinetic nature, it should not be used in inflammatory pain, nor is it effective in visceral pain. In turn, metamizole, despite the lack of anti-inflammatory activity, is characterized by an additional central spasmolytic activity, which makes it particularly effective in nociceptive visceral pain. In pain management, combined use of NSAIDs with paracetamol and/or metamizole should be considered, allowing to obtain an additional analgesic effect.

In the treatment of acute pain, intravenous forms of drugs are recognized to have the fastest analgesic effects. Dexketoprofen, ketoprofen, paracetamol and metamizole are recommended as first-line drugs. However, if oral analgesics can be administered first, due to the speed of the analgesic effect, granules for oral solution, soluble tablets and orodispersible tablets (ODT) should be preferred (tab. I). Currently, ketoprofen lysine salt is also available as granules for oral administration. Its pharmacokinetic parameters, and in particular fast absorption, cause a rapid analgesic effect while minimizing the risk of gastrointestinal side effects.

Threshold doses have been defined for all non-opioid analgesics, above which there is no increase in analgesic effect, while the risk of complications increases significantly (tab. II).

Metamizole

Metamizole belongs to the group of non-opioid analgesics. It is a drug with no anti-inflammatory activity, however its metabolites have an inhibitory effect on the synthesis of prostaglandins, mainly on the activity of cyclooxygenases 1 and 2 (COX-1, COX-2). In addition, metamizole impacts the cannabinoid system, and this guarantees both analgesic and antipyretic effects of the drug. In contrast, diastolic action in relation to smooth muscle is activated by inhibiting the reuptake of adenosine in the structures of the central nervous system and by affecting the cannabinoid system. Metamizole is proven to have synergistic action with NSAIDs, paracetamol and opioid analgesics and constitutes an important component of combined analgesic therapy [22]. Metamizole also has an additive spasmolytic effect both with musculotrophic spasmolytics (e.g., papaverine, drotaverine) as well as with hyoscine butylbromide.

Key information

- The analgesic strength of a 2.5 g dose of metamizole is comparable to a 10 mg dose of morphine (level II according to EBM). NNT (Number Needed to Treat), which stands for the number of patients to whom a certain drug should be given in order to achieve a 50% pain relief in one, for a 500 mg dose of metamizole (iv) is 2.5, and for a dose of 1000 mg (i.v.) is 1.9.
- Metamizole, demonstrating a synergistic action with tramadol, increases its analgesic effectiveness, and the combined use of both drugs reduces the need for tramadol by 35–40%.
- Metamizole should be administered intravenously in a slow infusion at a rate of 0.25-0.5 g/1-5 minutes, and the recommended single intravenous dose is 1-2.5 g. In the case of continuous IV infusion, the initial dose is 2.5 g (slow infusion for 15 minutes). It is then continued in the form of a continuous intravenous infusion at a dose of 100-150 mg/hour.
- Metamizole is available as an oral, intravenous and intramuscular preparation. In rare cases, parenteral administration may be accompanied by arterial hypotension.
- Available data indicate that metamizole does not cause side effects from the upper gastrointestinal tract and kidneys, as is the case with nonsteroidal anti-inflammatory drugs.
- Cases of sudden reduction in blood pressure are most often associated with rapid intravenous administration, because the risk of anaphylaxis with metamizole is low.
- An international study on agranulocytosis and aplastic anemia showed a total increase in risk after administration of metamizole estimated as 1 case per million patients. In Poland, there were no cases of agranulocytosis after the use of metamizole despite the total consumption of over 110 million tablets per year.
- The risk of agranulocytosis should be assessed in the context of other analgesics and related risks. The risk of agranulocytosis should be assessed in the context of other analgesics and related risks. Meta-analysis showed that the estimated additional mortality associated with severe adverse events was 185 per 100 million for aspirin, 592 per 100 million for diclofenac, but only 20 per 100 million for paracetamol and 25 per 100 million for metamizole

Tab. III. Equivalent doses of opioid analgesics [38].

OPIOID	INTRAVENOUS DOSE	ORAL DOSE
Morphine	10 mg	30 mg
Tramadol	100 mg	150 mg
Oxycodone	7.5-10 mg	20 mg
Fentanyl	0.1 mg	-
Buprenorphine	0.4 mg	0.8 mg
Tapentadol	-	100 mg
Methadone	1 mg	3 mg
Nalbuphine	10 mg	-

Tab. IV. Dosage of intravenous opioid analgesics in PCA system in adult patients [39].

OPIOID	DAWKA BOLUSA	OKRES REFRAKCJI (W MINUTACH)
Morphine	1-2.5 mg	10-15
Oxycodone	1-2 mg	10-15
Fentanyl	20-50 mcg	5-10
Nalbuphine	1-3 mg	6-10
Tramadol	10-25 mg	5-10

- With the use of metamizole, there is little risk of inducing interactions with other concomitant medications. The interaction with ciclosporin and methotrexate is clinically relevant, and hence caution is advised in patients taking both medicines at the same time. The interaction of metamizole with methotrexate increases the risk of agranulocytosis, whereas due to the fact that metamizole is a CYP3A4 inducer, it may reduce the concentration of cyclosporin in the blood serum and thus limit its effectiveness.

Paracetamol

Paracetamol works on all levels of the conduction of stimuli – from the receptors in the tissues, through the spinal cord, to the thalamus and the cerebral cortex, where pain sensations are perceived. The mechanism of paracetamol's analgesic effect is complex and associated with the effect on serotoninergic descending pathways inhibiting the transmission of nociceptive information, on the L-arginine/NO pathway and on the cannabinoid system, which induces both analgesic and antipyretic effects of the drug and inhibits neuroglial activation. Paracetamol exhibits a synergy of action with NSAIDs and opioid analgesics and constitutes a significant component of combination analgesia [28, 31].

Key information

- Paracetamol, exhibiting synergistic activity with tramadol, increases its analgesic effectiveness, and the combined use of both drugs reduces the need for tramadol by 35–40%.
- Extended period of gastric emptying after surgery limits the usefulness of oral paracetamol preparations as analgesics; the situation is aggravated by the simultaneous use of opioids.
- The paracetamol preparation for parenteral administration significantly increases the utility of this drug as an analgesic in the perioperative period, allowing for administration to patients unable to take medicines orally.
- Organ toxicity (hepatotoxicity) occurs primarily as a result

of overdose or chronic use of paracetamol in high doses, which does not happen in the postoperative period.
- The metabolism of paracetamol mainly takes place in the liver, so care should be taken in patients with active liver disease, chronically abusing alcohol with impoverishment of glutathione reserves (cachexia, starvation).
- Hematologic toxicity is extremely rare, but paracetamol can lead to hemolysis in patients homozygous for G6PD deficiency (glucose-6-phosphate dehydrogenase).
- In patients undergoing cardiac surgery in whom paracetamol was used, a 10% reduction in the cardiac index was observed.
- Paracetamol is effective as a painkiller (NNT 3.5-3.8 at a dose of 500-1000 mg) without significant adverse side effects.
- Combining paracetamol and morphine reduces the required daily dose of morphine by 20-33%.
- Paracetamol should not be used in patients taking oral anticoagulants from the K antivitamin group (warfarin, acenocoumarol) due to the increase in antithrombotic activity and risk of bleeding (pharmacokinetic interaction).

Nonsteroidal anti-inflammatory drugs (NSAIDs)

They belong to the group of non-opioid analgesics, which exhibit anti-inflammatory, analgesic and antipyretic effects. In addition to inhibiting synthesis, prostaglandins may affect other important pathophysiological processes that contribute to the formation of inflammatory nociceptive pain. The analgesic and anti-inflammatory effect of this group of drugs takes place by inhibiting prostaglandin synthesis, inhibiting the expression of the inducible nitric oxide synthase isoform, inhibiting the activation of NF-kappa B, substance P and by activating the lipoxin system. In addition, the effect of NSAIDs may result from the activation of both the cholinergic supraspinal pathways as well as from the activation of the endogenous opioid peptide system.

Patients treated with NSAIDs should be aware of the contraindications and limitations to their use resulting from concomitant diseases of the cardiovascular system, kidneys, upper and lower gastrointestinal tract. In terms of perioperative interaction, it is worth remembering that the combined administration of NSAIDs with SSRI and SNRI antipsychotics, heparin and anticoagulants increases the risk of perioperative bleeding, and combining NSAIDs with steroids may entail complications from the upper gastrointestinal tract. Similarly, the simultaneous use of NSAIDs with loop diuretics increases the risk of nephrotoxicity. More than one NSAID drug at the same time should never be used due to the fact that combining two or more NSAIDs not only does not increase therapeutic effectiveness, but significantly increases the risk of side effects [9]. In the NSAID group, selective COX-2 inhibitors are also currently used in the treatment of acute and postoperative pain. Celecoxib and etoricoxib are currently available in Poland for oral administration.

Key information

- NSAIDs co-administered with an opioid reduce the need for opioids and the incidence of nausea, vomiting and sedation associated with the use of opioids.
- NSAIDs combined with paracetamol increase the analgesic effect compared to paracetamol used alone (level I according to EBM).
- With proper selection of patients and compliance with dosage and contraindications, the incidence of perioperative impairment of renal function induced by NSAIDs is low (level I credibility).
- NSAIDs administered preoperatively increase the risk of severe bleeding after many types of surgery compared to placebo (level I credibility).
- Proton pump inhibitors (omeprazole, esomeprazole, pantoprazole, rabeprazole, dexlansoprazole) reduce the risk of NSAID-induced upper GI bleeding. They should be used only in groups at high risk of bleeding and in patients with polypharmacotherapy in whom drug interactions increase the risk of bleeding from the upper gastrointestinal tract.
- In patients taking antiplatelet dosage of acetylsalicylic acid, dexketoprofen and ketoprofen do not induce adverse interactions with acetylsalicylic acid. If the need occurs to use other NSAIDs with acetylsalicylic acid, a 2-hour interval should be observed between the administration of both the first and second medicine.
- In patients after an acute coronary event, NSAIDs should be avoided for 6 months.
- In patients with a significant risk of kidney damage, e.g., dehydrated, the use of NSAIDs should be strictly avoided.
- If the need arises to use NSAIDs in patients at high cardiovascular risk and low gastroenterological risk, the use of NSAIDs should preferably be celecoxib. Ketoprofen or dexketoprofen may also be used, as these drugs do not interact adversely with acetylsalicylic acid.
- If the need occurs to use NSAIDs in patients at high gastroenterological risk and low cardiovascular risk, celecoxib should be given in conjunction with proton pump inhibitors
- In patients with high gastroenterological risk and high cardiovascular risk, NSAIDs should be avoided. If necessary, celecoxib with a proton pump inhibitor should be preferred.

