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Multimodal analgesia in the postoperative period in patients with abdominal pathology in the Republic of Uzbekistan.

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Summary: Pain is an unpleasant sensory and emotional experience associated with actual or perceived tissue damage. (World Health Organization. International Classification of Diseases 11th Revision. Geneva: World Health Organization; 2019).
Postoperative pain of varying intensity occurs after any operation, both after minimal outpatient interventions and after highly traumatic hours-long operations.
Postoperative pain is not just an acute pain syndrome, it is also a strong trigger of the surgical stress response, which causes the activation of the autonomic nervous system and has a negative impact on almost all vital organs and systems.

Keywords: pain, analgesia, anesthesia, postoperative period, analgesics, opioids, multimodal analgesia.

Postoperative pain— pain sensations that arise in a surgical patient in the area of the performed surgical intervention [1, 2]. The World Health Organization and the International Association for the Study of Pain (IASP) have recognized pain relief as an inalienable human right [3]. Pain (nociceptive) is the natural response of the nervous system to nociceptive stimuli that are potentially harmful.

The biopsychosocial concept of pain is the concept that pain is a complex, multifaceted experience resulting from the interaction of biological, psychological and social factors. This concept serves as a basis for understanding the nature of pain and its treatment, taking into account the personality of the patient, his social environment and the social consequences of the impact of the disease on the individual. In this regard, it requires a multilateral, interdisciplinary and integrated approach to the treatment of pain.

Postoperative pain is not just an acute pain syndrome, it is also a strong trigger of the surgical stress response, which causes activation of the autonomic nervous system and has a negative impact on almost all vital organs and systems (Table 1).

Table number 1. The negative impact of postoperative pain on vital organ systems:

System	Changes due to the presence of acute pain syndrome
Cardiovascular	Tachycardia, hypertension, increased peripheral vascular resistance, increased myocardial oxygen demand, myocardial ischemia, reduced peripheral blood flow (risk factor for blood clots in the vessels of the lower extremities)
Respiratory	Decreased tidal volume (VR) and functional residual capacity (FRC), difficulty in adequate expectoration, sputum accumulation, atelectasis formation, pulmonary infection, hypoxemia
Gastrointestinal tract	Inhibition of gastrointestinal motility, increased risk of intestinal flora translocation
urinary	Difficulty urinating
Neuroendocrine	Increased plasma concentrations of catabolic hormones: glucagon, growth hormone (GH), vasopressin, aldosterone, renin and angiotensin.

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	Inhibition of the synthesis of anabolic hormones: insulin and testosterone. Catabolism is characterized by hyperglycemia, a sharp decrease in plasma protein levels. Negative nitrogen balance slows down the course of reparative processes and complicates postoperative rehabilitation of patients
Hemostasis system	Hypercoagulability, PE, deep vein thrombosis of the lower extremities
skeletal muscle	Increased muscle tone, immobilization (risk factor for deep vein thrombosis of the lower extremities)
central nervous system	The risk of developing chronic postoperative pain syndrome due to sensitization of the structures of the central nervous system against the background of intense acute pain

Postoperative pain syndrome is formed at all levels of both the peripheral and central nervous system, and reacts to damage.

The levels of formation of acute pain syndrome are as follows:

- transduction - activation of pain receptors (free endings of afferent axons) by mechanical action and the influence of pain mediators (serotonin,bradykinin, prostaglandins E2, etc.) with the formation of primary nociceptive stimuli (action potentials);
- transmission - transmission of nociceptive impulses from the area of damage along the afferent pathways to the spinal and supraspinal nerve structures;
- modulation - suppression of inhibitory interneurons of the II plate of the posterior horns of the spinal cord and descending inhibitory effects of activation of neurons of the 2nd order;
- perception is the processing of the received information by the cerebral cortex with the formation of a sensation of pain and its emotional-affective components.

The development of pain syndrome is associated with the formation of zones of hyperalgesia. There is primary and secondary hyperalgesia.

