

Ministry of Health of Belarus  
Gomel State Medical University

Department of Orthopedic, Trauma and military field surgery  
with the course of Anesthesiology and Critical Care Medicine

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SUBJECT: "Noninhalation general anesthesia"

Educational and methodical development  
for 4th year students of medical faculty

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Methodical development is designed for self-study. It provides:

- I. Relevance of the topic
- II. Purpose of the lesson
- III. Tasks
- IV. Basic Forums
- V. Recommended Reading
- VI. Questions for self-
- VII. Training Material
- VIII. Self-study
- IX. Clinical problems and test control

### I. Relevance of the topic

Intravenous anesthetics are widely used for induction of anesthesia, since the induction of these drugs proceeds smoothly and quickly, unlike the majority of inhaled agents. However, to achieve the level of surgical anesthesia and maintenance of anesthesia, many drugs should be used in high doses, which usually lead to the oppression of the cardiovascular activity and respiration, and waking delayed by several hours. In view of these circumstances, these drugs are combined with inhaled anesthetics and muscle relaxants. This educational-methodical development devoted to the pharmacokinetics and pharmacodynamics non-ingalations anesthetics, muscle relaxants, the combined use of schemes for narcosis.

### II. Purpose of the lesson

Learn the basics of clinical pharmacology non-ingalations anesthetics, especially their use in clinical anesthesiology. The scheme of a multi-component and combined anesthesia.

### III. Tasks

*The student should know:*

- Properties of an ideal anesthetic, route of administration non-ingalations anesthetics;
- Classification and clinical pharmacology non-ingalations anesthetics, muscle relaxants;
- Components of general anesthesia;

- Methodology for multi balanced anesthesia, its varieties: neuroleptic analgesia, ataralgesia, total intravenous anesthesia;

*The student should be able to*

- To justify the choice of drugs for intravenous anesthesia;
- To determine the indications for single-and multi-anesthesia;
- To justify the choice of drugs for the multicomponent anesthesia;
- Evaluate the effectiveness of anesthesia;

#### IV. Sections studied before and needed for the session

1. Normal and pathological human physiology. The value of the individual characteristics of the organism and its condition for the manifestation of the drug
2. General pharmacology (receptors, drug distribution in the body, biological barriers, biotransformation, metabolism of drugs in the body);
3. Clinical pharmacology of funds for inhalation anesthesia.

#### V. Recommended Reading

Books on anatomy, normal and abnormal physiology, general and clinical pharmacology for students of medical universities.

Suggested Reading on lessons

##### Main Reading

1. Bunyatyan, AA Anaesthesia and Intensive Care / AA Bunyatyan [and others] Ed. Ed. AA Buniatian. - M., Medicine. - 1997. - 565 p.;
2. Dale, OA Anaesthesia and Intensive Care / O. Valley [and others] Ed. Ed. OA Valley - M., Medicine - 2008. - 574 p.
3. Lecture material.

##### Further Reading

1. Morgan Jr., JE Clinical Anesthesiology, Book One / JE Morgan Jr., MS Magid: Per. from English. Under the general editorship of Professor. AA Buniatian, AM Zeitlin M, "Published Bean" - 2005. - 431 p.;
4. Kulagin, AE Fundamentals of clinical pharmacology for anesthesiologists and intensive care / AE Kulagin, VV Kurek. Teaching aid. - Mn.: BelMAPO, 2005.-45.
5. Calvey, TN Pharmacology for the anesthetist / TN Calvey, NE Williams. Per. from English. Under the general editorship of Professor. VM Mizikova, AM Zeitlin. - M, "Published Bean" - 2007. - 176;

## VI. Questions for self-working:

### Questions on basic knowledge

1. General Pharmacology, route of administration of drugs, absorption
2. Drug distribution in the body, biological barriers. Deposit.
3. Biotransformation. Drug metabolism in the body.
4. The mechanism of action of drugs, receptors, reversibility and selectivity.
5. Dependence pharmacotherapeutic effect on the properties of drugs and their conditions of use.
6. The value of the individual characteristics of the organism and its condition for the manifestation of the action of drugs.
7. Clinical pharmacology of non-ingalation anesthesia.
8. Neuromuscular synapse and neuromuscular transmission pulse
9. The mechanism of action of narcotic analgesics, tranquilizers, antipsychotics, side effects.

### Questions on this topic:

1. The concept of an "ideal" non-ingalation general anesthetic
2. The classification of types and methods general anesthesia: intravenous, intramuscular, intraosseous, rectal, etc.
3. Clinical and pharmacological characteristics non-ingalations anesthetics: barbiturates, propofol, ketamine, antipsychotics, ataraktiki analgesics.
4. Muscle relaxants, clinical application. Dangers, complications and their prevention and treatment.
5. Combined methods of general anesthesia. The main stages of combined general anesthesia during the administration of anesthesia, maintenance of anesthesia, duration of excretion. Combined general anesthesia with muscle relaxants, neuroleptic analgesia, ataralgeziya.

