IJCNP, Volume 4, Issue 01, 2025 ISSN: 2995-536X
https://medicaljournals.eu/index.php/IJCNP

INTERNATIONAL JOURNAL OF COGNITIVE NEUROSCIENCE AND PSYCHOLOGY

CURRENT PERSPECTIVES OF POSTOPERATIVE PAIN AND ITS REMEDIES: LITERATURE REVIEW

Ojum S., Dr. Nkadam, Nwizor Monday
Department of Anaesthesia, Rivers State University Teaching Hospital, Port Harcourt, Nigeria

Dr. Daniel Udobueze, Elem – Ojum
Sacred Heart Hospital, Abeokuta

Abstract: This study examines the current perspectives of postoperative pain and its remedies. The paper highlights the pathophysiological mechanisms of primary and secondary sensitization, as well as the possibilities of pharmacological management are considered. Multimodal analgesia - a combination of different analgesic medications - is the most justifiable approach of adequate postoperative pain relief. The advantages and disadvantages of possible combinations of analgesic medications depending on the type of surgical intervention are highlighted. The review underscores the significant protective potential in response to damaging factors. The occurrence of pain syndrome of varying intensity is an integral part and the result of the vast majority of operative interventions. Statistically more than 80% of patients experience acute pain in the postoperative period, 75% of which rate its intensity from moderate to severe and becomes unbearable. Drawing on contemporary literature, the study also explores the main reasons that hinder the early activation of patients, faster and more complete functional recovery after surgical intervention is insufficient postoperative analgesia. The paper argues that a high proportion of patients experience moderate to severe pain, which can delay recovery and increase the risk of chronic pain. Multimodal analgesia is identified as the most effective approach, combining different classes of analgesics such as opioids, NSAIDs, acetaminophen, local anesthetics, and adjuvant agents. Particular emphasis is placed on gabapentinoids, which provide significant opioid-sparing effects and improved pain control. Non-pharmacological methods also play a supportive role. In conclusion, effective postoperative pain management requires a comprehensive, patient-centered approach based on sound knowledge of pain mechanisms, careful drug selection, and continuous assessment. One of the reccomndation made was that healthcare providers should routinely implement multimodal analgesia strategies combining opioids, NSAIDs, acetaminophen, local anesthetics, and adjuvant drugs to achieve effective and balanced pain control.

Key words: Postoperative Pain, Analgesics, Opioid-saving Effect, Pregabalin.

Introduction

This is a review of modern perspective on postoperative pain syndrome and its correction. Having surgery is a common treatment in our hospital, many post operatively experience pain that become chronic. Correction of postoperative pain is important as it impacts on the duration and course of the recovery period. The pathophysiological mechanisms of the formation of primary and secondary sensitization and the possibilities of drug influence are considered. Multimodal analgesia – a combination of analgesics with different mechanisms of action – is the most justified approach for adequate postoperative analgesia. The advantages and disadvantages of possible combinations of analgesic drugs depending on the type of surgical intervention are highlighted. The place of application of adjuvant drugs, in particular gabapentinoids, in order to achieve an opioid-sparing effect and minimize the side effects of opioid analgesics, is necessary.

Naturally, pain has a significant protective potential in response to damaging factors. The occurrence of pain syndrome of varying intensity is an integral part and the result of the vast majority of operative interventions. Statistically more than 80% of patients experience acute pain in the postoperative

period, 75% of which rate its intensity from moderate to severe and becomes unbearable. Effective elimination of postoperative pain is noted in less than half of the patients, despite the advancement of pain clinics present in most medical institutions that are directly involved in the treatment of acute pain [1, 2].

It has been established that one of the main reasons that hinder the early activation of patients, faster and more complete functional recovery after surgical intervention is insufficient postoperative analgesia. Along with the elimination of physical suffering of patients caused by painful sensations, the purpose of using painkillers is creating psychological comfort and improving the quality of life of patients, which accelerates functional rehabilitation in the postoperative period, reduces the length of hospitalization, the frequency of complications and at the same time is a means of prophylaxis of the formation of chronic pain syndrome [3].