Primary hyperalgesia develops quickly, directly in the area of damaged tissues near the wound. This process is based on the sensitization of nociceptors (peripheral sensitization). The main role in triggering peripheral nociceptive mechanisms is played by bradykinin — it can have both direct and indirect effects on pain receptors. An important role is played by prostaglandins E2, which increase the sensitivity of nociceptors to the effects of other pain mediators.

The zone of secondary hyperalgesia is formed later and is located not only near the injury site, but also at a distance from it. Secondary hyperalgesia is due to the inclusion of central sensitization of nociceptive neurons that are located in the dorsal horns of the spinal cord. These neurons increase in excitability, sensitivity to mechanical stimulation, and spontaneous electrical activity. Further pain stimulation causes hypersecretion of neuropeptides (substance P, neurokinin A), which excite nociceptive neurons and enhance the excitatory effect of glutamate through N-methyl-D-aspartate receptors (NMDA receptors). Neurokinins cause cell membrane depolarization by removing blocking magnesium ions from NMDA receptor ion channels. Glutamate then acts on NMDA receptors, causing an abundant intake of calcium ions into the cell and prolonged depolarization. The increase in the zone of pain threshold reduction in the area of the surgical wound is associated with the expansion of the receptive fields of neurons located in the posterior horns of the spinal cord. This process occurs within 12-18 hours and often causes an increase in the intensity of postoperative pain on the second day of the postoperative period.

Chronic pain resulting from surgery and inadequate treatment of acute postoperative pain, the incidence of which reaches 30–70%, has a serious negative impact on the quality of human life and creates a significant financial burden on society [11].

The basis for choosing an effective and safe scheme of postoperative analgesia is an individual approach that takes into account the characteristics of each individual patient, assessment of pain intensity in dynamics, constant monitoring of the adequacy of pain relief, as well as timely detection of side effects of drugs and methods of analgesia.

The main principle of postoperative pain relief at present is the implementation of the concept of

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multimodal analgesia (MMA). It is recommended to use MMA, that is, the combined use of various analgesics and pain relief technologies in combination with non-pharmacological methods of postoperative pain relief in adults and children [16, 17]. Level of evidence - 1 (strength of recommendation - A).

All of the above was the reason for the implementation of this study, aimed at studying the effectiveness of the use of multimodal analgesia in our patients.

The main group received opioid analgesics for pain, as well as NSAIDs every 6 hours according to the scheme.

The test group received multimodal analgesia:

1. Before surgery, the patient received Paracetamol 500 mg and Diclofenac 100 mg in tablet form per day.

   In the first 24 hours after surgery:
2. NSAIDs every 6 hours according to the scheme
3. Paracetamol 500 mg in injection form (Infulgan, Fevalgan) 3-4 times a day.
4. Opioid analgesics every 12 hours.
5. TAP block under ultrasound navigation.
6. Ketamine 50mg on request.

Purpose of the study:

To improve the results of treatment of patients in the postoperative period in patients with abdominal pathology, to reduce the stay of these patients in the hospital.

Clinical materials and research methods:

In the intensive care unit of the TMA multidisciplinary clinic, we examined 24 patients with a diagnosis of postoperative ventral hernia (10 men and 14 women), whose average age was 46.1±2.4 years. These patients underwent surgery. We divided all patients into 2 groups: the control group, which included 12 patients who received standard therapy (antibacterial, infusion-transfusion, anticoagulant (low molecular weight heparins), analgesic and symptomatic therapy) and the study group, which included 12 patients who, in addition to this therapy, received multimodal analgesia both before surgery and in the postoperative period.

Both groups were randomized by us according to gender and age, the nature of the standard examination and surgical treatment.

All patients underwent clinical and biochemical studies, radiography, computed tomography (CT), during therapy, monitoring of blood pressure (BP), mean arterial pressure MAP, central venous pressure (CVP), blood glucose, thermometry and saturation of the venous (jugular) blood.

In addition to general clinical research methods, pain intensity was assessed.