### ***Topics UIRS***

1. Features use of muscle relaxants in children and elderly patients.
2. Anesthetics used in multiple trauma and other hypovolemic states.
3. Intravenous anesthetics in outpatient practice.

### Teaching tools for organization of independent work of students

1. Computer database.
2. Objectives, test control.
3. Thematic patients.

4. Patient records and other documentation.
5. Safety instructions, aseptic and antiseptic.
6. Bank jobs for self-study.

## VII. Training Material

Non-ingalation general anesthesia - a variant of anesthesia at which anesthetics enter the body by different ways.

Classification of non-ingalation general anesthesia:

*intravenous*, –

*intramuscular* –

*oral*; –

*iliac* –

*intraosseous*, –

The greatest value of these options has an intravenous general anesthesia.

Clinical effect of intravenous anesthetics depends on the concentration of the drug in the brain tissue. Any injection of the drug quickly redeployed from richly vascularized tissues (brain, heart, kidneys) in the muscles, and finally, in poor vascular tissue (fat, bone). On the pharmacokinetics and pharmacodynamics of drugs administered intravenously, is influenced by:

the binding to plasma proteins, –

the volume of distribution of the drug, –

the proportion of different tissues in the body, –

value of cardiac output and its distribution, –

metabolism and excretion, –

rate intravenous administration. –

The mechanism of action is not fully understood, it is believed that the main point of their applications - reticular activating system of the brain. All intravenous anesthetics are readily soluble in lipids and quickly penetrate the blood-brain barrier (BBB). The rapidity of the onset of the conditioned velocity passing BBB and cerebral blood flow (CBF). Clinical use of intravenous anesthetics have both positive and negative.

***The "ideal" intravenous anesthetic must meet the following requirements:***

- To have a small amount (up to 10 ml) required for the induction of anesthesia;
- To cause rapid development of clinical effect (for one cycle of blood) and a short

duration of action;

- Rapidly metabolized without the formation of toxic metabolites;
- To be water soluble, stable in aqueous solution, chemically stable;
- Do not interact with muscle relaxants;
- Quickly restore the original level of consciousness;
- Does not cause the release of histamine and anaphylactic reactions;
- Does not cause depression of systems and organs (except CNS depression): cardiovascular, respiratory, liver and kidney, gastrointestinal tract;
- Not to have undesirable side effects (nausea, vomiting, headache, vision);
- Do not cause pain at the injection site and safety accidental introduction into the artery.

### ***Classification of intravenous anesthetic***

- I. Short-duration (15 minutes): propofol, midazolam
- II. Average duration (20 minutes): barbiturates, ketamine.
- III. Long-lasting (up to 60 minutes): sodium hydroxybutyrate.

### ***Propofol (Diprivan)***

*Mechanism of action:* Not known, but it is proved that there is an inhibition of GABA transmission mediator, as in the action of benzodiazepines.

Effect of structure on the activity. Propofol is used (10 mg / ml) in the form of an emulsion containing soybean oil, glycerol and egg lecithin. No preservatives, so it is extremely important to follow a strict sterility during treatment, within 6 hours after the opening of the ampoule propofol unusable.

#### ***Pharmacokinetics.***

*Distribution.* Propofol - a highly lipophilic compound, is rapidly distributed in the richly vascularized organs, resulting in a rapid onset of action and its acceptability to the induction of anesthesia. The end effect is due to a redistribution of the drug on the one hand and the rapid hepatic and renal clearance on the other.

Metabolized in the liver, the end product is excreted in the urine. About 0.3% of administered drug is excreted in the urine unchanged. Propofol clearance is directly related to the rate of hepatic blood flow. At the same time, and the possibility extrahepatic metabolism, the process involves active participation of the lungs. Propofol does not have a pronounced ability to cumulation.

#### ***Effects on the body:***

*Cardiovascular system:* reduces PR, myocardial contractility, preload; a significant

decrease in blood pressure; inhibits pressosensitive reflex; no compensatory tachycardia in response to a decrease in blood pressure.

*Respiratory system:*

cause respiratory depression, induction dose usually causes apnea; inhibits airway reflexes with more than thiopental, which allows for the installation of tracheal intubation and laryngeal mask without muscle relaxation.

*Central Nervous System:*

reduces cerebral blood flow—

reduce intracranial pressure—

*Dosage:* Adult dose induction of anesthesia is 1.5-2.5 mg / kg, intravenous sleep occurs within 20-40 seconds, the duration of about 5 minutes. Dose maintenance of anesthesia in adults 4-15 mg / kg per hour. Awakening occurs without stimulation, orientation is restored immediately, no postanesthetic depression of consciousness. Is the drug of choice for anesthesia in patients in day care, and in the case of suspected porphyria or malignant hyperthermia.

*Contraindications:* early childhood - up to 3 years of life and obstetrics, ie anesthesia for caesarean section.