OPIOID DRUGS USED IN POSTOPERATIVE PAIN RELIEF

Opioids are a very effective tool in relieving moderate to severe postoperative pain, provided that their use is prudent and is supported by good knowledge of the mechanisms of action, potential adverse effects and interaction with other medicines used concomitantly. It is important to remember about the possibility of some medicines inducing immunosuppression during the administration of opioid drugs [40], as well as the risk of so-called opioid induced hyperalgesia (opioid paradox) which manifests by the intensification of pain, despite the increased dose used in the opioid drug therapy [26].

A broad range of side effects which opioid drugs may induce, including nausea, vomiting, sedation, gastrointestinal motility disorders, pruritus and potentially life-threatening complication, which is respiratory depression causes that the current recommendations of scientific societies for postoperative pain relief recommend the use of multidirectional combination therapy, an important element of which are techniques of block anesthesia and combined pharmacotherapy with non-opioid analgesics (paracetamol, metamizole, nonsteroidal anti-inflammatory drugs) as well as coanalgesics (lidocaine, ketamine, dexamethasone, magnesium sulfate, gabapentin or pregabalin). This allows for a significant reduction of opioid dosing in the perioperative period while ensuring good postoperative pain control [7, 25].

In the postoperative period, opioids can be administered in various ways. Most often it is intravenous, oral or in the case of nervous system block, endocardial (epidural or subarachnoid) or perineural. In contrast, in acute postoperative pain, due to frequent changes in

Tab. V. Opioid analgesics used most often in relieving postoperative pain [30].

OPIOID NAME	DOSAGE
Tramadol	Intravenously: in fractionated doses of 50-100 mg every 4-6 hours or continuous intravenous infusion. Orally: 5–20 drops every 6–8 hours (1 drop –2.5 mg tramadol) or in a short-acting preparation 50-100 mg every 4-6 hours, or in a 50-200 mg controlled-release formulation every 12 hours. Maximum dose is 400 mg/day.
Morphine	Intravenously: PCA (bolus 0.5-2.5 mg, refraction period 10-15 minutes) or titration: 1-2 mg every 3-5 minutes to achieve the desired effect with the continuation of continuous infusion (according to the scheme). Orally: at a dose of 5–10 mg every 4 hours (short-acting preparations) or 10–20 mg every 12 hours (controlled release formulations). *The conversion of intravenous morphine to oral is 1:3, i.e., orally, a three-fold higher dose of morphine should be given compared to that effective in intravenous use of the drug.*
Oxycodone	Intravenously: PCA (bolus 1-2 mg, refraction time 10-15 minutes) or titration: 1-2 mg every 3-5 minutes for optimal effect with continued infusion (according to the scheme). Orally: in controlled release formulation initially 10-20 mg every 12 hours. *The conversion of intravenous oxycodone into oral is 1:2, i.e., twice the dose of oxycodone should be given orally compared to that effective in intravenous use of oxycodone.*
Fentanyl	Intravenously: in a continuous infusion at a dose of 0.5-3 µg/kg/hour or PCA: bolus 0.02-0.05 mg, refractory period 5-10 minutes.
Tapentadol	Orally: immediate release tablets used at a dose of 50–100 mg every 4–6 hours (maximum daily dose 600 mg) and controlled release tablets administered at a dose of 50-250 mg every 12 hours (up to a maximum of 500 mg per day).
Nalbuphine	Intravenously: bolus 0.1-0.3 mg/kg (maximum 20 mg), the dose can be repeated after 3-6 hours; continuous infusion of 004-0.32 mg/kg/hour.
Buprenorphine	Intravenously: 0.3-0.6 mg every 6-8 hours Orally: 0.2-0.4 mg every 6-8 hours.

Tab. VI. Dosage of coanalgesics in perioperative pain management.

KOANALGETYK	DOSAGE
Lidocaine	Intravenous dosage: · during induction of anesthesia - 1-1.5 mg/per kg body weight · continuous i.v. infusion during procedure 1-1.5 mg/per kg body weight/hour · in postoperative period (24-48 hours) – 0.5-1.5 mg/minute.
Ketamine	Intravenous dosage: · surgical procedures (< 60 min); 0.1-0.3 mg/kg bolus i.v. during induction · surgical procedures (> 60 min), without planned infusion i.v. in the postoperative period; 0.1-0.3 mg/kg bolus i.v. during induction followed by boluses in dose of 0.1-0.3 mg/kg every 30-60 minutes · surgical procedures (> 60 min), with planned infusion i.v. in postoperative period; 0.1-0.3 mg/kg bolus i.v. during induction, followed by i.v. infusion at a dose of 0.1-0.2 mg/per kg body weight/hour for a period of 24-72 hours. After 24 hours, a dose reduction of ketamine to 10 mg/hour may be considered.
MgSO4	Intravenous dosage: · During induction for anesthesia – 30-50 mg/per kg body weight · During surgery, infusion of 10-15mg/kg/hour · In postoperative period (24-48 hours) – 10-15 mg/kg/hour
Dexamethasone	Intravenous dosage: 0.1-0.2 mg/per kg body weight in 10-15 minutes intravenous infusion intraoperatively
Gabapentin	Oral administration: 2 hours before surgery at a dose of 300-600 mg,
Pregabalin	Oral administration: 1-12 hours before surgery in a dose of 150-300 mg
Dexmedetomidine	Intravenous dosage: · in premedication up to 30 min. intravenous infusion (5-10 min), at a dose of 0.5-2 mcg/per kg body weight · intraoperatively and/or postoperatively, intravenous infusion 0.2-0.5 mcg/kg/hour.
Clonidine	Oral administration or slow intravenous infusion (30-60 min.) · in premedication 30-90 min. before surgery at a dose of 3-5 mcg/per kg body weight · intraoperatively and/or postoperatively, intravenous infusion 0.2-0.3 mcg/kg/hour.

the severity, opioids should not be used in transdermal systems (patches). They are dedicated primarily to the treatment of chronic pain. It should be emphasized that administering a dose of an opioid in an arbitrary dose determined by the doctor at specific intervals (e.g., every 4-6 hours) makes it difficult to adjust the analgesic therapy to the patient's individual needs. However, the dependence of opioid administration on the patient's complaints about pain (the "in case of pain, administer..." pattern) is fraught with the risk of insufficient treatment, because usually many factors affect both the delay of drug administration and the reduction of the dose used [39]. Postoperative analgesia should aim to achieve the minimum effective analgesic concentration (MSSA) in blood serum and its maintenance throughout the treatment period. The opioid drug dose should be determined in the titration procedure, in which small doses of opioids, for example morphine (1-2 mg) or oxycodone (1-2 mg) are administered slowly intravenously every 3-5 min, until a significant reduction in the severity of postoperative pain. Maintaining the concentration of the drug at the level of MSSA is then followed by administering the analgesic by continuous intravenous infusion. The dose supporting the effective level of analgesia is, for the time interval corresponding to the opioid half-life, 1/2 of the loading dose [39].

Opioid analgesic titration chart

In a patient whose saturation/effective dose was 6 mg morphine, 3 mg morphine (6 mg/2) was eliminated during one half-life. This means that the hourly morphine demand for this patient is 1 mg (3 mg/3h- the half--life of morphine is 3 hours) and such a dose of morphine (1 mg/h) should be given to the patient by continuous intravenous infusion to maintain minimum effective concentration of serum morphine.

After titrating the demand for morphine, it can be converted into another opioid analgesic by means of equivalent doses of opioids, which are defined as doses of various opioids resulting in the same analgesic effect. They are shown in Table III. It should be emphasized that in the postoperative period, the so-called piercing pain associated with painful procedures (e.g., dressing changes, stent reposition) or rehabilitation. Performing these activities should be preceded by intravenous administration of an additional dose of a painkiller.

Accurate adjustment of analgesics dosage to the patient's current demand is ensured by the so-called Patient Controlled Analgesia, or PCA, developed based on the concept of negative feedback. It assumes that if the patient does not feel the pain because it has been relieved by the previous dose of the medicine, he does not request the administration of another dose until the pain stimulation reappears. In this method, when the patient begins to feel pain, he himself starts the dosing system (microprocessor-controlled automatic syringe) by pressing the switch within reach of his hand. After switching on the PCA system, the patient receives a dose of medicine programmed by the medical team, and the PCA system secures the so-called lockout time, which is a temporary blockage of the dispensing system that will remain inactive until the end of the lockout time (despite the patient's attempts to activate it). This limit the possibility of opioid overdose. The PCA method allows optimal adjustment of the opioid dosage to the severity of postoperative pain. The dosage of the opioids most commonly used in the PCA system is presented below in Table IV.

It should be noted that PCA has also been used in local anesthesia techniques for the administration of LA (local anaesthetics) through a catheter inserted into the epidural space (Patient Controlled Epidural Analgesia; PCEA), in the area of nerve plexus, peripheral nerves, intraoperative or surgical wound (Patient Controlled Regional Analgesia; PCRA). NCA (Nurse Controlled Analgesia) is a certain modification to this method, in which the care team, at the patient's request, administers an analgesic intravenously in a dose and time interval determined earlier by the physician.