Pain Intensity Assessment

1. According to the scale of verbal assessments (SVR) (measured in points with a joint decision of the doctor and the patient):
   - 0 - no pain;
   - 1 - mild pain;
   - 2 - moderate pain;
   - 3 - severe pain;
   - 4 - unbearable pain.
2. On a visual analog scale (VAS) (from 0 to 100%). Performed by the patient individually using a ruler (see Fig. 1).

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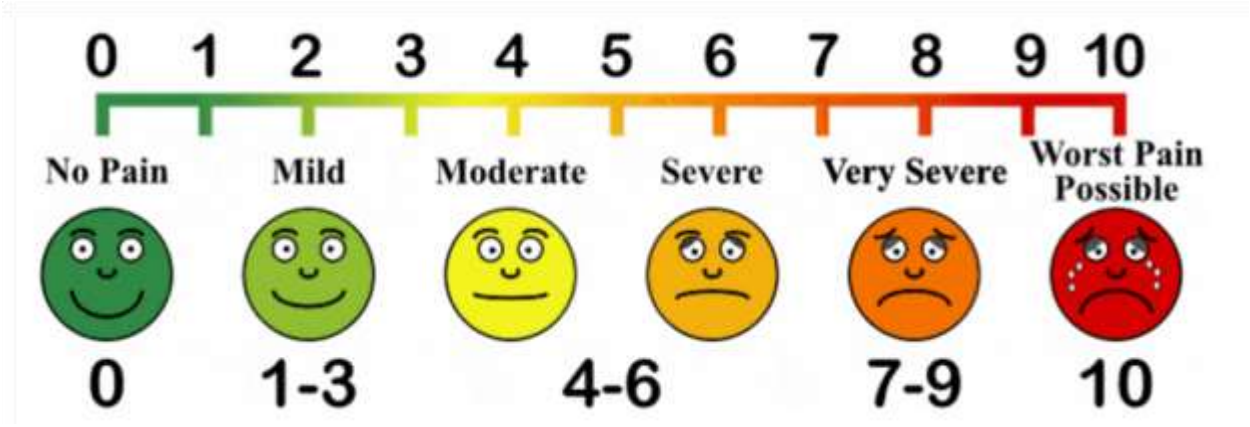
Figure 1. Scales for assessing the intensity of pain. VISUAL ANALOGUE SCALE



3. Assessment of the quality of night sleep:
    - good (6–8 hours);
    - satisfactory (4–6 hours);
    - bad (less than 4 hours).
4. Evaluation of the effectiveness of analgesic therapy:
    - assessment of the time of onset of analgesia after a single dose of the drug;
    - the duration of action of a single dose of the drug;
    - calculation of single and daily doses of the main analgesic in dynamics at the stages of therapy;
    - calculation of daily doses of additional analgesics;
    - assessment of the duration of analgesic therapy (days).
5. Pain therapy tolerance assessment:
    - accounting for side effects (AE) of previous therapy;
    - identification (presence) of the main AEs associated with taking an analgesic (sedation, dizziness, nausea, vomiting, increased sweating, dry mouth, headache, decreased appetite, digestive tract disorders (constipation, diarrhea), urinary retention, general weakness, mental disorders);
    - the severity of PE on a four-point scale:
        - – 0 – no PE (excellent tolerance);
        - - 1 - mild (good tolerance);
        - – 2 – moderate (satisfactory tolerance);
        - - 3 - strong degree of severity (poor tolerance).
6. To diagnose the neuropathic component of pain, the DN4 questionnaire (Neuropathic Pain Diagnostic Questionnaire - French Neuropathic Pain Group. - D. Bouhassiraa, 2004) is used (Appendix 1).

The length of stay of patients in the ICU and in the TMA multidisciplinary clinic as a whole was studied.

