

Ministry of health of the Republic of Belarus
Educational institution
«Gomel State Medical University»

Department of general and clinical pharmacology

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METHODOLOGICAL 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 13: «ANTICONVULSANTS. ANTIPARKINSON DRUGS.
ANTIPSYCHOTIC DRUGS»**

Time: 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

Currently, there is an unfavorable epidemiological situation in the world regarding the prevalence of mental disorders of various origin among the population. The scale and urgency of the problem of mental health is confirmed by WHO specialists who found that 5 of the 10 leading causes of disability are associated with mental disorders, namely unipolar major depression, alcohol dependence, bipolar disorder, schizophrenia and obsessive-compulsive disorder.

Epilepsy and Parkinson's disease are common diseases of the central nervous system and are not inferior in relevance to mental disorders. According to world statistics, up to 0.8-1% of the population suffer from epilepsy. Approximately in 10% of patients with epilepsy, the course of the disease is complicated by epileptic status, which requires immediate and effective care. Parkinson's disease (trembling paralysis) and parkinsonism are among the four most common neurodegenerative diseases in the elderly. This pathology affects an average of 100 to 150 people per 100 000 population worldwide. In the European Region, the percentage of people with serious mental disorders varies between 1% and 6%.

All these diseases significantly reduce the quality of life of patients whose post-penum invalidization causes significant economic and social costs for the state. In connection with this, the need for the knowledge of future physicians of the specific features of drugs for lifelong individual pharmacotherapy of these diseases increases, which is justified pathogenetically and is justified from the economic point of view.

Learning objective:

- formation of scientific knowledge about the main pharmacological effects, providing therapeutic and preventive effect of drugs on the topic of the class, indications and contraindications for their use, the interaction of drugs, their combined use for use in medical and preventive activities.

Educational purpose:

- to develop their value-personal, spiritual potential, to form the qualities of a patriot and 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 follow academic and work discipline, standards of medical ethics and deontology.

Tasks:

As a result of the study lesson, the student should

know:

- classification and basic characteristics of the studied drugs, pharmacodynamics and pharmacokinetics, indications and contraindications for their use, side effects;
- features of pharmacokinetics and pharmacodynamics, advantages and disadvantages of different dosage forms of these drugs;
- principles of research and testing of new drugs; information and reference and search systems;

be able to:

- analyze the effect of the studied drugs on the set of their pharmacological properties and the possibility of their use in medical practice; to write them in prescriptions;

- use different dosage forms of these drugs, based on the peculiarities of their pharmacodynamics and pharmacokinetics;
- work with scientific literature, search for information about the use and action of the studied drugs;

possess:

- skills in choice of drugs on the topic of the lesson;
- the rules of prescribing the studied drugs in the treatment of various diseases and pathological conditions, taking into account the indications;
- skills of dosage regime correction in case of pathological changes in functions of organs or systems responsible for biotransformation and elimination of drugs or in case of joint use of different drugs;
- skills to search, analyze and summarize information about the use and effects of the studied drugs.

Motivation for learning the topic:

- the specifics of training doctors in this specialty determines the need for students to purposefully study the main pharmacological effects, providing therapeutic and preventive effects of drugs on the topic of the class, indications and contraindications for their use, the interaction of drugs, their combined use, which will successfully complete the specialized disciplines of the specialty.

MATERIAL EQUIPMENT

Reference and informational literature, charts, tables, presentations, drug collections.

CONTROL QUESTIONS FROM RELATED DISCIPLINES

1. Physiological basis of motion control.
2. Pathogenetic factors of epilepsy and biochemical disorders underlying spontaneous hyperreactivity of neurons of epileptogenic foci.
3. Pathogenetic mechanisms and biochemical bases of Parkinson's disease and parkinsonism.
4. Concept of physiological features of mental activity and psychoses.

CONTROL QUESTIONS ON THE TOPIC OF THE CLASS

1. The basic forms of epilepsy and the principles of their pharmacotherapy.
2. Anticonvulsants (antiepileptic) drugs: valproic acid, carbamazepine, phenytoin, lamotrigine, phenobarbital, ethosuximide, clonazepam, gabapentin. Classification. Mechanisms of anticonvulsant action, criteria for the choice of agents for arresting seizures, side and toxic effects. Comparative characteristics of individual drugs depending on the form of epilepsy.
3. Definition of epileptic status and drugs for its treatment.
4. Antiparkinsonian drugs: levodopa, amantadine, selegiline, trihexyphenidil, pramipexole. The use of DOPA-decarboxylase inhibitors (carbidopa, benserazide) and COMT inhibitors (entacapone) to reduce side effects and increase the effectiveness of levodopa.