Sequential therapy is an interesting treatment strategy in the treatment of postoperative pain. It consists in changing the parenteral analgesic form to oral after prior determination of the drug's optimal dosage (e.g., the titration method described above) and obtaining effective pain relief. In sequential treatment, drugs with good bioavailability and good absorption via the gastrointestinal tract are available, both in parenteral form and oral (morphine*, oxycodone**). This way of conduct allows for a change in the pathway of analgesics from parenteral to oral. It is the most convenient for patients, especially when the drug is used in a controlled release formulation, which is administered only twice a day (every 12 hours). Such therapy can be initiated in a hospital and later continued at home.

** conversion rate of morphine administered intravenously into oral route is 1:3. This means that a higher dose of morphine should be administered orally compared to that which was effective when using the drug intravenously.*

*** conversion rate of oxycodone administered intravenously into oral route is 1:2. This means that a higher dose of oxycodone should be administered orally compared to that which was effective when using the drug intravenously.*

Opioids most frequently used in the perioperative period and their dosage are presented in Table V and in algorithms 2 and 3.

Opioid drugs not recommended

Current standards for treating postoperative pain do not recommend the use of pethidine whose active metabolite - norpethidine - causes a neurotoxic effect, especially when using repetitive doses of pethidine. Half-life prolongation of norpethidine is particularly important in the pediatric population. If pethidine is used during labor, the newborn may be exposed following placental transfer, which can affect the drug's neurological status and, in some cases, lead to seizures. However, in the case of patients over 65 years of age, due to the risk of accumulation of norpethidine, caused by the possibility of impairment of liver and kidney function - there is an increased risk of CNS adverse effects, including agitation, confusion, movement disorders, dizziness, as well as nausea and vomiting. It should also be emphasized that there is no data indicating the better effectiveness of pethidine in the pharmacotherapy of pain compared to other opioids.

Also, pentazocine (kappa opioid receptor agonist), in addition to poor analgesic activity (5–10-fold weaker than morphine) also exhibits an increased risk of hallucinogenic and dysphoric effects. For this reason, this drug should not be used in the treatment of postoperative pain.

Key information:

- The use of opioids may cause side effects. From the point of view of safety of therapy, their knowledge and monitoring of the patient's condition is of fundamental importance.
- Due to the risk of excessive sedation, hypoventilation, hypoxia or respiratory depression, patients who are given opioids in the postoperative period should be monitored (state of consciousness, respiratory rate, pulse oximetry).
- The combination of tramadol with paracetamol allows to reduce the doses of both drugs, while improving both the therapeutic effectiveness (better analgesic effect) as well as the tolerance of drugs (reducing the frequency and severity of side effects). The synergism of the action of tramadol and paracetamol has been confirmed clinically.
- Due to the additional action on opioid kappa receptors (in addition to acting on opioid receptors), oxycodone should be preferred in relieving visceral postoperative pain of high severity.
- Pethidine and pentazocine are not recommended for pain relief in the perioperative period.
- In acute postoperative pain, opioids in transdermal patches should not be used because of frequent postoperative pain intensity. They are primarily intended for the treatment of chronic pain.
- Combined pharmacotherapy of postoperative pain includes the use of different groups of analgesics with different mechanisms of action, including nonsteroidal anti-inflammatory drugs, metamizole or paracetamol in combination with opioids. This induces "the effect of reduced demand for opioids": 25-30% reduction in the need for morphine when combined with NSAIDs and a 20% reduction when combined with paracetamol in the first 24 hours after surgery.
- Significant reduction of opioid dosing and side effects associated with their use in the perioperative period is

also possible due to the use of block anesthesia techniques (central block, plexus and peripheral nerve block, interfascial nerves block, operative wound infiltration) and/or coanalgesics (lidocaine, ketamine, dexamethasone, magnesium sulfate, gabapentin or pregabalin).

THE USE OF COANALGESICS IN POSTOPERATIVE PAIN RELIEF

Due to adverse reactions that may be caused by opioid analgesics, the currently proposed strategies to optimize perioperative management significantly reduce or completely eliminate analgesics (opioid free anesthesia/analgesia; OFA) [5]. These strategies rely on the use of multimodal therapeutic approaches using both block anesthesia techniques and multidirectional pharmacotherapy with the inclusion of coanalgesics, that is, drugs that "per se" are not analgesic, but by means of various mechanisms modify the phenomenon of pain formation [37]. Coanalgesics most commonly used in the perioperative period are: lidocaine, ketamine, dexamethasone, magnesium sulfate, gabapentin or pregabalin, clonidine or dexmedetomidine. The dosage of individual drugs from this group is shown in Table VI.

Lidocaine

The mechanism of action of intravenous lidocaine consists in quenching spontaneous excitations of foci in nerve fibers damaged during surgery. This drug, administered intravenously in perioperative period, also exhibits an anti-inflammatory effect by limiting the action of proinflammatory factors and inhibiting the phenomenon of "priming" of granulocytes, which prevents excessive release of pro-inflammatory cytokines and free radicals. The mechanisms leading to the development of so-called neurogenic inflammation are limited in the area of tissue damage, and this reduces peripheral sensitization and hyperalgesia. It should be emphasized that the therapeutic concentrations of lidocaine administered intravenously at the recommended doses are significantly lower than the drug serum levels, at which cardio- and neurotoxic effects occur [3].

Lidocaine - as a component of multimodal analgesia - used intravenously in the perioperative period allows reduction of opioid doses or complete abandoning. It significantly reduces the intensity of pain in the early postoperative period at rest and during activity (deep breathing, coughing), as well as frequent nausea and vomiting. It accelerates the return of gastrointestinal function after surgery (especially after abdominal surgery) and shortens the time of hospitalization. It has also been demonstrated that perioperative intravenous infusion of lidocaine induces preventive analgesia, i.e., with an action time greater than 5.5 times the lidocaine half-life, i.e.> 8 hours after the end of administration. Intravenous infusion of lidocaine is indicated primarily in open and laparoscopic abdominal surgery.

Meanwhile, the effectiveness of intravenous administration of lidocaine in this group of procedures is also confirmed by many studies; the limited number of clinical trials indicates the benefits use in patients undergoing prostate, breast, thoracic and spine surgery. However, the benefits of intravenous lidocaine infusion in patients after cardiac surgery, laparoscopic nephrectomy, transabdominal hysterectomy and hip replacement have not been confirmed. So far, neither optimal dosage, nor starting point of intravenous infusion of lidocaine or the time of duration have been clearly established. Published clinical trials suggest that intravenous lidocaine infusion may be initiated 30 minutes before skin incision (induction of preventive analgesia) or (most commonly) during induction of anesthesia. The most common is an initial bolus dose of 1.5 mg/kilogram of body weight (dose range: 1-3 mg/kilogram of body weight), then, a continuous intravenous infusion of lidocaine at a dose of 1.5 mg/kilogram of body weight/h (dose range 1.0 - 3.0 mg/kilogram of body weight/hour) is continued intraoperatively. The infusion is usually continued in the postoperative period – for a few dozen to 48 hours after the surgery. At the above dosing, plasma concentrations of lidocaine are in the safe range of 1 to 5 mcg/ml. In these concentrations, lidocaine does not block the conductivity in the peripheral nerves [11, 30].

The dose of lidocaine should be reduced in conditions where the free fraction of drug increases: acidosis, hypercapnia, hypoxia, hypoproteinemia and impaired liver or kidney function. In patients with circulatory, hepatic and/or renal insufficiency, the dose of lidocaine should be reduced and the cardiovascular function monitored.

Ketamine

Ketamine, acting through inhibition of NMDA receptor activation, induces effective analgesia and prevents the development of persistent postoperative pain, and by activating the sympathetic system ensures the patient's hemodynamic stability in the perioperative period [14]. Ketamine is also characterized by:

- no inhibitory effect on the respiratory center,
- expanding effect on the bronchioles,
- no inhibition of reflexes from the upper respiratory tract,
- no hypotensive effect,
- no immunosuppressive effect,
- blocking the activation of pro-inflammatory mediators (cytokines).

In addition to analgesia, the use of ketamine in the perioperative period is associated with a significantly lower incidence and severity of postoperative nausea and vomiting. In addition, the antidepressant action of ketamine used in subanesthetic doses prevents the development of post-traumatic stress disorder in patients after extensive surgery [18, 34].

Magnesium sulphate ($MgSO_4$)

A blocker of the ion channel coupled to the NMDA receptor which acts as an inhibitor for the activation of proinflammatory cytokines. Used as an intravenous infusion in the perioperative period, it reduces both the need for opioid analgesics and the intensity of postoperative pain, especially after operations in the colon, cholecystectomies, urological and orthopedic procedures. [15,30].

Corticosteroids

The mechanism of analgesic effect of corticosteroids used in the perioperative period is associated with their anti-inflammatory, anti-edematous action, inhibiting the activation of proinflammatory cytokines and probably also with direct action inhibiting the electrical activity of the damaged nerve by stabilizing the neuronal cell membranes and facilitating repair processes in intraoperatively damaged nerve fibers. An additional effect of glucocorticosteroids

Tab. VII. Epidural analgesia — recommended drugs and doses [39].

TREATMENT - LOCATION	LEVEL OF EPIDURAL CATHETERIZATION	INITIAL DOSE	CONTINUOUS INFUSION
Lower extremities	L 3 - L 5	1–2 ml per segment	0.125-0.2% bupivacainum or 0.2% ropivacaine
Abdominal and pelvic surgery	Th 8-Th 10	Titration: 5 ml every 10 min	+ fentanyl 2mcg/ml or Sufentanil 0.5–1 mcg/ml
thoracic surgery and epigastric surgeries	Surgical incision midline Th 4-Th 8	0.5 ml per segment Titration: 5 ml every 10 min	flow 2–8 ml/hour

Tab. VIII. Block of peripheral nervous system structures in perioperative period - indications, methods, and dosage of local anaesthetics (LA) [39].