Postoperative pain is mixed in nature and includes 3 components, the severity of which varies depending on the type and extent of surgical intervention. In particular, the somatic component of pain syndrome, which is the result of tissue damage as a result of incision, is distinguished; neuropathic – damage to nerve fibers during surgery, as well as visceral - intraoperative mechanical trauma (mesenteric tractions, the use of expanders, traumatic manipulations on the gastrointestinal tract (GIT), placement of drains, etc.). The pathophysiology of the occurrence of pain syndrome is based on the sequence of formation of pain sensations at different levels of the three-neuron nociceptive system: the first neuron - the peripheral pain receptor (nociceptor) and central neurons located in different structures of the central nervous system (CNS): the second - spinothalamic; the third - thalamocortical with appropriate processes at each of the levels. [4, 5].

Activation of nociceptors, the so-called transduction process, is caused by mechanical stimuli and the action of pain mediators (bradykinin, serotonin, prostaglandins E and others). Trans-Nociception is the process of transmitting nociceptive stimuli along afferent axons from the lesion area to the spinal and supraspinal structures. The next stage is modulation, which occurs at the level of the dorsal horns of the spinal cord (DHSC) through the inhibitory effect of interneurons of the second layer or due to the descending inhibitory effect on activated 2^{nd} order neurons. The final stage is the processing of nociceptive information in the cerebral cortex with the formation of sensations an emotional affective component of pain - the so-called perception. As you know, surgical trauma induces the occurrence of hyperalgesia, which leads to the formation of a persistent pain syndrome in the postoperative period. [6].

The basis of any postoperative pain is plastic changes in the nervous system with the formation of zones of primary hyperalgesia, that is, zones with a reduced pain threshold, due to a complex of changes directly at the site of incision and surgical manipulations. In addition to the zones of primary hyperalgesia, a decisive role in the formation of postoperative pain syndrome belongs to secondary hyperalgesia, which is a consequence of changes at different levels of the central nervous system. In particular, the "inclusion" of central mechanisms of sensitization of nociceptive neurons at the level of the DHSC occurs by increasing their excitability, spontaneous electrical activity and sensitivity to mechanical stimulation. With prolonged nociceptive stimulation, hypersecretion of neuropeptides (substance P, neurokinin A) occurs, which, by acting on the corresponding receptors, activate nociceptive neurons and potentiate the effect of glutamate through N-methyl-D-aspartate (NMDA) receptors. Neurokinins depolarize the cell membrane by eliminating Mg' ions that block ion channels of NMDA receptors. After that, glutamate affects NMDA receptors, increasing the active influx of Ca ions into the cell and leading to prolonged depolarization of the cell membrane.

As a result, the so-called "expansion" of the zone of reduced pain threshold outside the boundaries of the surgical wound occurs. This process takes place within 12–18 hours and in a significant number of cases leads to an increase in the intensity of postoperative pain sensations on the second day after surgery [5]. Among the pathological effects of pain, it is necessary to highlight the emotional and physical suffering of the patient, sleep disturbances, undesirable reactions from the cardiovascular and respiratory systems, gastrointestinal tract, decreased diaphragmatic excursion, weakening of the Cough

reflex, which leads to a decrease in the patient's physical activity, prolongs the terms of reconvalescence and underlies the formation of a pathological postoperative syndrome complex [7–9].

The problem of postoperative pain syndrome remains relevant, despite the significant number of studies in the field of postoperative analgesia, the introduction of methods of systemic and local anesthesia, the use of analgesic drugs of various groups. These facts are confirmation that a single treatment approach or means to eliminate pain has not been found. The most justified and scientifically based is the concept of multimodal analgesia, which involves the simultaneous use by clinicians of 2 or more analgesics and/or methods of anesthesia with different mechanisms of action to achieve adequate analgesia and minimize side effects [10, 11].