5. Classification of antiparkinsonian drugs, mechanisms of action of drugs. Comparative evaluation of the effectiveness of individual drugs. Indications for use and side effects of antiparkinsonian drugs.

6. Principles of drug correction of extrapyramidal disorders. Pharmacological effects of antiparkinsonian drugs, pharmacokinetics, side effects.

7. Means for reducing spasticity - muscle relaxants of central action (baclofen, tizanidine, tolperisone): mechanisms of action, side and toxic effects.

8. Antipsychotics (neuroleptics): chlorpromazine, flupentixol, haloperidol, droperidol, clozapine, risperidone. Antipsychotics as a special class of psychopharmacological agents. The concept of neuroplegia. Classification of antipsychotics.

9. Neurophysiological effects and mechanisms of antipsychotic action, pharmacokinetics, main indications and principles of use, use of depot injectable dosage forms of antipsychotics.

10. Side and toxic effects of neuroleptics (effects on the central nervous system, autonomic functions, endocrine system).

11. Comparative characteristics of antipsychotics. "Atypical" antipsychotic drugs.

PROCESS OF THE STUDY

Theoretical part

Theoretical questions are described in the appendix to the methodological recommendations.

Practical part

1. Take notes on theoretical material demonstrated by the teacher.
2. Master the methods of solving the tasks and writing out prescriptions on the topic of the class.

Theme learning control

Conducted in the form of independent written work (solution of practical problems and prescriptions for individual task).

METHODOLOGICAL RECOMMENDATIONS FOR ORGANIZATION AND EXECUTION OF STUDENTS' INDEPENDENT WORK (SIW)

The time given for independent work can be used by students for:

- preparing for the practical classes;
- completing the tasks on the topic of the class in the workbook;
- preparing thematic reports, essays and presentations;
- taking notes from academic literature.

The main methods of organizing independent work:

- completing tests and practical tasks of the electronic educational-methodical complex (EEMC) for self-monitoring and self-assessment.

The list of tasks of the SIW:

- solving practical problems in the EEMC;
- completing the test tasks of the EEMC.

Control of the SIW is carried out in the form of:

- assessment of an oral answer to a question, report, report, or solution of a task in a practical class;
- individual conversation.

METHODOLOGICAL RECOMMENDATIONS FOR ORGANIZATION AND EXECUTION OF CONTROLLED INDEPENDENT WORK OF STUDENTS (CIWS)

Recommended forms of CIWS organization:

- doing exercises on the topic of the class in the workbook;
- writing an essay on a given topic;
- preparing a report and a multimedia presentation on a given topic.

The list of tasks of the CIWS:

Topics of essays / multimedia presentations:

1. Sleeping pills: strong sleep and unpleasant consequences. Modern methods of treatment of parkinsonism and epilepsy (complete the teaching workbooks).
2. Social adaptation of patients with epilepsy. Errors of patients during epilepsy treatment.
3. Characteristics of the new drug form of antipsychotics - prolongation, difference from depot preparations.
4. Pharmacological incompatibilities for anticonvulsants.

Forms of control of CIWS realization:

- checking and grading an essay on a given topic;
- checking and grading 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: 23.05.2022.
2. Кратко о лекарственных средствах: учебно – методическое пособие для студентов 3 и 6 курсов факультета иностранных студентов, учреждений высшего мед. образования: в 2 ч.=Drugs in short: partical workbook for 3 and 6 year students Faculty for International Students of medical higher educational institutions: in 2 parts / Е.И. Михайлова [и др.]. – Ч. 1. – Гомель: ГомГМУ, 2020. – 56с. – Режим доступа: <http://elib.gsmu.by/xmlui/handle/GomSMU/7128> – Дата доступа: 23.05.2022.
3. Кратко о лекарственных средствах: учебно – методическое пособие для студентов 3 и 6 курсов факультета иностранных студентов, учреждений высшего мед. образования: в 2 ч.=Drugs in short: partical workbook for 3 and 6 year students Faculty for International Students of medical higher educational institutions: in 2 parts / Е.И. Михайлова [и др.]. – Ч. 2. – Гомель: ГомГМУ, 2020. – 76с. – Режим доступа: <http://elib.gsmu.by/xmlui/handle/GomSMU/7129> – Дата доступа: 23.05.2022.
4. Rang and Dale's Pharmacology / J.M. Ritter [et al.]. - 9th ed. - Edinburg [et al.]: Elsevier, 2020. - xvi, 789 p.: ill., tab. + Student consult online.