Results of own research:

In both groups of postoperative patients, we managed to maintain hemodynamic and respiratory parameters within acceptable limits. But due to pain syndrome and/or discomfort in the area of the postoperative wound, patients of the 1st group had slightly elevated hemodynamic parameters, namely BP, MAP, and pulse. And also because of the pain syndrome and / or fear (expectation) of pain in patients, the respiratory rate slightly increased: in patients of the 1st group 24-26 times per minute, in patients of the 2nd group 20-22 times per minute. Graph No. 1 shows that in the patients of the study group, the MAP values correspond to the norm after 3-6 hours, while in the patients of the first group, the hemodynamic parameters remain overestimated.

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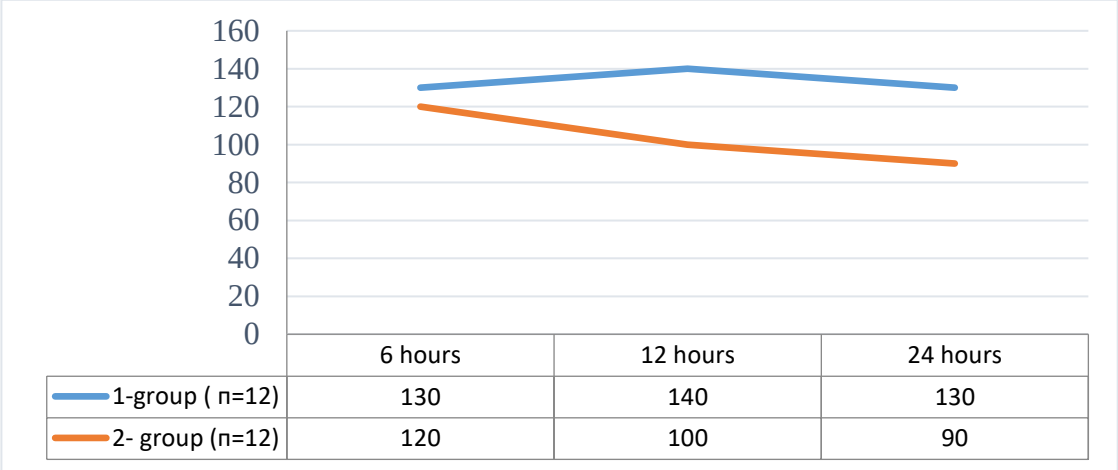
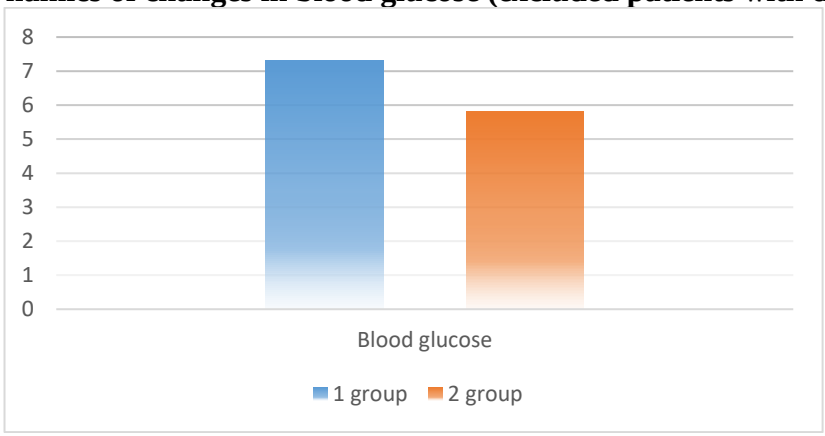
Schedule #1. Dynamics of change in MAP (mm Hg)



Graph No. 2 shows the dynamics of changes in blood glucose. Due to the fact that there is an inhibition of the synthesis of anabolic hormones due to pain syndrome, namely insulin, in patients of group 1, blood glucose values were7.3 ± 0.3 mmol/l, while in patients of group 2 this indicator was 5.8 ± 0.5 mmol/l, this indicates better analgesia in patients of group 2. DReliability: p*- <0.05.

