

**Ministry of health of Republic Belarus**  
**Educational institution**  
**«Gomel state medical university»**

Department of General and Clinical Pharmacology

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**METHODICAL RECOMMENDATIONS**  
for a practical lesson on the discipline "Pharmacology"  
for the third-year students of the Faculty of Foreign Students,  
studying at the specialty 1-79 01 01 "General medicine"

**TOPIC 12: « ANALGESICS »**

Time is 3 hours

Approved at the meeting of the department of general and clinical pharmacology  
the protocol № 18 of 30.06.2022

## **LEARNING AND EDUCATIONAL GOALS, OBJECTIVES, MOTIVATION FOR LEARNING THE TOPIC**

Pain is one of the most frequent complaints that physicians of all specialties have to face. It is known, for example, that pronounced postoperative pain is associated with a higher risk of perioperative complications, while adequate postoperative analgesia provides early painless activation of the patient and allows overall improvement of surgical outcomes. However, there are still a lot of challenges in chronic pain treatment. Therefore, the problem of pain and anesthesia throughout the world is still important.

Narcotic analgesics are characterized by a strong analgesic effect, which makes it possible to use them in traumas and such diseases that are accompanied by a severe pain syndrome, for example, malignant tumors, myocardial infarction, etc. However, they affect the central nervous system of a person, and it is manifested in the development of euphoria, and with the repeated application of addiction and drug dependence can happen. In addition, an increase in the dose of the drug is accompanied by an increased risk of depression of the respiratory center. Therefore, the knowledge in pharmacological features, rules for storage, delivery and dispensing from pharmacies of this group of drugs are needed by doctors of different profiles.

Non-narcotic analgesics have anti-inflammatory, antipyretic and peripheral analgesic actions and, in contrast to narcotic analgesics, do not affect the breathing center and do not cause long-term development of drug dependence. This feature provided their wide application in the clinic. Moreover, many patients use non-narcotic analgesics for headache, dental, muscular and joint pain. Over-the-counter delivery of these drugs in pharmacies requires active medical education by doctors, who must explain to patients the benefits and possible risks from their use.

In a number of cases, so-called co-analgesics can also be used to reduce pain. Such drugs in addition to their main action can have analgesic effect antioxygent agents (clonidine, carbamazepine, amitriptyline, etc.). Knowledge and successful use of co-analgesics will help the doctor in a timely and effective manner to complete with the pain syndrome from those situations when the basic analgesic drugs do not have the proper effect.

### **Learning purpose:**

-systematize the knowledge of students. Analyze the effects of drugs on the totality of their pharmacodynamic and pharmacokinetic properties, efficacy and safety of use. Take into account the possible side effects of analgesic agents, determine the necessary medication for emergency treatment for poisoning with opioid analgesics. Pre-scribe medicines on the topic of the lesson, based on their pharmacodynamic and pharmacokinetic characteristics, taking into account the underlying pathology, concomitant diseases and the patient's age.

### **Educational purpose:**

- to develop one's value-personal, spiritual potential, to form the qualities of a patriot and a citizen, ready for active participation in the economic, industrial, socio-cultural and public life of the country; to realize the social significance of their future professional activities, to learn to observe educational and labor discipline, the norms of medical ethics and deontology.

**Tasks:**

As a result of the training session, the student must

**know:**

- pathophysiological mechanisms of pain;
- classification of analgesics and co-analgesics;
- features of their pharmacokinetics and pharmacodynamics, indications and contraindications for use;
- side effects of analgesics, the clinic and treatment of their overdose;
- features of drug dependence and the concept of withdrawal syndrome, arising from the use of narcotic analgesics, methods of treatment;
- the importance of drug abuse as a social and biological problem.

**be able to:**

- justify the choice of analgesic, taking into account its pharmacological characteristics, the main pathology and individual characteristics of the patient;
- evaluate the benefit / risk ratio when using narcotic analgesics;
- correctly choose and calculate the dose and route of administration of the drug taking into account the nature of the pathological process, concomitant diseases and the patient's age;
- prescribing medicines from the above groups in the form of medical prescriptions.