When choosing a multimodal analgesia regimen, the type of surgical intervention should be taken into account. In highly traumatic operations, the use of opioid analgesics remains justified. These drugs have a powerful analgesic effect with the possibility of various routes of administration (oral, intramuscular, intravenous, subcutaneous, epidural and spinal). Morphine hydrochloride and its synthetic analogues, as well as mixed opioid receptor agonists-antagonists – butorphanol tartrate; partial antagonists of opioid receptors are most often used. However, the widespread and prolonged use of drugs of this group is limited by a number of side effects (nausea, vomiting, respiratory and peristaltic depression, sedation, skin itching with intrathecal use), which are dose-dependent [12]. The effectiveness of anesthesia with the traditional prescription of opioid analgesics as monotherapy does not exceed 25–30% [13].

According to the results of a meta-analysis of 27 randomized clinical trials dedicated to opioid-free postoperative analgesia in the USA (2017), multicomponent analgesia using non-steroidal anti-inflammatory drugs (NSAIDs), acetaminophen, tramadol and gabapentinoids is effective and safe. More than 50% of patients did not require the prescription of opioid analgesics, and the rest showed a significant opioid-sparing effect [14]. Considering these data and current trends, aimed at reducing the frequency of use of narcotic analgesics, or their effective analgesic dose, let us dwell in more detail on the main classes of drugs for multimodal postoperative analgesia (see table).

Tissue inflammation play important role in the mechanisms of peripheral and central sensitization, which necessitates the use of NSAIDs in postoperative pain treatment regimens. Preparations of this group are used to treat mild to moderate pain. The mechanism of their action is to reduce the level of inflammatory mediators at the site of surgical trauma, as well as to block the synthesis of prostaglandin E by inhibiting the activity of cyclooxygenase (COX) of the 1st and 2nd type. Among NSAIDs, non-selective drugs that are used includes diclofenac, ibuprofen, naproxen, ketoprofen, ketorolac, dexketoprofen; selective COX-2 inhibitors – meloxicam, celecoxib, lornoxicam and specific COX-2 inhibitors – parecoxib sodium.

The advantages of NSAIDs include the absence of hemodynamic effects, respiratory depression, impaired gastric motility and transit time through the small intestine. The main side effects of NSAIDs are gastrointestinal dysfunction (NSAID-induced gastropathy), increased bleeding, renal dysfunction, especially in patients with kidney disease with reduced circulating blood volume [15]. The risk of negative effects of NSAIDs increases with electrolyte disturbances (hypokalemia), hypotension, the use of nephrotoxic drugs and angiotensin-converting enzyme inhibitors. One example of the implementation of a multimodal approach in clinical practice is the use of various pain relief techniques – regional (subcutaneous infiltration of the incision site, irrigation of the abdominal cavity with an anesthetic solution) and/or Neuroaxial in combination with systemic opioids or other analgesics. Among the advantages of local anesthetics, it is worth noting the high effectiveness of pain relief, especially in patients with concomitant pathology, which ensures a more stable course of the postoperative period, a stimulating effect on intestinal peristalsis, and improved blood circulation in the blockade area. The main side effects are neuro- and cardiotoxicity, especially when a large amount of local anesthetics enters the systemic bloodstream [16].

The use of multimodal analgesia is also recommended today non-pharmacological approaches that stand out fewer side effects, however the level of evidence of these methods is sufficient low (see

table). Despite the large selection of drugs and different effectiveness among opioid analgesics, NSAIDs, local anesthetics, availability certain side effects and insufficient level of analgesia, encourages the search for new approaches to postoperative pain relief with the most greater effectiveness and leveling of side effects on the body. A special place in the multimodal approach belongs to the group of preparations called gabapentinoids, to which include gabapentin and pregabalin, which, in addition to anticonvulsant action, exhibit analgesic properties, in particular in the treatment of chronic pain syndromes and neuropathic pain [19, 22]. The above-mentioned preparations have a central mechanism of action and influence on sensitization processes.