Anticonvulsants [1-15]

Anticonvulsants – are medicines used to prevent and treat seizures.

Classification	GABAergic system activators			Na ⁺ - channel blockers		Ca ²⁺ -channel blockers
Drugs	<i>Barbiturates</i> 1. Phenobarbital (Luminal) 2. Benzobarbital 3. primidon	<i>Benzodiazepines</i> 4. diazepam (Sibazol, Relanium) 5. Clonazepam 6. midazolam 7. lorazepam 8. Phenazepam	<i>GABA analogues</i> 1. gabapentin	<i>Valproates</i> 10. Valproic acid 11. sodium valproate 12. combined preparations: "Depakin-chrono", "Depakin chrono-sphere" (valproic acid + sodium valproate)	<i>Others:</i> 13. carbamazepine 14. Phenytoin 15. Topiramate 16. lamotrigine	17. ethosuximide 18. pregabalin (lyric)
Mechanism of action	The synaptic transmission in the cerebral neurons is inhibited by ion channels blockage or activation of the inhibitory mediators. <ul style="list-style-type: none"> • enhance the processes of inhibition through the GABA system: ↑ sensitivity of receptors to GABA (1-7), ↑ GABA amount (8-11) • • inhibit excitation processes due to blockade of ion channels of neurons: block Na-K-ATPase (12-15), ↓ Ca²⁺ flow into the cell (16-17) 					
Pharmacological effects	1. Anticonvulsant 2. Anxiolytic (4-8) 3. Sleeping pills (1-8) 3. Sedative (4-8) 4. Miorelaxing (4-8)			1. Anticonvulsant 2. The normotimic (14-16) 3. Antiarrhythmic (14) 4. Analgesic (13) 5. Antipsychotic (13) 6. Timoleptic (13)		1. Anticonvulsant (17-18) 2. Analgesic (18) 3. Miorelaxing (17)
Indications for use	1. Epilepsy 2. Eclampsia (4-8) 3. Chorea (1) 4. Sleep disorders (4-8) 5. Convulsive syndrome in organic brain damage (9-12) 6. Neuroses (6, 7) 7. Postherpetic neuralgia (9) 8. Hemolytic disease of newborns (2) 9. Hyperbilirubinemia (1, 2)			1. Epilepsy 2. Bipolar disorder (13-14, 16) 3. Neuropathic pain syndrome (13-14) 4. Alcohol abstinence (13) 5. Ventricular tachyarrhythmias (14) 6. Migraines (15)		1. Epilepsy 2. Neuropathic pain syndrome (18) 3. Anxiety disorders (18) 4. Fibromyalgia (18)
Side effects	1. Drowsiness 2. Ataxia (1, 4-8) 3. Dizziness 4. Nausea 5. Nystagmus (4, 5) 6. Depression 7. Hallucinations (1, 4-8) 8. Drug dependence (1-8) 9. Dry skin (9)-11) 10. Bradycardia (1, 4, 5, 6) 11. ↓ BP (1, 4-8)			1. Hepatotoxicity 2. Excitation (13, 15) 3. Visual impairment (13, 14, 15) 4. Skin rash (15, 16) 5. Sleep disorders (13, 15) 6. Ataxia (13, 14) 7. Slow-motion thinking (15) 8. Violation of speech (13) 9. Depression (13) 10. Osteomalacia (13) 11. Hallucinations (13)		1. Parkinsonism (17) 2. Dyspeptic disorders 3. Dizziness and drowsiness (17, 18) 4. Dyskinesia 5. Depression 6. Hallucinations 7. ↑ appetite (18) 8. Ataxia (18)

	12. Inhibition of the respiratory center (1-8) 13. Retrograde amnesia (4-8) 14. Peripheral edema (9)	12. Infringement of a hemopoiesis (13) 13. Muscle stiffness (15) 14. Dry skin (10-12) 15. Hair loss (10-12)	
Contraindications	1. Hypersensitivity 2. Hepatic / renal Failure 3. Blood clotting disorders (9) 4. Closed-angle glaucoma (3-7) 5. Anemia (2) 6. Leukopenia (2-7) 7 Myasthenia gravis (3-7) 8. Cerebral and spinal ataxia (4-9)	1. AV blockade (13-14) 2. Adams–Stokes syndrome (14) 3. Hepatic / renal heart failure (14)	1. Hypersensitivity 2. Hepatic / renal failure