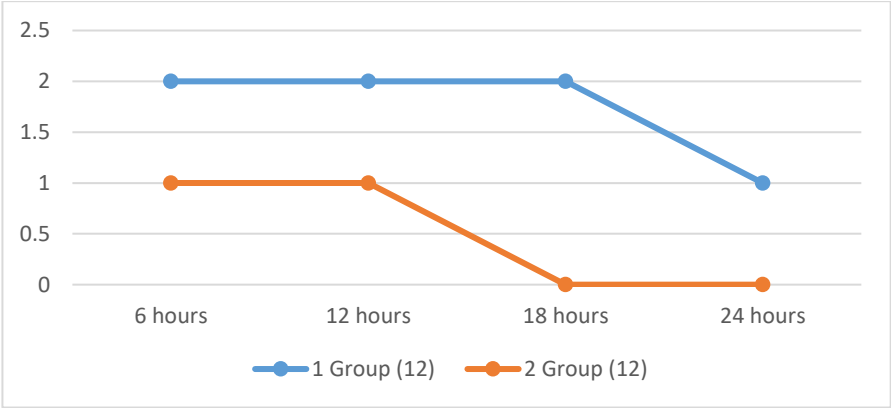
Schedule #2. Dynamics of changes in blood glucose (excluded patients with diabetes) mmol/l



Graphs 3 and 4 show the dynamics of changes in the pain syndrome in both groups according to the assessments of the patients themselves. Both graphs clearly demonstrate that patients of the second group feel much less pain than patients of the first group.

In addition, both graphs demonstrate the dynamics of pain reduction over time, so in patients of the 2nd group in the first hours they indicated severe (14%) or moderate pain (86%), then after 6-12 hours the pain was either weak, or patients felt no pain at all. In addition, the DN4 neuropathic pain diagnostic questionnaire also showed slightly better results in patients in the second group.

Schedule #3. According to the scale of verbal assessments (SVA)



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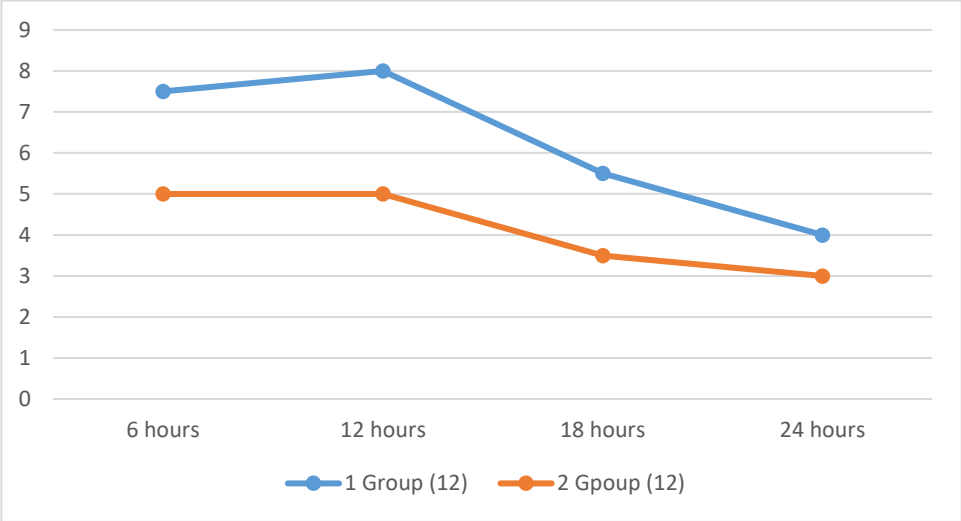
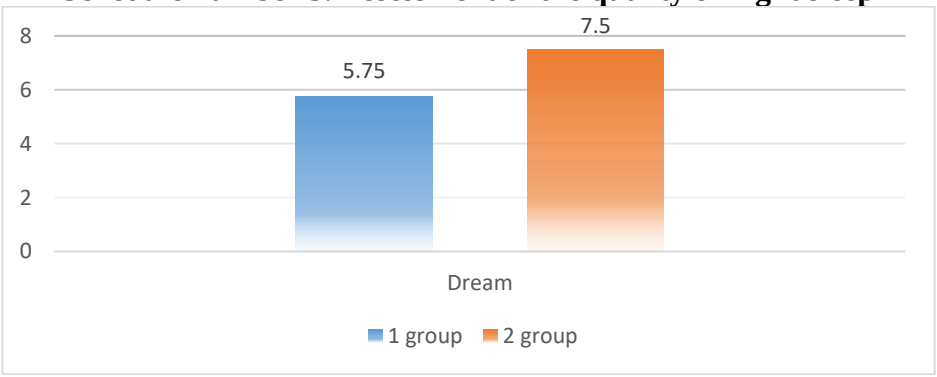
Graph No. 4. Dynamics of readings on the VAS scale:



Graph #5 shows the ratio of sleep quality. So patients of the 2nd group slept on average 7.5 hours, which corresponds to normal physiological needs. In addition, almost 90% of patients in group 2 did not have any complaints after waking up. Whereas patients of group 1 complained of poor sleep, and after waking up they complained of headache, fatigue, general weakness, pain in the postoperative wound

Schedule number 5. Assessment of the quality of night sleep



This table shows the ratio of side effects of anesthetic therapy. So in patients of group 2, side effects are slightly less, this is due to the fact that due to adequate anesthesia in patients, the number of opioid analgesics has decreased.

Table No. 2. The ratio of side effects of anesthetic therapy in the postoperative period in groups 1 and 2.

No.	Side effect	1 group	2 group
1	Sedation	3	5
2	Dizziness	6	6
3	Nausea	7	4
4	Increased sweating	2	1
5	Dry mouth	4	2
6	Headache	3	1
7	Violation of the functions of the gastrointestinal tract	5	3

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When comparing the final values of the studied parameters in the control and study groups, the following data were obtained: the length of stay of patients in the ICU was 24 and 18 hours in the postoperative period, and in the hospital as a whole, 6 and 4 days, respectively.

Conclusions:

Based on the foregoing, it must be assumed that multimodal, adequate analgesia contributes to a more rapid return of the patient to normal life, without compromising its quality.

This anesthesia demonstrated:

- ✓ Absolute elimination of discomfort caused by pain;
- ✓ Creating conditions for psychological comfort (good memories after surgery are important for a speedy recovery);
- ✓ According to the FTS approach, the rehabilitation period is significantly reduced, the patient returns to the usual level of life faster;
- ✓ It has been proven that in the absence of pain, the risk of complications in the postoperative period is reduced;
- ✓ It is a method of preventing the development of chronic pain.

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Appendix 1. DN4 Neuropathic Pain Diagnostic Questionnaire

INTERVIEW WITH THE PATIENT

Question 1: Does the patient's pain fit one or more of the following definitions?

		Yes	Not
one.	Burning sensation	☐	☐
2.	Painful sensation of cold	☐	☐
3.	Feeling like an electric shock	☐	☐

Question 2: Is the pain accompanied by one or more of the following symptoms in the area of pain?

		Yes	Not
one.	Tingling, crawling sensation	☐	☐
2.	tingling	☐	☐
3.	Numbness	☐	☐
four.	Itchy	☐	☐

EXAMINATION OF THE PATIENT

Question 3: Is the pain localized in the same area where examination reveals one or both of the following symptoms:

		Yes	Not
one.	Decreased sensitivity to touch	☐	☐
2.	Decreased sensitivity to tingling	☐	☐

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Question 4: Is it possible to cause or increase pain in the area of its localization:

		Yes	Not
one.	Sweeping in this area with a brush	☐	☐

Sum of points (number of "Yes" answers): _____

Key (interpretation): If the sum is 4 or more points, this indicates that the patient's pain is neuropathic, or there is a neuropathic component of pain (in mixed nociceptive-neuropathic pain syndromes).