Clinical studies show that the use of the use of gabapentin reduces acute postoperative pain and reduces the need for opioids analgesics. Thus, 150 mg of pregabalin or 800mg of gabapentin significantly reduced postoperative pain and the minimum effective dose narcotic analgesics after laparoscopic cholecystectomy [20]. According to L. Ajori and L. Nazari taking 600 mg of gabapentin before performing abdominal hysterectomy significantly influenced the severity of acute postoperative pain. Pain assessment was performed using visual analogue scale (VAS) after 1, 4, 6, 12 and 24 hours after surgery. The study showed that gabapentin significantly reduces the number of points on the VAS in each time interval. The total dose of meperidine to eliminate acute pain syndrome was significantly lower compared to the group placebo. Researchers also note a decrease reduction in the frequency of postoperative nausea and vomiting, and, accordingly, the need for the use of antiemetics [21].

Pregabalin is a structural analogue of g-aminobutyric acid – a neurotransmitter that inhibits transmission of nerve impulses from neurons to muscles. Interacting with α 2-delta- protein of calcium channels, pregabalin reduces depolarization caused by influx calcium and the release of excitatory neurotransmitters tors, including glutamate, noradrenaline, dopamine and serotonin, which prevents the transmission of pathological nerve impulses to the muscles, and thus exhibits an analgesic effect [22].

Table. Summary of recommendations for postoperative pain control [16]

Methodology/preparation	Recommended application	Comments	Contraindications and precautions
Non-pharmacological approaches			
Transcutaneous electrical nerve stimulation (class Ia, level C)	Supplement to others methods of p/o pain control	Most often used in place incision	Implanted rhythm drivers or cardioverter - defibrillator, lymphedema, violation of the integrity of the skin
Cognitive methodologies	Supplement to others methods of p/o pain control	Relaxation techniques, hypnosis music therapy intraoperatively	Absent. With caution in patients with psychosis in anamnesis
Systemic pharmacological approaches			
Peroral opioid analgesics (class I, level C)	As a component of multimodal analgesia	The peroral route of administration has more advantages [17]	Respiratory depression, addiction formation, sedation, nausea and vomiting, constipation
Patient-controlled IV administration of opioid analgesics (class I, level C)	In cases of need for parenteral systemic p/o analgesia for more than	Avoid initial opioid infusion	See opioid analgesics (per os)

	several hours		
Acetaminophen and NSAIDs (class I, level A)	As a component of multimodal analgesia	No data on the advantages of IV administration or per os. Use of opioids in the p/o period. Celecoxib at a dose of 200-400 mg 30-60 minutes before surgery, then after surgery 200 mg 2 r./day Acetaminophen at a dose of 500-1000 mg IV or per os every 6 hours Data on increased bleeding of Intestinal anastomoses, in surgery for fractures and spinal interventions [15, 18]. NSAIDs are contraindicated in ACS	Acetaminophen: hepatotoxicity NSAIDs :gastrointestinal bleeding, ulcerogenic effect, cardiovascular events, renal dysfunction
Gabapentin and pregabalin (class I, level B)	As a component of multimodal analgesia. Studies in groups of patients who underwent major surgical interventions [21, 23, 24]. Opioid-sparing effect [24].	Gabapentin doses varied depending on the study: 600 - 1200 mg 1-2 hours preoperatively and 600 mg p/o in one or several doses. Pregabalin doses varied depending on study: 150 - 300 mg 1-2 hours preoperatively and 150-300mg after 12 hours p/o. Higher doses are more effective, but Ĺ sedation	Dizziness, sedation, dose reduction in renal dysfunction
Ketamine (IV) (class Ia, level B)	As a component of multimodal analgesia. Studied in groups of patients who underwent major	Doses vary widely: 0.5 mg/kg bolus before surgery, 10 mcg/kg/min intraoperatively with or without	Patients with psychosis in anamnesis. Hallucinations, nightmares, dissociative