NB!	<p>Separately, a new drug levetiracetam (keppra), which has a mechanism of action different from other groups: it blocks the SV2 protein that improves synaptic transmission in the cerebral cortex.</p> <p>The choice of the drug depending on the type of seizures:</p> <table> <tr> <th></th><th>Primary generalized</th><th>Myoclonic</th><th>Absence seizures</th><th>Partial</th><th>Secondarily generalized</th><th>Undifferentiated</th></tr> <tr> <td>First line</td><td>Valproate Lamotrigine Topiramate</td><td>Valproate Levetiracetam</td><td>Valproate Ethosuximide</td><td colspan="2">Valproate Topiramate Levetiracetam Carbamazepine</td><td>Valproate Topiramate</td></tr> <tr> <td>Second line</td><td>Carbamazepine Phenobarbital Pregabalin Levetiracetam</td><td>Lamotrigine Topiramate Levetiracetam</td><td>Lamotrigine Topiramate Levetiracetam Ethosuximide</td><td>Phenytoin Pregabalin Gabapentin Levetiracetam</td><td>Phenytoin Pregabalin Gabapentin Levetiracetam Phenobarbital</td><td>Topiramate Lamotrigine Levetiracetam</td></tr> </table> <p>Epileptic status is an emergency characterized by a series of recurrent episodes of epilepsy, in the interval between which the patient does not come to consciousness. Diazepam is given intravenously, and in the absence of effect – non-inhalational anesthetics are given (propofol, thiopental).</p> <p>Febrile convulsions are not epilepsy. They are symptomatic seizures in children under 4 years of age because of hyperthermia. As a treatment, NSAIDs as antipyretic agents, phenobarbital and diazepam are used.</p>							Primary generalized	Myoclonic	Absence seizures	Partial	Secondarily generalized	Undifferentiated	First line	Valproate Lamotrigine Topiramate	Valproate Levetiracetam	Valproate Ethosuximide	Valproate Topiramate Levetiracetam Carbamazepine		Valproate Topiramate	Second line	Carbamazepine Phenobarbital Pregabalin Levetiracetam	Lamotrigine Topiramate Levetiracetam	Lamotrigine Topiramate Levetiracetam Ethosuximide	Phenytoin Pregabalin Gabapentin Levetiracetam	Phenytoin Pregabalin Gabapentin Levetiracetam Phenobarbital	Topiramate Lamotrigine Levetiracetam
	Primary generalized	Myoclonic	Absence seizures	Partial	Secondarily generalized	Undifferentiated																					
First line	Valproate Lamotrigine Topiramate	Valproate Levetiracetam	Valproate Ethosuximide	Valproate Topiramate Levetiracetam Carbamazepine		Valproate Topiramate																					
Second line	Carbamazepine Phenobarbital Pregabalin Levetiracetam	Lamotrigine Topiramate Levetiracetam	Lamotrigine Topiramate Levetiracetam Ethosuximide	Phenytoin Pregabalin Gabapentin Levetiracetam	Phenytoin Pregabalin Gabapentin Levetiracetam Phenobarbital	Topiramate Lamotrigine Levetiracetam																					

Antiparkinson agents [1-15]

Antiparkinson agents are medications used to treat Parkinson's disease and Parkinson's syndrome.