SURGICAL PROCEDURES/INJURY	TYPE OF BLOCK	RECOMMENDED LA DOSAGE
Surgical operations in the abdominal cavity via midline incision	Rectus Sheath Block - RSB	Bilateral: 10-15 ml 0.25% bupivacaine or 0.375% ropivacaine per side
Surgical procedures in the abdominal cavity with access other than median-sector	Transversus Abdominis Plane Block - TAP block	Unilateral: 20-30 ml of 0.25% bupivacaine or 0.375% ropivacaine Bilateral: 10-15 ml 0.25% bupivacaine or 0.375% ropivacaine per side
	Quadratus Lumborum Block - QLB	Unilateral: 20-30 ml 0.25% bupivacaine or 0.375% ropivacaine Bilateral: 10-15 ml 0.25% bupivacaine or 0.375% ropivacaine per side
Surgical procedures in the thoracic area (thoracotomy, VATS), abdominal cavity (in the epigastric region, nephrectomy), analgesia after chest injuries	Erectus Spinae Block - ESP	Unilateral: 20-30 ml 0.25% bupivacaine or 0.375% ropivacaine Bilateral: 10-15 ml 0.25% bupivacaine or 0.375% ropivacaine per side
Breast surgery	Pectoral Nerve Blocks I and II - PECS I and PECS II), Serratus Plane Block - SPB or Erectus Spinae Block - ESP.	10-20 ml (PECS I, PECS II), 20-30 ml (SPB, ESP) 0.25% bupivacaine or 0.375% ropivacaine
Surgical procedures in the area of the shoulder and proximal arm	Brachial plexus block, access between scalene muscles	Initial bolus: 15-20 ml 0.5% ropivacaine or 0.375% bupivacaine Continuation of continuous infusion via implanted catheter at a rate of 2-6 ml/hour: 0.15-0.3% of ropivacaine or 0.125-0.25% bupivacaine
Operative procedures in the area of the distal arm, elbow, forearm, wrist and hand	Brachial plexus block, supraclavicular, subclavicular or axillary access (the last access: distal forearm, wrist, hand)	Initial bolus: 20 ml 0.5% ropivacaine or 0.375% bupivacaine Continuation of continuous infusion via implanted catheter at a rate of 3-8 ml/hour: 0.15-0.3% of ropivacaine or 0.125-0.25% bupivacaine
One-sided: thoracotomy, extensive breast surgery (Th 4-5), rib fracture, nephrectomy (Th7) Bilateral: laparotomy (Th 8), resection of bladder (Th 10)	Thoracic paravertebral block	Unilateral: initial bolus 15-20 ml 0.5% ropivacaine or 0.375% bupivacaine Continuation of continuous infusion through an implanted catheter at a speed of 4-8 ml/hour: 0.15-0.3% of ropivacaine or 0.125-0.25% bupivacaine Bilateral: 10-15 ml 0.25% bupivacaine or 0.375% ropivacaine per side
Hip arthroplasty, femur arthroplasty	Lumbar plexus block	Initial bolus: 20 ml 0.25-0.5% of ropivacaine or 0.25-0.375% bupivacaine Continuation of infusion through implanted catheter at a speed of 4-8 ml/hour 0.15-0.3% of ropivacaine or 0.125-0.25% bupivacaine
Femoral fracture, selected knee surgeries	Femoral nerve block	Initial bolus: 20 ml 0.25-0.5% of ropivacaine or 0.2-0.375% bupivacaine Continuation of continuous infusion through implanted catheter at a speed of 4-8 ml/hour 0.15-0.3% of ropivacaine or 0.125-0.25% bupivacaine
Knee alloplasty posterior cruciate ligament reconstruction	Femoral and sciatic nerve block	Initial bolus: 10-15 ml 0.25-0.5% ropivacaine or 0.25-0.375% bupivacaine/nerve Continuation of infusion: 3-6 ml/hour 0.15-0.25% ropivacaine or 0.1-0.2% bupivacaine
Surgeries in the lower thigh, ankle, and foot	Sciatic and femoral nerve block	Initial bolus: 10-15 ml 0.25-0.5% ropivacaine or 0.25-0.375% bupivacaine/nerve Continuation of infusion: 3-6 ml/hour 0,15-0.25% ropivacaine or 0.1-0.2% bupivacaine.

in the postoperative period is antiemetic activity. The steroid most commonly used in the perioperative period is dexamethasone [35]. In operated patients after administration of a single dose of dexamethasone, there was no increase in infection rate or delayed healing of postoperative wounds, but during the first 24 hours after surgery, an increase in blood glucose was observed, compared to the group of patients who did not receive dexamethasone [35].

Gabapentin and pregabalin

Gabapentin and pregabalin are medicines considered as anti-epileptic. These drugs are blockers of voltage-gated ion channels for calcium ions in the structures of the nervous system. Blocking the transport of calcium ions in damaged neurons during surgery causes a significant reduction in the release of "probiotic" neurotransmitters and inhibition of the transmission of pain information from the area of surgical trauma, especially after extensive surgery [10, 42]. The use of gabapentin and pregabalin in the preoperative period reduces the severity of postoperative pain and reduces the need for opioids in the postoperative period [42]. Patients receiving gabapentin and pregabalin may experience excessive sedation, dizziness and blurred vision in the postoperative period.

α-2 adrenergic receptor agonists (clonidine, dexmedetomidine)

These drugs, acting in the structures of the nervous system, inhibit the release of pronociceptive neurotransmitters (substance P and stimulant amino acids), as well as "open up" potassium channels

Tab. IX. Dosage of local anesthetic drugs during infiltration of surgical wound or applications into administration into peritoneal cavity [39].

SURGICAL PROCEDURES/INJURY	TECHNIQUE	RECOMMENDED DOSAGE/CONTINUOUS INFUSION OF LOCAL ANAESTHETICS (LA)
Applicable for any type of surgery	Infiltration anesthesia of planned incision line/ postoperative wound/or implantation of catheter into the postoperative wound	Bolus: 10-30 ml of 0.25% bupivacaine or 0.375% ropivacaine Continuous infusion: 3–8 ml/hour 0.125-0.25% bupivacaine or 0.2% ropivacaine through a catheter implanted into the wound
Laparoscopic abdominal surgery	Infiltration of planned trocar entry site and/or intraperitoneal administration via laparoscopic ports after surgery.	0.25% bupivacaine or ropivacaine, 5 ml for each trocar entry site and/or 20-30 ml of 0.25% bupivacaine or ropivacaine

inducing hyperpolarization of neurons. The corollary of these processes is sedation (associated with the activation of α-2 receptors in the locus coeruleus) and inhibition of transmission of pain information from the operative field, manifested by a reduction in the severity of postoperative pain, and the possibility of reducing opioid doses used in the postoperative period [4, 30]. The most common side effects that limit the use of α-2 adrenergic receptor agonists are arterial hypotension, bradycardia and sedation.

Key information

- An important element of combined pharmacotherapy in postoperative pain are coanalgesics, which "per se" do not act as analgesics, but modify the phenomenon of pain in various mechanisms: they contribute to the improvement of postoperative analgesia and reduce the dose of analgesics required, including opioids, and therefore reduce the frequency of complications associated with their use.
- The most commonly used coanalgesics in the perioperative period are: lidocaine, ketamine, dexamethasone, magnesium sulphate, gabapentin or pregabalin, clonidine or dexmedetomidine.
- Intravenous infusion of lidocaine is indicated primarily in open and laparoscopic abdominal surgery. A certain number of clinical trials also indicates the benefits of intravenous lidocaine infusion in patients undergoing prostate, breast, thoracic and spine surgery.
- In addition to analgesic activity, the use of ketamine in the perioperative period is associated with a significantly lower incidence and severity of postoperative nausea and vomiting. Furthermore, the antidepressant action of ketamine prevents the development of post-traumatic stress disorder in patients after extensive surgery.
- Dexamethasone used in the perioperative period is anti-inflammatory, anti-edematous, inhibits the activation of proinflammatory cytokines and the electrical activity of intraoperatively damaged nerve fibers. It also has an antiemetic effect. After administering a single dose of dexamethasone in patients, no increase in the frequency of infections or delayed healing of postoperative wounds was observed, but the possibility of increased blood glucose level should be expected.
- Magnesium used as an intravenous infusion in the perioperative period reduces both the need for opioid analgesics and the intensity of postoperative pain, especially after operations in the field of colon, cholecystectomies, urological and orthopedic procedures.
- The use of gabapentin and pregabalin in the preoperative period reduces the severity of postoperative pain and reduces the need for opioids in the postoperative period. Patients receiving these medicines may experience excessive sedation, dizziness and blurred vision in the postoperative period.
- α-2 adrenergic receptor agonists (dexmedetomidine, clonidine) inhibit the transmission of pain information from the operative field. This allows to reduce the severity of postoperative pain and enable the reduction of opioid doses used in the postoperative period. The most common side effects that limit their use are arterial hypotension, bradycardia and sedation.

TECHNIQUES OF BLOCK ANESTHESIA IN POSTOPERATIVE PAIN RELIEF

Techniques of block anesthesia are very important methods of relieving postoperative pain. They allow effective relief of pain which appears not only at rest, but also - what is extremely important - in dynamic conditions. This is essential for fast mobilization and effective rehabilitation of patients after surgery. In addition, these techniques reduce the dose of block analgesics to be used, including opioids, which also improves the safety of postoperative pain therapy. However, it should be emphasized that the real benefits of using block anesthesia techniques are closely related to the experience and skills of the anesthesia team, the ability to supervise the patient and knowledge and training of the entire medical and care team dealing with patient care in the postoperative period.

In everyday practice, central block (most often continuous epidural analgesia), paravertebral block, plexus and peripheral nerve block, and interfascial block are used [7].