	surgical interventions. Opioid-sparing effect	administration in smaller doses p/o	symptoms
Lidocaine (IV) (class Ia, level B)	As a component of multimodal analgesia. Open and laparoscopic abdominal interventions.	Doses range from initial 1.5 mg/kg to 2 mg/kg/hour intraoperatively	Conduction (conductive) block. mg/kg to 2 mg/kg/hour intraoperatively Dizziness, seizures, bradycardia
Local anesthesia (infiltration, intra-articular administration) (class Ia, level B)			

Note: class – class of recommendation; level – level of evidence; p/o – postoperative; IV – intravenous; per os – peroral

Compared to gabapentin, pregabalin is absorbed faster and has a higher bioavailability (90% vs. 60%). Food intake does not affect the bioavailability of the drug. Important advantages of pregabalin compared to gabapentin are a clear linear dependence of the drug concentration in the blood within the therapeutic window (75–600 mg), a smaller daily dose, faster titration of the drug, and fewer side effects. A meta-analysis of 74 randomized, controlled studies showed that pregabalin reduced the quantitative assessment of pain and morphine costs after cardio- surgical, gynecological, orthopedic operations and laparoscopic cholecystectomy [23].

Perioperative administration of pregabalin significantly reduced the number of points on the VAS after 2 and 24 hours after the above-mentioned surgical interventions, with the exception of cardiothoracic and spinal procedures. The total amount of morphine consumption within 24 hours after surgery was significantly reduced in all surgical interventions, with the exception of cardiothoracic ones [24]. Side effects included significant sedation after pregabalin use in cardiothoracic, orthopedic, and spinal procedures.

It should be noted that postoperative nausea and vomiting were recorded less frequently after pregabalin administration in all types of interventions. The above data indicate the possibility of using pregabalin for the treatment of postoperative pain, as well as reducing morphine consumption and the frequency of postoperative nausea and vomiting.

According to the results of a meta-analysis conducted by Zhang J. against the background of pregabalin administration at a dose of <300 mg, the total consumption of opioid analgesics in the first day after surgery decreased by 8.8 mg (weighted mean difference), with an increase in the in mg. Perioperative use of pregabalin led to a significant reduction in the severity of side effects associated with the use of opioid analgesics, in particular vomiting (risk ratio – 0.73; 95% confidence interval 0.56 – 0.95) [25].

It is known that most patients who undergo thoracotomy for lung cancer experience fairly intense ipsilateral shoulder pain after surgery. In a study by Y. Imai et al., patients in the postoperative period received pregabalin at a dose of 150 mg orally in combination with NSAIDs, the control group - only NSAIDs. The

severity of postoperative shoulder pain was significantly lower in the group of patients who received pregabalin, compared with the control group [26]. Scientific data substantiated the use of pregabalin at a dose of 75–300 mg 2 times/day as an effective means for treating neuropathic postoperative pain [16, 19].

According to current recommendations of the American Pain Association (2016), clinicians should consider using gabapentin or pregabalin as components of multimodal analgesia (recommendation class ², level of evidence B) in surgical patients. A number of studies have shown a decrease in the

need for the use of opioids after major operations or minor surgical procedures. There is also data on a decrease in the severity of postoperative pain syndrome when assessed by VAS [16]. The above data allow the use of this drug both before surgery (1–2 hours) and postoperatively (after 12 hours). Typical doses evaluated in studies were 150 and 300 mg of pregabalin. Although higher doses may be more effective, their administration is associated with greater sedation of patients. The drug is available in a form for oral administration. Thus, pregabalin should be used in patients undergoing highly traumatic surgical interventions or surgical interventions associated with significant pain as components of multimodal therapy.