Classification	↑ activity of the dopaminergic system			↓ glutamatergic effects	↓ activity of the cholinergic system
Drugs	<i>Dopamine precursors</i> 1. Levodopa (in combination with carbidopa / benserazide)	<i>Dopamine receptor agonists</i> 2. Bromocriptine 3. Pramipexole (mirapex)	<i>COMT inhibitors</i> 4. Entacapone 5. Tolcapone <i>MAO inhibitors</i> 6. Selegiline	7. Amantadine (PK-Merz, midantan)	8. Cyclochol
Mechanism of action	<ul style="list-style-type: none"> transformation of the drug into dopamine in the central nervous system (1) stimulation of dopamine receptors in the brain (2-3) inhibition of enzymes that destroy dopamine (4-6) stimulation of dopamine synthesis (7) 			<ul style="list-style-type: none"> Stimulation of dopamine synthesis blockage of glutamate NMDA receptors ↑ sensitivity of receptors to dopamine 	weakening of cholinergic effects due to blockage of central nicotinic and peripheral muscarinic cholinergic receptors
Pharmacological effects	Antiparkinsonian			1. Antiparkinsonian 2. Antiviral	Antiparkinsonian
Indications for use	1. Parkinson's disease 2. Parkinson's Syndrome (1, 2, 4, 6, 7, 8) 3. Influenza A (prevention, including in combination with vaccination and treatment) (7) 4. Extrapyramidal disorders when taking antipsychotics (2, 7, 8) 5. Neuralgia with shingles caused by Varicella zoster (7)				
Side effects	1. Dyskinesia (1-3) 2. Orthostatic hypotension (1-3) 3. Mental and behavioral disorders (depression, hallucinations, euphoria) (1-3) 4. Nausea and vomiting 5. Arrhythmias (1-3) 6. Acute toxic hepatitis (5)			1. Hallucinations 2. Irritability 3. Insomnia 4. Psychosis 5. Convulsions	1. Psychosis 2. Hallucinations 3. Excitation 4. Dry mouth 5. Constipation
Contraindications	1. Mental diseases 2. Arrhythmias (2)			1. Mental diseases 2. Epilepsy 3. Thyrotoxicosis 4. Glaucoma	1. Mental diseases 2. Glaucoma 3. Adenoma of the prostate 4. Elderly age
NB!	Levodopa is converted to dopamine in the CNS due to DOPA-decarboxylase enzyme. Carbidopa and benserazide block peripheral DOPA-DC and prevent the formation of dopamine outside the CNS (reducing side effects). The selection of an individual dose of levodopa is difficult, severe for the patient and is accompanied by a pronounced emetic reaction, for the prevention of which motilium is administered (antiemetic). After a few years of levodopa intake, it loses its effectiveness.				

Antipsychotic drugs (neuroleptics) [1-15]
Antipsychotic drugs are psychotropic drugs used to treat psychoses and other mental disorders.

Classification	<i>Typical antipsychotics</i>			<i>Atypical antipsychotics</i>
	<i>Phenothiazines</i>	<i>Butyrophenones</i>	<i>Thioxanthenes</i>	
Drugs	1. Chlorpromazine (aminazine) 2. Levomepromazine 3. Promazine 4. Periciazine 5. Fluphenazine 6. Thioproperazine	7. Droperidol 8. Haloperidol	9. Chlorprotixene 10. Flupentixol 11. Zuclopentixol	12. Sulpiride 16. Quetiapine 13. Sertindole 17. Risperidone 14. Clozapine 18. Amisulpride 15. Paliperidone 19. Olanzapine
Mechanism of action	Typical: they disrupt the action of many mediators in the central nervous system by blockage of various receptors (dopamine, adrenergic, muscarinic, H1-histamine and serotonin-5-HT ₂ receptors) Atypical: block dopamine and serotonin receptors in the brain			
Pharmacological effects	1. Antipsychotic 3. Stimulating (12-19) 5. Miorelaxing 7. Hypotensive 2. Sedative (1-11) 4. Antiemetic 6. Antihistamine (1-11)			
Indications for use	1. Acute and chronic psychoses 3. Schizophrenia 5. Intractable vomiting (1-11) 7. Migraine (12) 2. Hallucinatory conditions 4. Neuroleptanalgesia (7) 6. Depression (12) 8. Hypertensive crisis due to psychomotor agitation (1)			
Side effects	1. Extrapyramidal disorders 2. Severe cognitive and affective disorders 3. Malignant neuroleptic syndrome 4. Hyperprolactinemia			1. Extrapyramidal disorders (much less often than because of typical) 2. Hyperprolactinemia
Contraindications	1. Glaucoma 2. Parkinson's disease 3. CNS depression 4. Organic diseases and brain trauma 5. Hyperprolactinemia 6. Severe cardiovascular diseases 7. Exacerbation of erosive and ulcerative diseases of the digestive tract (1) 8. Pheochromocytoma (4) 9. Benign prostatic hyperplasia (6)			1. Hypertension (12) 2. CNS depression (14) 3. Myasthenia gravis (14) 4. Alcoholic and intoxication-caused psychoses (12, 14) 5. Hyperprolactinemia (12) 6. Severe cardiovascular diseases (13)
NB!	Typical neuroleptics (especially aminazine and haloperidol) cause pronounced neurological extrapyramidal disorders (neuroleptic parkinsonism, motor anxiety and involuntary spastic contractions of muscles), remove the productive symptoms of schizophrenia (delirium, hallucinations), but have a depressing effect on mental processes. Atypical far less likely to cause extrapyramidal disorders and neuroendocrine disorders due to a lesser affinity for dopamine D ₂ receptors and in addition to productive remove negative symptoms of schizophrenia (blunted affect, emotional and social detachment, lack of speech), i.e. have a stimulating effect on mental processes.			