**own:**

- skills in using basic pharmacokinetic parameters and information about the dependence of pharmacodynamics on the properties of the analgetics, conditions of their use, features of their release forms, dose regimen and ways of delivering drugs to the body;
- the rules of prescribing the studied drugs for the treatment, prevention of various diseases and pathological conditions, taking into account the indications;
- skills in choosing the analgetics for medical measures for the most common diseases and conditions in the adult population and adolescents;
- skills of searching, analyzing and summarizing information about the use and operation of tools on the topic of the lesson.

**Motivation for mastering the topic:**

The specifics of the training of doctors in this specialty determines the need for students to purposefully study knowledge about the classification, pharmacokinetic and pharmacodynamic properties, indications for prescribing and side effects of analgetics.

**MATERIAL EQUIPMENT**

Reference and information literature, diagrams, tables, presentations, collection of medicines.

**CONTROL QUESTIONS FROM RELATED DISCIPLINES**

1. Definition of the pain.
2. Pain pathway.
3. Structure and functions of the antinociceptive system.
4. Metabolites of arachidonic acid and their main effects.

## CONTROL QUESTIONS ON THE TOPIC OF THE LESSON

1. Modern ideas about the systems of perception and regulation of pain in the body. Nociceptive system - a specific and nonspecific pathway for the pain impulse; pain mediators. Antinociceptive system, mediators of the antinociceptive system and their precursors, mechanisms of pain relief. Opiate receptors - localization, heterogeneity ( $\mu$ -,  $\kappa$ -,  $\delta$ -,  $\sigma$ -), activation effects, endogenous ligands.

2. Classification of analgesic agents.

3. Narcotic analgesics (opioids) and their antagonists. Opioid receptor agonists (morphine, codeine, trimeperidine, fentanyl, methadone). Antagonist agonists (pentazocine) and opioid receptor partial agonists (buprenorphine). Opioid antagonists (naloxone, naltrexone). Molecular and cellular mechanisms of action, main pharmacological effects, pharmacokinetics of opioids.

4. Characteristics of the main groups of opioids. Areas of medical use of narcotic analgesics, side and toxic effects, contraindications.

5. Acute opioid poisoning and the principles of its pharmacotherapy. Chronic toxicity and drug dependence. Principles of pharmacotherapy for drug addiction and withdrawal symptoms. Interaction of opioids with other drugs.

6. Non-narcotic analgesics (nefopam, paracetamol, ibuprofen, ketorolac, acetylsalicylic acid, combined agents) and mixed-type analgesics (tramadol): mechanisms of analgesic action, other pharmacological effects, use, side effects, contraindications.

7. Comparative characteristics of non-narcotic and narcotic analgesics, selection criteria for the relief of pain syndromes of various origins. The concept of neuro-leptanalgesia.

8. Drugs used for neuropathic pain syndromes.

9. Principles of pharmacotherapy for migraine. Drugs for the relief of acute attacks: acetylsalicylic acid, paracetamol, 5HT<sub>1</sub> receptor agonists (sumatriptan), ergot alkaloids (ergotamine), antiemetics (methoclopramide). Means for the prevention of migraine attacks: pizotifen,  $\beta$ -blockers, tricyclic antidepressants, valproic acid, calcium channel blockers, cyproheptadine.

10. Agents for the treatment of acute and chronic pain syndromes (adjuvants): clonidine, amitriptyline, carbamazepine, ketamine, benzofurocaine, baclofen, diphenhydramine, phenytoin, valproic acid. Mechanisms of pain-relieving action, the use of drugs for the treatment of pain syndromes.

## THE COURSE OF THE LESSON

### The theoretical part

Theoretical questions are set out in the appendix to the methodological recommendations.

### The practical part

1. Take notes of the theoretical material demonstrated by the teacher;
2. To master the methodology of solving problems and prescribing prescriptions on the topic of employment.

### **Monitoring the assimilation of the topic**

It is carried out in the form of independent written work (solving practical tasks and prescribing prescriptions for individual tasks).

## **METHODOLOGICAL RECOMMENDATIONS FOR THE ORGANIZATION AND IMPLEMENTATION OF THE INDEPENDENT WORK OF STUDENTS**

### **The time allotted for independent work can be used by students on:**

- preparation for practical classes;
- completing assignments on the topic of the lesson in the workbook;
- preparation of thematic reports, abstracts, presentations;
- taking notes of educational literature.

### **The main methods of organizing independent work:**

- performing test tasks and practical tasks of the EEMC for self-control and self-assessment.