Conclusion

In conclusion, effective postoperative pain management requires a comprehensive, patient-centered approach based on sound knowledge of pain mechanisms, careful drug selection, and continuous assessment. The integration of pharmacological and non-pharmacological strategies remains essential for achieving optimal clinical outcomes.Postoperative pain is an inevitable consequence of most surgical procedures and remains inadequately managed in a significant proportion of patients. It is a complex condition involving multiple physiological mechanisms, including peripheral and central sensitization, which contribute to both acute and chronic pain development. Poorly controlled postoperative pain negatively impacts patient recovery, delays mobilization, prolongs hospital stay, and increases the risk of complications.Despite advances in pain management, no single analgesic agent or technique has proven sufficient in providing optimal pain relief. Opioids, although effective, are limited by dose-dependent adverse effects, while other agents such as NSAIDs and local anesthetics also carry specific risks. Therefore, reliance on a single method of analgesia is no longer considered appropriate in modern clinical practice.

Recommendations

1. Healthcare providers should routinely implement multimodal analgesia strategies combining opioids, NSAIDs, acetaminophen, local anesthetics, and adjuvant drugs to achieve effective and balanced pain control.
2. Greater emphasis should be placed on reducing opioid use by incorporating alternatives such as gabapentinoids, regional anesthesia, and non-opioid analgesics to minimize adverse effects and dependency risks.
3. Postoperative pain management should be tailored to the patient's clinical condition,type of surgery, and pain severity to optimize outcomes and reduce complications.

REFERENCES

1. Apfelbaum J.L. Postoperative pain experience: Results from a national survey suggest postoperative pain continues to be undermanaged / J.L. Apfelbaum, C. Chen, S.S. Mehta et al. // Anesthesia. Analgesia. – 2003. – ¹ 97. – P. 534-540.
2. Gan T.J. Incidence, patient satisfaction, and perceptions of postsurgical pain: Results from a US national survey / T. J. Gan, A.S. Habib, T.E. Miller et al. // Curr. Med. Res. Opinion. – 2014. – ¹ 30. – P. 149-160.
3. Kehlet H. Persistent postsurgical pain: Risk factors and prevention / H. Kehlet, T. Jensen, C. Woolf // Lancet – 2006. – ¹ 367. – P. 1618-1625.
4. Trachuk M.E. Physiology of pain (literature review) / M.E. Trachuk // Ukr. scientific-medical youth journal – 2010. – ¹ 2. – pp. 10-16.
5. Purves D. Pain. In: Neuroscience / D. Purves, G.J. Augustine, D. Fitzpatrick et al. // 5th ed. Sunderland, MA: Sinauer Associates, Inc. – 2012. – P. 209-228.
6. Malik O.S. Perioperative Hyperalgesia and Associated Clinical Factors / O.S. Malik, A.D. Kaye, R.D. Urman //Curriculum. Pain Headache Rep. – 2017. / ¹ 21 (1). – P. 4. doi: 10.1007/s11916-017-0602-3.