Central block

Continuous epidural analgesia is a very effective method of relieving postoperative pain, especially after extensive chest and abdominal surgery associated with significant tissue damage and, as a result, high-intensity postoperative pain. Particular benefits of continuous epidural analgesia can be observed in patients at high risk of cardiac and pulmonary complications and prolonged intestinal atony and postoperative ileus. Many studies indicate a reduction in the incidence of postoperative cardiovascular, pulmonary and thromboembolic complications, as well as a faster return of gastrointestinal tract function in patients undergoing extensive intervention in the field of gastrointestinal surgery, in whom continuous epidural anesthesia was used compared to classical analgesia using opioids [32].

Epidural analgesia allows for a significant reduction in the opioid doses required for use, which translates into a decrease in the frequency and severity of side effects associated with their use. Compared to analgesia, which can be provided with the use of systemic opioids, it more effectively relieves pain in dynamic conditions, which allows early rehabilitation and rapid activation of patients even after extensive surgery. In the case of thoracotomy, continuous epidural anesthesia further reduces the incidence of persistent

postoperative pain, which is a very real problem and depending on the surgical technique used, it occurs at a frequency of 30-50% [41].

It should be remembered that continuous epidural analgesia is an invasive technique that requires skills and experience and strict adherence to contraindications from the anesthesiologist, also such resulting from anticoagulant therapy used in many patients [17].

It should be emphasized that the decision to use epidural analgesia in the treatment of postoperative pain must be considered in relation to a number of conditions, including considering the possibility of adequate postoperative surveillance of the patient as well as adverse effects and complications of this method of analgesia (arterial hypotension, bradycardia, respiratory failure, hematoma or epidural abscess). The team providing medical care to the patient taking epidural analgesia should be trained and prepared to implement prevention methods, early diagnosis and treatment of adverse events and complications (modification in doses of drugs, treatment of arterial hypotension or bradycardia, removal of epidural catheter with safe intervals from the last dose of anticoagulant, administration of opioid antagonists in the event of respiratory depression, decompression with laminectomy for hematoma or perispinal abscess) [20].

Table VII presents the proposed dosing regimens for epidural drugs and the optimal choice of insertion site for epidural catheter depending on the location of the surgical procedure.

Blockade of peripheral nervous system structures

The component of multimodal postoperative pain therapy may also be other techniques of block anesthesia, including plexus and peripheral nerve block and interfascial block [33].

In the case of procedures performed within the limbs, a safe and effective technique allowing to ensure intra- and postoperative analgesia are plexus block (brachial in the case of the upper limb and lumbar in the case of the lower limb) or relevant peripheral nerves (radial, median and ulnar for the upper limb and sciatic and femoral for the lower limb). Implantation of the catheter in the vicinity of the aforementioned nerve structures allows for the continuation of analgesia for many hours or days after surgery and contributes to the reduction of non-opioid analgesics and opioids necessary for the application and, which is extremely important, facilitates postoperative rehabilitation [19].

The techniques described above are more and more widely used thanks to the introduction of ultrasound into the daily practice of anesthesia, which allows the identification of nerve structures and observation of local anesthetic spread, which significantly contributes to the improvement of efficacy and safety of ultrasound guided anesthesia.

Another group of regional analgesic techniques, increasingly used after many surgical procedures within the chest and abdominal cavity, are interfascial block [2, 12, 13].

In these blocks (under the guidance of ultrasonography), a local anesthetic is administered to the space between the fasciae of particular muscles where there are sensory nerves supplying the appropriate areas of the chest or abdominal cavity. These blocks performed before surgery allow to reduce the intraoperative demand for opioids, reduce pain intensity in the immediate postoperative period, and use lower doses of analgesics in the postoperative period.

The following may be performed for intra-abdominal surgery [6]:

- Rectus Sheath Block, RSB,
- Transversus Abdominis Plane Block, TAP,
- Quadratus Lumborum Block – QLB.

Rectus Sheath Block (RSB) assumes the reciprocal administration of LA to the space between the rectus abdominal muscle and the posterior layer (lamella) of rectus sheath, where intercostal nerves from IX to XI run, or more precisely, where the frontal cutaneous branch which supply the skin of the anterior abdominal wall pass. RSB can be an element of intra- and postoperative multimodal analgesia for the treatment of umbilical and abdominal hernia as well as other procedures performed via median incision [21].

The transverse abdominis plane (TAP) block procedure involves the administration of LA to the space between the internal and transverse oblique muscles in which the anterior branches of the spinal nerve pairs from Th7 to L1 run, supplying the anterolateral abdominal wall. This technique can be used as a component of multimodal intra- and postoperative analgesia for abdominal surgery (gynecological procedures, Caesarean section, appendectomy, inguinal hernia repair) and for laparoscopic procedures [1].

Quadratus Lumborum Block (QLB) involves the administration of LA in the antero-lateral border of the quadratus lumborum muscle, which causes wide distribution of LA into the paravertebral space in the thoracic region and ensures long-lasting analgesia after abdominal surgery. It may be an alternative to paravertebral block or epidural analgesia, however, it should be remembered that in the case of laparotomy it must be performed bilaterally [43].

For surgical operations in the chest and in the breast gland, interfascial block are used: W

- PECS I and PECS II (Pectoral Nerve Block I and II),
- Serratus Plane Block (SPB),
- Erectus Spinae Block (ESP).

PECS I and PECS II are interfascial block within the thoracic wall. Most often they are performed jointly (PECS I + PECS II), and the block technique involves the administration of LA to interfascial spaces between the larger and smaller breast muscles and between the pectoralis minor and major muscles, which block the lateral branches of the Th2-4 intercostal nerve, the intercostobrachial nerve and the long thoracic nerve. This block is performed primarily during breast surgery - mastectomy, quadrantectomy, and breast surgery with extended axillary revision [24].

SPB is an interfascial block within the chest, which consists in the administration of LA at Th5 height between the midaxillary line and posterior axillary line, to the interfascial compartment between the latissimus dorsi and the serratus anterior. The scope of block includes intercostal Th3-9 nerves and thoracodorsal nerve, and the indications for performance are intra- and postoperative analgesia for chest procedures (VATS – videothoracoscopy, chest

tube drainage) and extensive mammary gland reconstruction with the shift of musculocutaneous flaps from the latissimus dorsi [29].

The last of the aforementioned interfascial block of the chest is erector spinae plane (ESP) block. It consists in administering LA under ultrasound guidance to the interfascial space between the erector spinae and the intercostal muscles at the level of the transverse processes on Th5 level. The clinical effect of this block is due to anesthesia of the neural structures of the paravertebral space (branches of the spinal nerves and the sympathetic trunk). The range of block after execution at Th5 height usually includes segments from Th1 to L1. This technique is applicable to procedures performed within the chest (thoracotomy, VATS), abdominal cavity (epigastrium surgeries, nephrectomies), as a method of analgesia after chest injuries or chronic pain therapy (e.g., in the case of intercostal neuralgia or developing chronic postoperative pain after thoracic surgery) [8]. Interfascial block performed as a "single shot" technique have a time limit limited by the duration of LA operation, in addition only some of them have the potential to relieve visceral pain. Nevertheless, the right choice of blockade adapted to the extent and location of the surgical procedure and, if appropriate, the insertion of a catheter into the appropriate interfascial space and continuation of the continuous block allows to optimize the strategy of postoperative pain relief selected individually for each patient. Table VIII presents peripheral nerve block most frequently used in relieving postoperative pain.

When planning postoperative analgesia, in the case of contraindications or lack of the possibility to perform one of the central or peripheral block described above, it is also worth remembering the simple and safe technique of block anesthesia, or infiltration of the surgical wound with an anesthetic nerve block [16]. The performance of this procedure during surgery (optimally before the beginning) relieves postoperative pain and allows the use of lower doses of analgesics in the immediate postoperative period. In addition, implantation into the surgical wound of a special catheter connected to an elastomeric pump, which is small in size and requires no power supply, allows for continuation of this method of analgesia for a long time (even a few days), also in dynamic conditions, during the patient's mobilization and rehabilitation. It should be emphasized that the use of "closed systems" (catheter + elastomeric pump filled once in sterile conditions) eliminates the risk of postoperative wound infection. Table IX presents the dosage of local anesthetic drugs during infiltration of the surgical wound or intraperitoneal injection.

In conclusion, it is currently considered that the standard in the treatment of postoperative pain should be the use of multimodal analgesia, because combining drugs with different mechanisms of action with regional anesthetic techniques allows optimal control of postoperative pain and reduction of analgesics necessary to provide effective analgesia, including opioids. This strategy helps to reduce postoperative complications, improve the comfort and satisfaction of patients with surgery [37].

Key information

- Continuous epidural analgesia is an effective method of relieving postoperative pain, especially after extensive chest and abdominal surgery associated with high-intensity postoperative pain. Particular benefits of continuous epidural analgesia may be associated with patients at high risk of cardiac and pulmonary complications as well as prolonged intestinal atony and postoperative gastrointestinal obstruction.
- Epidural analgesia allows for a significant reduction in the opioid doses required for use, which translates into a decrease in the frequency and severity of side effects associated with their use. Compared to analgesia, which can be provided with the use of systemic opioids, epidural analgesia relieves pain more effectively in dynamic conditions, which allows early rehabilitation and rapid mobilization of patients even after extensive surgery.
- The safe use of epidural analgesia requires proper postoperative supervision of the patient. The team providing medical care to patients should be trained and prepared to implement methods for preventing, early diagnosis and treatment of adverse events and complications of this method.
- An alternative to epidural analgesia or paravertebral block in many clinical situations may be more widely used interfascial block. In these blocks, under the guidance of ultrasound, the local anesthetic drug is deposited into the space between the fascia of individual muscles, in which there are sensory nerves supplying the appropriate areas of the chest or abdomen.
- The most commonly performed in abdominal surgery are: Rectus Sheath Block (RSB), Transversus Abdominis Plane Block (TAP) or Quadratus Lumborum Block (QLB).
- The following interfascial blocks are used for surgical operations within the throat or breast gland: PECS I and PECS II (Pectoral Nerve Block I and II), Serratus Plane Block (SPB) or Erectus Spinae Block (ESP). ESP block can also be performed during selected abdominal cavity procedures (epigastrium surgeries, nephrectomies) and as a method of analgesia after chest injuries or in the treatment of selected chronic pain syndromes.
- The techniques described above are more and more widely used thanks to the introduction of ultrasound into the daily practice of anesthesia, which allows the identification of nerve structures and observation of the local anesthetic drugs' spread, which significantly contributes to the improvement of efficacy and safety of ultrasound guided anesthesia.