### **The list of tasks of the independent work of students:**

- solving practical tasks of the EEMC;
- execution of test tasks of the EEMC.

### **The control of the independent work of students is carried out in the form of:**

- evaluation of an oral answer to a question, a message, a report or a solution to a problem in practical classes;
- individual conversation.

## **METHODOLOGICAL RECOMMENDATIONS FOR THE ORGANIZATION AND IMPLEMENTATION OF THE USRS**

### **Recommended forms of independent work of students organization:**

- completing assignments on the topic of the lesson in the workbook;
- writing an abstract on a given topic;
- preparation of a report and multimedia presentation on a given topic.

### **List of independent work of students tasks:**

Topics of abstracts / multimedia presentations:

1. Addiction - a global social problem and its assessment (complete the teaching workbooks).

2. Negative effects of morphine use on health and society.

3. The risk of using opioids for mental health.

4. Negative physical consequences of the use of opioids.

5. Treatment of opioid dependence. Prevention measures.

### **Forms of control over the implementation of independent work of students:**

- review and evaluation of the abstract on a given topic;
- checking and evaluating a multimedia presentation on a given topic.

## **LIST OF REFERENCES**

1. Kharkevitch, D. A. Pharmacology : textbook for med. students : transl. of 12th ed. of Russ. textbook "Pharmacology" (2017) / D.A. Kharkevitch. - 2nd ed. -

Москва : ГЭОТАР-Медиа, 2019. - 676 с. : ил., табл. - Рек. ФГАУ "ФИРО".—Режим доступа: <http://www.studmedlib.ru/book/ISBN5970402648.html> – Дата доступа: 03.05.2021.

2. Конорев, М. Р. Курс лекций по фармакологии. В 2 т. Т. 2, ч. 1 : для студентов 3 и 4 курсов фармацевт. фак. учреждений высш. образования, обучающихся по специальности 1 - 79 01 08 "Фармация" / М. Р. Конорев, И. И. Крапивко, Д. А. Рождественский ; УО "ВГМУ", Каф. общей и клинической фармакологии с курсом ФПКиПК. - Витебск: ВГМУ, 2019. - 294 с.: ил., табл. - Рек. УМО по высш. мед., фармацевт. образованию.

3. Конорев, М. Р. Курс лекций по фармакологии. В 2 т. Т. 2, ч. 2 : для студентов 3 и 4 курсов фармацевт. фак. учреждений высш. образования, обучающихся по специальности 1 - 79 01 08 "Фармация" / М. Р. Конорев, И. И. Крапивко, Д. А. Рождественский ; УО "ВГМУ", Каф. общей и клинической фармакологии с курсом ФПКиПК. - Витебск: ВГМУ, 2019. - 165 с.: ил. - Рек. УМО по высш. мед., фармацевт. образованию.

4. Кратко о лекарственных средствах: учебно – методическое пособие для студентов 3 курса лечебного., мед.-диагност., фак. подг. спец. для зарубеж. стран, 6 курса лечебного факультета и фак. подг. спец. для зарубеж. стран, аспирантов, магистрантов, учреждений мед. образования: в 2 ч. / Е. И. Михайлова [и др.]. – Гомель: ГомГМУ, 2019. – Ч. 1. – 56 с.

5. Кратко о лекарственных средствах: учебно – методическое пособие для студентов 3 курса лечебного., мед.-диагност., фак. подг. спец. для зарубеж. стран, 6 курса лечебного факультета и фак. подг. спец. для зарубеж. стран, аспирантов, магистрантов, учреждений мед. образования: в 2 ч. / Е. И. Михайлова [и др.]. – Гомель: ГомГМУ, 2019. – Ч. 2. – 84 с.