7. Kehlet Í. Postoperative pain / H. Kehlet, J.B. Dahl // World J. Surg. – 1993. – ¹ 17. – P. 215-219.
8. Breivik Í. Postoperative pain management / H. Breivik //Bailliere's Clinical Anesthesiology. – 1995. – ¹ 9. – P. 403-585.
9. Ovechkin A.M. Postoperative pain: state problems and modern trends of postoperative analgesia / A.M. Ovechkin // Regional. anest. and treatment of acute pain –2015. – Vol. 11, ¹ 2. – pp. 29-39.
10. Kehlet H. The value of "multimodal" or "balanced analgesia" in postoperative pain treatment pain / H. Kehlet, J.B. Dahl // Anesthesia. Analgesics. – 1993.- ¹ 77 (5). -P. 1048–1056.
11. Brown E.N. Multimodal General Anesthesia: Theory and Practice / E.N. Brown, K. J. Pavone, M. Naranjo // Anesthesia. Analgesia. – 2018. – ¹ 127(5). – P. 1246-1258.
12. Shafi S. Association of Opioid-Related Adverse Drug Events with Clinical and Cost Outcomes Among Surgical Patients in a Large Integrated Health Care Delivery
13. System / S. Shafi, A.W. Collinsworth, L.A. Copeland et al. // JAMA Surg. – 2018. – ¹ 153 (8). – P. 757-763. doi: 10.1001/jamasurg.2018.1039.
14. Macintyre P. Acute Pain Management: Scientific Evidence. Australian and New Zealand College of Anesthetists, 3-rd edition / P. Macintyre, D. Scott, S. Schug // 2010.
15. Wick E. C. Postoperative Multimodal Analgesia Pain Management with Nonopioid Analgesics and Techniques: A Review / E.C. Wick, M.C. Grant, C.L. Wu // JAMA Surg. – 2017. – ¹ 152 (7). – P. 691–697.
16. Gorissen K.J. Risk of anastomotic leakage with nonsteroidal anti-inflammatory drugs in colorectal surgery / K.J. Gorissen, D. Benning, T. Berghmans et al. // Br. J. Surg. – 2012. – ¹ 99. – P. 721-727.
17. Chou R. Management of Postoperative Pain: A Clinical Practice Guideline From the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists' Committee on Regional Anesthesia, Executive Committee and Administrative Council / R. Chou, D. B. Gordon, O. A. de Leon-Casasola et al. // J. of Pain // – 2016. – ¹ 17 (2). – P. 131–157.
18. Ruetzler K: A randomized trial of oral versus intravenous opioids for treatment of pain after cardiac surgery / K. Ruetzler, C. Blome, S. Nabecker et all. // J. Anesthesia. – 2014. – ¹ 28. – P. 580-586.
19. Rutegard J., Rutegard M: Non-steroidal anti-inflammatory drugs in colorectal surgery: A risk factor for anastomotic complications? / J. Rutegard, M. Rutegard // World J. Gastro intestine. Surg. – 2012. – ¹ 4. – P. 278-280.
20. Eidy M. Effects of pregabalin and gabapentin on postoperative pain and opioid consumption after laparoscopic cholecystectomy / M. Eidy, M.R. Fazel, H. Abdolrahimzadeh // Korean J. Anesthesiology. – 2017. – ¹ 4 (70). – P. 434–438.
21. Ajori L. Effects of gabapentin on postoperative pain, nausea and vomiting after abdominal hysterectomy: a double blind randomized clinical trial / L. Ajori, L. Nazari, M.M. Mazloomfard et al. // Archives of Gynecology and Obstetrics – 2016. – ¹ 285. – P. 677–682.
22. Ben-Menachem E. Pregabalin pharmacology and its relevance to clinical practice / E. Ben-Menachem //Epilepsy. – 2004. – ¹ 45 (6). – Ð. 13–18.
23. David M.H. Efficacy of Pregabalin in Acute Postoperative Pain Under Different Surgical Categories. A Meta-Analysis/ M.H. David, S.C. Stanley, G.I. Michael // Medicine (Baltimore). – 2015. – ¹ 94 (46). – P. 320-326.
24. Ittichaikulthol W: Effects of pregabalin on post-operative morphine consumption after abdominal hysterectomy with/without salphingophorectomy: A randomized, double-blind trial / W.

Ittichaikulthol, T. Virankabutra, M. Kunopart et al. // J. Med. Assoc. Thai – 2009. – ¹ 92. – P. 1318-1323.

25. Zhang J: Efficacy of pregabalin in acute postoperative pain: A meta-analysis / J. Zhang, K.Y. Ho, Y. Wang // Br. J. Anesthesia. – 2011. – ¹ 106: – P. 454-462.
26. Imai Y. Evaluation of postoperative pregabalin for attenuation of postoperative shoulder pain after thoracotomy in patients with lung cancer, a preliminary result / Y. Imai, K. Imai, T. Kimura et al. //Gen. Thoracic. Cardiovasc. Surg. – 2014. – ¹ 29. – P. 186–194.