ANALGESIC TREATMENT DEPENDING ON THE EXTENT AND DEGREE OF TISSUE INJURY

Comments

- The categorization of treatments according to the severity of pain refers to treatments performed in planned mode.
- In the case of emergency procedures, with severe inflammatory, ischemic lesions etc., the pain category is usually increased by one degree, e.g., laparotomy in OZT is category IV.
- Classic bariatric procedures are within the scope of surgery of the stomach and small intestine.
- In case of severe postoperative pain, the patient should receive a strong analgesic, regardless of the category of surgery.
- The patient's discharge report should contain precise information for the patient - what medicines and doses should be used at home (a prescription for these medicines should be written for the patient), information for the general practitioner - regarding the need to continue using analgesics at home.

SURGERY COMBINED WITH MINOR TISSUE INJURY – ALGORITHM OF CONDUCT 1

Surgical procedures in which postoperative pain intensity is <4 on the NRS scale, e.g.

- excision of skin lesions,
- excision of subcutaneous tissue and soft tissues lesions,
- incision of soft tissue abscesses,
- excision of regional lymph nodes (cervical, axillary and inguinal),
- inguinal, femoral and umbilical hernia surgeries,
- replacement of expander with prosthesis,
- local breast tumor excision, breast quadrant excision, mastopexy, reduction plastic surgery,
- surgery of lower extremity varicose veins (classic and mini-invasive procedures).

Pharmacotherapy – before surgery

In order to induce the effect of analgesia in advance, intravenous administration of the following drugs should be considered (drug dosage according to table I):

- metamizole,
- and/or paracetamol,
- and/or NSAIDs before surgery (increased risk of intraoperative bleeding after NSAID administration).

Pharmacotherapy – after surgery:

Monotherapy or combination therapy consisting of non-opioid analgesics, intravenous administration of the following drugs should be considered (drug dosage according to table II):

- metamizole,
- and/or paracetamol,
- and one medicine from the NSAIDs group.

For pain with an intensity ≥ 4 on the NRS scale despite the use of combination therapy with non-opioid analgesics, tramadol should be administered intravenously or orally at a dose of 25 mg by NCA (Nurse Controlled Analgesia) until satisfactory pain control.

In case of contraindications to the use of tramadol, intolerance or lack of effect, a strong opioid (e.g., oxycodone or morphine) should be used at a low dose, e.g., 2 mg i.v. administered every 3-5 minutes until satisfactory relief of pain.

Regional analgesia

Before surgery in order to induce the effect of analgesia in advance, it is recommended to:

- infiltrate the planned incision line with local anesthetic (LA); dosage of LA according to table IX.
- TAP block or iliohypogastric and ilioinguinal nerve or RSB in the case of hernioplasty; dosage of LA according to table IX.
- PECS I and PECS II or SPB block in the case of breast implants from category; dosage of LA according to table IX.

After surgery depending on the type, it is recommended to:

- Reinfiltrate wound with LA

in the case of a large surgical wound, the following can be considered:

- continuous infusion of LA through a catheter implanted into the wound or interfascially (using an automatic syringe or an elastomeric pump).

SURGERY COMBINED WITH MODERATE TISSUE INJURY - ALGORITHM OF CONDUCT 2

Surgeries in which intensity of postoperative pain is > 4 points according to NRS, but after which duration of pain is usually shorter than 3 days:

- thyroid surgery,
- surgical treatment of Zenker's diverticulum,
- mastectomy (simple, modified radical),
- placement of expander beneath pectoralis major (1st stage of breast reconstruction),
- diagnostic versus exploratory laparoscopy,
- removal of the appendix (classic, laparoscopic),
- laparoscopic cholecystectomy,
- incisional hernia repair and large abdominal wall hernias (classic, laparoscopic access),
- laparoscopic surgery of esophageal hiatus hernia,
- laparoscopic bariatric procedures,
- procedures carried out using robotic-assisted surgery techniques,
- tracheostomy,
- varicose veins surgery or rectal fissure,
- embolectomy,
- procedures using TEMs,
- amputations including loss of fingers, feet, hands.

Pharmacotherapy – before surgery:

In order to induce the effect of analgesia in advance, intravenous administration of the following drugs should be considered (drug dosage according to table II):

- metamizole,
- paracetamol,
- and/or NSAIDs before surgery (increased risk of intraoperative bleeding after NSAID administration).

In order to reduce the necessary doses of analgesics, including opioids, and to improve the quality of analgesia, preoperative use of selected coanalgesics (during the induction of anesthesia) should be considered (dosage according to table VI):

- lidocaine administered intravenously (do not use if one of the regional analgesia techniques given below is performed),
- magnesium sulphate,
- ketamine.

Pharmacotherapy - intraoperatively:

In selected category II treatments, intraoperative administration of coanalgesics should be considered (dosage according to table VI):

- lidocaine administered by intravenous infusion (do not use if one of the regional analgesia techniques given below is performed)
- magnesium sulphate via intravenously infusion

Pharmacotherapy

use of the following should be considered to induce the effect of analgesia in advance

- metamizol (1–2.5 g) *i.v.*
- and/or paracetamol (0.5-1.0 g) *i.v.*

in combination with NSAIDs, for example:
- ketoprofen 50–100) mg *i.v.*
- or dexketoprofen (25-50 mg) *i.v.*

after excluding specific contraindications, including the risk of increased intraoperative bleeding after NSAIDs

Regional analgesia:

use of the following is recommended to induce the effect of analgesia in advance:

- infiltration of planned incision line with LA - LA dosage *according to table IX*
- TAP block oriliohypogastric nerve and ilioinguinal nerve block or RSB in the case of hernioplasty - dosage of LA *according to table VII*
- PECS I and PECS II or SPB blocks in the case of category I breast surgeries - dosage of LA *according to table VII*

surgery

Pharmacotherapy

Monotherapy or combined therapy consisting of non-opioid analgesics administered intravenously or orally (drug dosage according to Table II):

- metamizol 1–2.5 g, every 6–12 hours (max. 5.0 g/day) *i.v. /per os*
- and/or paracetamol 0.5-1.0 g every 6 hours. (max. 4 g/day) *i.v. /per os*

in combination with NSAIDs, for example:
- ketoprofen (50–100 mg) *i.v./per os* every 12 hours
- or dexketoprofen (25-50 mg) *i.v./per os* every 8 hours

In the case of pain ≥ 4 on the NRS scale, despite combined therapy consisting in non-opioid analgesics, tramadol should be administered intravenously or orally at a dose of 25 mg by NCA. In case of contraindications to the use of tramadol, intolerance or lack of effect, a strong opioid should be used (*e.g. oxycodone or morphine*) at a low dose, e.g. ,2 mg i.v. administered every 3 – 5 minutes until satisfactory relief of pain.

Regional analgesia:

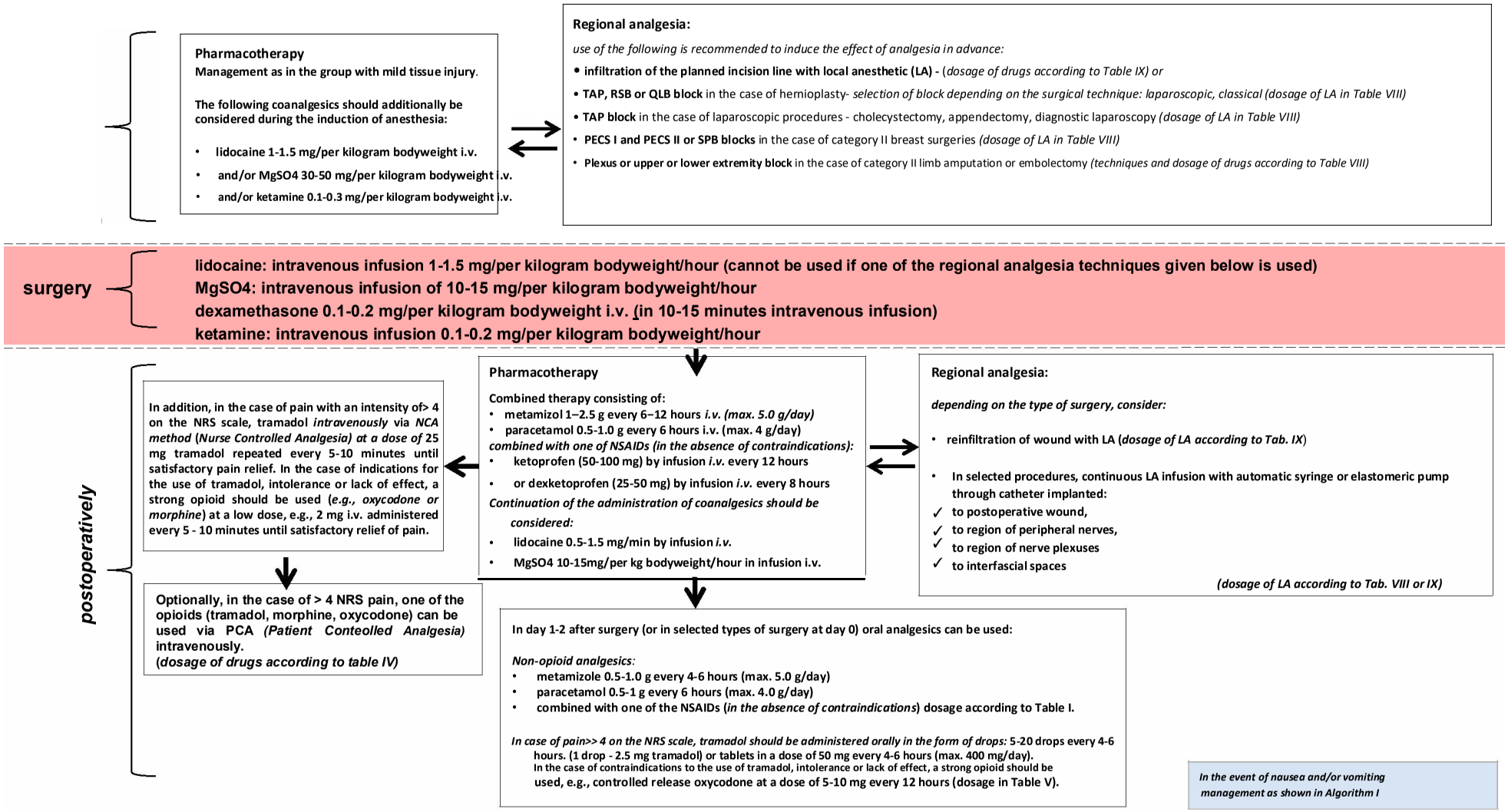
depending on the type, the following is recommended:

- reinfiltration of wound with LA (*dosage of LA according to Tab. IX*)
- in case of extensive surgical wound, a continuous LA infusion can be considered using an automatic syringe or an elastomeric pump through a catheter implanted to:
  - ✓ postoperative wound,
  - ✓ interfascially,
  - ✓ in the area of peripheral nerves.

(dosage of LA according to Tab. VIII or IX)

In case of nausea and/or vomiting: metoclopramide 10 mg i.v. or ondansetron 4-8 mg i.v. Caution! Metoclopramide and ondansetron should not be used in patients receiving tramadol, these patients may be given levomepromazine as an antiemetic at a low dose (12.5-25 mg) i.v.

Algorithm 1. Postoperative pain relief combined with minor tissue injury.



Algorithm 2. Postoperative pain relief combined with mediocre tissue injury.

- ketamine via intravenous infusion
- dexamethasone by intravenous infusion.

Pharmacotherapy – after surgery:

Combination therapy consisting of non-opioid analgesics administered intravenously or orally (dosage according to table II):

- metamizole,
- paracetamol,
- one of the NSAIDs

When using NSAIDs, contraindications for their use should be kept in mind and the use of a proton pump inhibitor should be considered for protection of the gastrointestinal tract. Protection of the GI with a proton pump inhibitor should be obligatorily applied if NSAIDs and dexamethasone are used as a coanalgesic. Administration of coanalgesics in the postoperative period may be considered (dosage according to table VI):

- lidocaine administered by intravenous infusion (do not use if one of the regional analgesia techniques given below is performed)
- magnesium sulphate via intravenously infusion

For pain with an intensity ≥ 4 on the NRS scale, occurring despite the combination therapy with non-opioid analgesics, tramadol should be administered intravenously or orally at a dose of 25 mg by NCA (Nurse Controlled Analgesia) until satisfactory relief of pain. In case of contraindications to the use of tramadol, intolerance or lack of effect, a strong opioid (e.g., oxycodone or morphine) should be used at a low dose, e.g., 2 mg i.v. administered every 3-5 minutes until satisfactory relief of pain. Optionally, one of the opioids (tramadol, morphine, oxycodone) administered by PCA (Patient Controlled Analgesia) in intravenous form can be used (drug dosage according to table IV). In 1-2 days after surgery (or in selected types of surgery on the same day), oral painkillers can be used – dosage of drugs in Tables I and IV.

Regional analgesia:

Before surgery, one of the following techniques should be used:

- infiltration of the planned incision line with LA (dosing of LA in Table IX),
- TAP, RSB or QLB block in the case of hernioplasty; selection of block depending on the surgical technique used: laparoscopic, classic- (dosing of LA in Table VIII),
- TAP block for laparoscopic procedures - cholecystectomy, appendectomy, diagnostic laparoscopy, other (dosing of LA in Table VIII),
- PECS I and PECS II or SPB block for stage II breast treatments (dosing of LA in Table VIII),
- plexus block, lower or upper extremity block in the case of type II limb amputation or embolectomy (techniques and dosage of drugs in Table VIII).

After surgery depending on the type, it is recommended to:

- reinfiltrate wound with LA.
- in selected type II treatments, a continuous LA infusion may be considered through implantation into the wound - interfascially or in the area of the plexus or nerve/nerves (the choice of techniques is given above) - catheter with an infusion pump or (optimally) elastomeric infusion pump
- fractionated dose method may also be considered, which is less recommended due to the higher risk of infectious complications (dosage of LA in the aforementioned techniques is given in Table VIII).

SURGERY COMBINED WITH SIGNIFICANT TISSUE INJURY – ALGORITHM OF CONDUCT 3

Surgeries in which intensity of postoperative pain> 4 points according to NRS, but after which duration of pain is usually not longer than 3 days:

- exploratory laparotomy, adhesiolysis,
- gastric surgery,
- small intestine surgery,
- colon surgery (classic and laparoscopic),
- pancreatic surgery,
- hepatic surgery,
- bile duct surgery (except for laparoscopic cholecystectomy),
- resection of spleen, kidneys, adrenal glands,
- breast reconstruction with pedicled flaps,
- fasciotomy,
- amputation of shin, thigh, arm.

In the absence of contraindications, the principle of standard application of multimodal analgesia consisting of combined pharmacotherapy and one of the techniques of regional analgesia (algorithm 3) should be adopted.

Pharmacotherapy – before surgery

The use of the following should be considered to induce the effect of analgesia in advance:

- metamizole,
- paracetamol,
- and/or NSAIDs (administered intravenously – caution, increased risk of intraoperative bleeding after NSAID administration)
- (drug dosage according to table II).

In order to reduce the necessary doses of analgesics, including opioids, and to improve the quality of analgesia, preoperative use of selected coanalgesics should be considered (dosage according to table VI):

- lidocaine administered intravenously (do not use if one of the regional analgesia techniques given below is performed),
- magnesium sulphate,
- ketamine,
- α-2 adrenergic receptor agonists (dexmedetomidine, clonidine),
- gabapentin, pregabalin.

Pharmacotherapy - intraoperatively:

Intraoperative use of coanalgesics drugs should be considered (dosage according to table VI):

- lidocaine administered intravenously (do not use if one of the regional analgesia techniques given below is performed)
- magnesium sulphate
- ketamine
- dexamethasone
- α-2 adrenergic receptor agonists (dexmedetomidine, clonidine)

Pharmacotherapy – after surgery:

Combined pharmacotherapy consisting of:

- strong opioid drug (e.g., oxycodone, morphine) administered:
- intravenously via the PCA method (Patient Controlled Analgesia), drug dosage according to table IV.
- or continuous intravenous infusion of a strong opioid at a dose determined in titration (for example: oxycodone or morphine is administered intravenously at a low dose of 2 mg i.v. every 3-5 minutes, until a satisfactory pain relief and then the injection of this medicine should be continued intravenously according to the scheme described in the opioid analgesic titration procedure).

Therapy combined with non-opioid analgesics administered intravenously (dosage of drugs according to table III):

- metamizole,
- paracetamol,
- and/or one of the NSAIDs.

When administering NSAIDs, the contraindications for their use and the increased risk of intraoperative bleeding should be borne in mind and the administration of a proton pump inhibitor should be considered for protection of the GI tract. The protection of the gastrointestinal tract using a proton pump inhibitor should be obligatorily applied if NSAIDs and dexamethasone are used as a coagulant.

Combined with coanalgesics.

Continuing the administration of selected coanalgesics in the postoperative period should be considered (dosage according to table VI):

- lidocaine administered intravenously (do not use when one of the regional analgesia techniques given below is performed),
- magnesium sulphate,
- ketamine,
- α-2 adrenergic receptor agonists (dexmedetomidine, clonidine).

When using opioids via a method other than PCA, it is essential to remember about relief of the so-called piercing pain. Additional doses of oxycodone or morphine of 2 mg i.v. should be used. In subsequent days, depending on the specific clinical situation and the severity of pain, combined pharmacotherapy should be modified through the option of changing the administration route of opioid analgesics from intravenous to oral (drug dosage in Tables V).

Regional analgesia

Before surgery, one of the following techniques should be used:

- continuous epidural analgesia - LA in combination with an opioid (drug dosage in Table VII); continuous epidural analgesia should then be continued in the postoperative period – optimally using a continuous infusion or PCEA method,
- interfascial block: QLB or ESP blocks for abdominal or epigastric surgeries using the classical method; alternatively, RSB for abdominal cavity surgeries, TAP block - for laparoscopic procedures, subcostal TAP block - for classic cholecystectomy (drug dosage in Table VIII).
- paravertebral block, SPB or ESP block in the case of breast reconstruction with pedicled flaps – drug dosage according to table VIII.
- plexus or upper or lower extremity nerve block in the case of amputation of the limbs or fasciotomy (drug dosage according to table VIII).

In the event of contraindications or inability to use one of the -mentioned techniques,

- infiltration of the planned LA incision line should be considered - drug dosage according to table IX.

Then, at the end of the surgical procedure, implantation of a catheter in the surgical wound with continuous infusion in the postoperative period via an elastomeric pump (optimally), infusion pump or fractional dose method (less recommended due to the higher risk of infectious complications - LA dosage according to Table IX.