<b>NB!</b>	<ol style="list-style-type: none"> <li>1. <b>Neuroleptanalgesia</b> – A combination of a narcotic analgesic (eg, fentanyl) and a neuroleptic (eg, droperidol). <b>Ataralgesia</b> – Combination of narcotic analgesics and tranquilizers.</li> <li>2. <b>Fentanyl</b> is stronger than morphine, but acts for a short time (up to 30 minutes).</li> <li>3. <b>Trimiperidine (promedol)</b> is weaker than morphine and less depresses the respiratory center (of choice in obstetrics, pediatrics and geriatrics), and also has a moderate spasmolytic effect on smooth muscles (can be used to treat renal, hepatic and intestinal colic).</li> <li>4. <b>Methadone</b> causes a softer abstinence syndrome due to prolonged action, therefore it is used to treat opioid addiction.</li> <li>5. <b>Loperamide</b> does not have a morphine-like effect on the central nervous system, does not have an analgesic effect.</li> </ol>
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### Morphine and its analogues intoxication [1-15]

<b>Main reasons</b>	<p><b>Acute intoxication:</b></p> <ol style="list-style-type: none"> <li>1. Accidental or intentional overdose with addiction.</li> <li>2. Overdose during premedication or in the postoperative period in patients with chronic respiratory or hepatic insufficiency, as well as with rapid bolus administration of narcotic analgesics for the treatment of pulmonary edema, myocardial infarction, etc.</li> <li>3. Hypersensitivity to narcotic analgesics.</li> <li>4. Children are more likely as a result of accidents or overdose of antitussive drugs.</li> </ol> <p><u>The lethal dose of morphine: 0.5-1 g for oral intake, 0.2 g for IV administration. The fatal blood concentration is 0.14 mg</u></p> <p><u>1. Chronic intoxication:</u> long-term administration of morphine and its analogues (opioid dependence).</p>
<b>Clinic</b>	<ol style="list-style-type: none"> <li>1. <b>Acute intoxication:</b> redness of the face, neck, chest, puffiness of the face, skin itch, fainting ("mediator" syndrome). Instead of euphoria, dysphoria begins with the development of hallucinations. Then the depression of consciousness develops up to the coma, the breath is rare (up to 10 per minute), superficial with apnea. There is a "cholinergic" syndrome - bradycardia, urinary retention. The main diagnostic symptoms of opiate poisoning are pinpoint pupils and the loss of their reaction to light (with the exception of trimeperidine). However, with severe hypoxia of the brain, the pupils dilate (!). With prolonged hypoxia, pulmonary and cerebral edema and hyperkinesia or tonic-clonic seizures develop. Death most often occurs as a result of blockade of the respiratory center.</li> <li>2. <b>In chronic intoxication</b> the drug discontinuation leads to withdrawal syndrome (a sign of physical drug addiction). Initially, there are signs of mental addiction: nervousness, sweating, the need for taking a drug. Then there are signs of severe physical addiction, mostly associated with a violation of the autonomic nervous system ("vegetative storm"): mydriasis, tachycardia, goosebump, intestinal colic, muscle pain, vomiting, diarrhea, dyspnea, fever, yawning, tremor, lacrimation, as well as anorexia and depression. The duration of the withdrawal syndrome depends on the specific drug (for example, for morphine – about 5 days, the peak falls on 1-2 days). Death can come from pain shock, myocardial infarction.</li> </ol>
<b>Therapy</b>	<ol style="list-style-type: none"> <li>1. <b>Acute intoxication:</b> Intravenous administration of opioid analgesics antagonists – naloxone, nalmefene. The effect of naloxone is short (1-2 hours), therefore, when long-acting opioids intoxication (methadone, etc.), it is necessary to re-administer naloxone (!) or administer an antagonist with a longer duration of action – nalmefene (8-10 hours). Restoration of airway passages (artificial lung ventilation and other methods), oxygen therapy, pathogenetic, detoxification and symptomatic therapy are also needed.</li> <li>2. Opioid addiction treatment: methadone is used. It is a long-acting strong opioid agonist opioid with properties close to morphine. Peak of withdrawal syndrome is week 1 (flows more smoothly, unlike morphine), duration is 3 weeks. Instead of methadone, buprenorphine is often used. Both substances are administered orally with a gradual decrease in the daily dose until withdrawal. For the treatment of drug addiction, a long-acting (48 hours) opioid antagonist, naltrexone, is also used to eliminate the use of opioid drugs. . For the treatment of drug addiction, a long-acting (48 hours) opioid antagonist, naltrexone, is also used to eliminate the use of opioid drugs. Clonidine is also used in addiction treatment to eliminate hyperactivity of nervous system during opioid abstinence.</li> <li>1.</li> </ol>

AH - arterial hypertension ICP - intracranial pressure CNS - central nervous system

Non-narcotic analgesics

See the topic "Anti-inflammatory and antispasmodic agents"