After surgery (depending on the type of procedure)

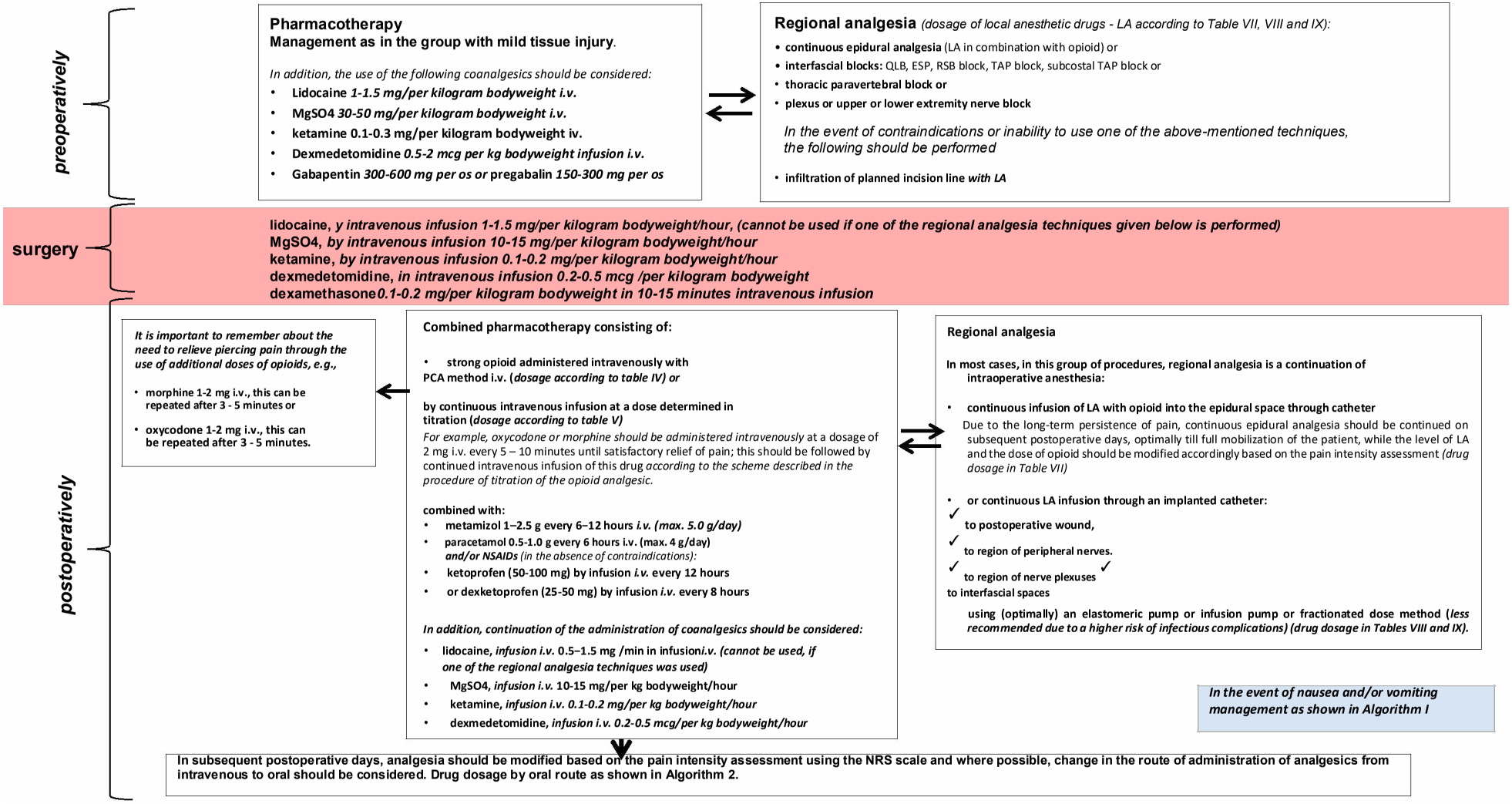
- continuous infusion of LA with opioid into the epidural space through the catheter (drug dosage in Table VII).
- (or) continuous infusion of LA through a catheter implanted:
- interfascially,
- in the region of the plexus or nerve/nerves
- for surgical wound, using (optimally) elastomeric or infusion pump or fractional dose method, which is less recommended due to the higher risk of infectious complications (dosage of LA in the aforementioned techniques is given in Tables VII and VIII).

SURGERY COMBINED WITH EXTENSIVE TISSUE INJURY – ALGORITHM OF CONDUCT 3

Single-stage surgeries involving more than one body cavity and reconstructive treatments after significant injuries. The expected level of pain intensity in the postoperative period is> 6 points according to VAS, and the duration of pain in the postoperative period is longer than 7 days:

- esophageal resection through thoracolaparotomy,
- reconstructive surgeries in polytrauma with the opening of two body cavities.

The standard of analgesic treatment does not significantly deviate from the standard defined for patients after surgical procedures connected with significant tissue injury (category III). On the other hand, an additional problem in this group of patients is long-term persistence of painful aches and pains.



Algorithm 3. Postoperative pain relief combined with significant and extensive tissue injury.

In the absence of contraindications, the principle of the application of multimodal analgesia consisting of combined pharmacotherapy and one of the techniques of regional analgesia continued for a sufficient period of time should be adopted (algorithm 3).

Pharmacotherapy – before surgery:

In order to induce the effect of analgesia in advance, use of the following should be considered:

- metamizole,
- paracetamol,
- and/or NSAIDs (caution, increased risk of intraoperative bleeding after NSAID administration).

When administering NSAIDs, the contraindications for their use and the increased risk of bleeding should be considered. Dosage of nonopioid analgesic drugs according to table II. In order to reduce the necessary doses of analgesics, including opioids, and to improve the quality of analgesia, preoperative use of selected coanalgesics should be considered (dosage according to table VI):

- lidocaine administered intravenously (do not use if one of the regional analgesia techniques given below is performed),
- magnesium sulphate,
- ketamine,
- α-2 adrenergic receptor agonists (dexmedetomidine, clonidine),
- gabapentin, pregabalin.

Pharmacotherapy - intraoperatively:

The possibility of intraoperative continuation of the administration of drugs coanalgesics be considered (dosage according to table VI):

- lidocaine administered intravenously (do not use if one of the regional analgesia techniques given below is performed),
- magnesium sulphate,
- ketamine,
- dexamethasone,
- α-2 adrenergic receptor agonists (dexmedetomidine, clonidine).

Pharmacotherapy – after surgery:

Combined therapy consisting of:

- strong opioid (e.g., oxycodone, morphine) administered intravenously using the PCA method (Patient Controlled Analgesia), drug dosage according to table IV.
- or continuous infusion at a dose determined in titration; for example: oxycodone or morphine is administered intravenously at a low dose of 2 mg i.v. every 3-5 minutes, until a satisfactory pain relief and then the injection of this medicine should be continued intravenously according to the scheme described in the opioid analgesic titration procedure.

In combination with non-opioid analgesics:

- metamizole
- paracetamol
- and/or one of the NSAIDs,
- administered intravenously (drug dosage according to table II).

When administering NSAIDs, the contraindications for their use and the increased risk of intraoperative bleeding should be borne in mind and the use of a proton pump inhibitor should be considered for protection of the GI tract. Gastrointestinal protection should be obligatorily administered when NSAIDs and dexamethasone are used as a coanalgesic.

Combined with coanalgesics.

Continuing the administration of selected coanalgesics in the postoperative period should be considered (dosage according to table VI):

- intravenous lidocaine (cannot be used if one of the regional analgesia techniques given below was performed),
- magnesium sulphate,
- ketamine,
- α-2 adrenergic receptor agonists (dexmedetomidine, clonidine).

When using opioids via a method other than PCA, it is essential to remember about relief of the so-called piercing pain. Additional doses of opioids, e.g., oxycodone or morphine in a dose of 2 mg i.v should be used. In subsequent days, depending on the specific clinical situation and the severity of pain, combined pharmacotherapy should be modified with the option of changing the administration route of opioid analgesics from intravenous to oral (drug dosage in Tables V).

Regional analgesia:

Before surgery, one of the following techniques should be used:

- continuous epidural analgesia - LA in combination with an opioid (drug dosage according to table VII). Continuous epidural analgesia should then be continued in the postoperative period – optimally using a continuous infusion or PCEA method,
- interfascial blocks: QLB block, ESP or paravertebral block in the case of selected abdominal or chest surgery; alternatively, RSB for abdominal cavity surgery with midline incision (drug dosage according to table VII),
- plexus or upper or lower extremity nerve block in the case of limb repair (drug dosage according to table VII),
- in the event of contraindications or in the case of inability to use one of the above-mentioned techniques, infiltration of the planned LA incision line, and then - at the end of the surgical procedure - implantation of a catheter into the surgical wound with continuous infusion in the postoperative period using the elastomeric pump (optimally), infusion pump or fractional dose method (less recommended due to the higher risk of infectious complications (dosage of LA according to table IX).

After surgery, depending on the type of procedure:

- continuous infusion of LA with opioid to epidural space through the catheter - drug dosage in Table VII. Due to the long-term persistence of pain, continuous epidural analgesia should be continued on subsequent postoperative days, optimally until the patient's full mobilization. The concentration of LA and the dose of opioid should be modified accordingly.

- or continuous LA infusion through an implanted catheter:
- interfascially,
- in the region of the plexus or nerve/nerves,
- to the surgical wound, using (optimally) an elastomeric or infusion pump or fractionated dose method (less recommended due to the higher risk of infectious complications) - dosage of LA in the aforementioned techniques is given in Tables VIII and IX.

It should be emphasized that the predicted pain in category IV, due to the extent of surgical trauma, is intensified, and the time of persistence is also longer. This puts the medical team before a specific task of conducting analgesia adapted to a specific clinical situation changing by the day, both in the immediate postoperative period, but also later, during wound healing and rehabilitation, as well as, what is extremely important, in the case of complications (necessity of reoperation, prolonged wound healing, etc.). This requires an interdisciplinary approach and close cooperation of the entire team dealing with the treatment of the patient.

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