***Barbiturates***

*Methods of administration*

intravenously for induction of anesthesia in adults and children.—

rectally for induction of anesthesia in children.—

*Pharmacokinetics.*

loss of consciousness with a / Venn introduction begins about 30 seconds and lasts about 20 minutes; oxidized in the liver to inactive water-soluble metabolites.—

allocated kidneys (metogeksital excreted in faeces).

*Pharmacodynamics*

*Cardio-vascular system.*

reduce blood pressure, increase in heart rate;—

expand peripheral vessels, which leads to the sequestration of blood and decreases venous return to the right atrium;—

Slow administration of the drug and a full load of fluid before surgery in most cases weaken adverse circulation.

*The respiratory system.*

- depress the respiratory center of the medulla, which inhibits the compensatory response of ventilation to hypoxia and hypercapnia;  
an induction dose of barbiturates causes apnea;–
- barbiturates not completely inhibit nociceptive reflexes of the respiratory tract, which can be manipulated to cause bronchospasm in bronchial asthma or laryngospasm during light anesthesia;  
after applying metogeksitala incidence of laryngospasm and hiccups are higher than with the use of thiopental.–

#### *Central nervous system.*

- cause narrowing of the blood vessels of the brain, which reduces cerebral blood flow and intracranial pressure;–
- reduce oxygen consumption by the brain (up to 50% of the physiological values);–
- sometimes give antianalgetichesky effect, reducing the pain threshold;–

#### *Kidney, liver,*

- reduce renal and hepatic blood flow and glomerular filtration rate is proportional to the decrease in blood pressure;–
- induce hepatic enzymes;–
- stimulate the formation of porphyrin (intermediate metabolite in the synthesis of heme) that individuals at risk can provoke an attack of porphyria.

#### ***Thiopental***

Available in vials of 500 mg or 1 g of distilled water and dissolved for 2.5% or 1% solution. The peak effect of the drug when administered intravenously occurs in 30-40 seconds, the duration of 5-15 minutes, maximum 20 minutes.

*Dosage.* Used for induction of anesthesia, at a dose of 3-5 mg / kg as a 2-2.5% solution. Maintenance dose in children is or 3-5 mg / kg per hour for adults 25-100 mg. Dose for sedation - 0.5-1.5 mg / kg intravenously.

#### *Indications:*

- induction of anesthesia, maintenance of anesthesia for short procedures (threatening accumulation after repeated administration);  
therapy convulsions, decreased intracranial pressure.–

#### *Contraindications:*

- heart failure, a common disorder and coronary hemodynamics;–
- functional failure of the liver;–
- shock;–



asthma and chronic respiratory disease;–  
porphyria;–

### ***Ketamine (Kalipsol, ketalar)***

Ketamine has a multifaceted effect on the central nervous system, it separates or dissociates, thalamus and limbic cortex. The clinical condition of dissociative anesthesia characterized by the fact that the patient seems to be awake (he opens his eyes, swallowing, muscles contract), but he does not have the ability to analyze sensory stimuli and react to them.

#### *Pharmacokinetics*

Ketamine is used IV or IM

*Distribution.* Ketamine is stronger than thiopental, soluble in fat and less protein bound. The presence of these properties leads to a rapid uptake of ketamine in the brain and the subsequent redistribution.

*Biotransformation.* Metabolized in the liver, the end products of biotransformation are allocated through the kidneys.

#### *Pharmacodynamics:*

##### *Cardio-vascular system.*

– stimulates the sympathetic nervous system, which leads to increased blood pressure, heart rate, cardiac output, myocardial oxygen consumption, increased heart.

increases the pressure in the pulmonary artery;–

improves atrioventricular conduction and conduction in accessory pathways, improves functional status of sino-atrial node.–

##### *The respiratory system.*

powerful bronchodilator, which makes it an ideal anesthetic agent for the induction of bronchial asthma.

##### *Central nervous system.*

increases oxygen consumption by the brain–

increases cerebral blood flow, increased intracranial pressure, causing undesirable effects (eg, illusions, frightening dreams, delirium) during waking, rarely occur with the use of benzodiazepines in premedication in children.

most "full" of anesthetics - causes analgesia, amnesia, loss of consciousness.

#### *Contraindications:*

patients with CNS disorders, including intracranial hypertension (cerebrovascular accidents, brain injury, birth injury);

any illnesses with convulsive;

corneal damage (compared to ketamine anesthesia by 30% increased intraocular pressure);

arterial hypertension of any cause, severe heart failure, and congenital heart disease, when the myocardium is working against a mechanical resistance (coarctation of the aorta); continued bleeding; severe disturbance of renal excretory function.

Dosage. IM dosage - of 6-8 mg / kg, the maximum effect occurs within the first 5-10 minutes. The duration of analgesic effect of a single dose of 20-25 minutes.

IV dosage - 0.5-3 mg / kg, maximum effect develops within 40-60 seconds, the duration of 5-15 minutes. The usual dose of induction of anesthesia, 1-2.5 mg / kg. Maintenance of anesthesia administration is in fractional doses, constituting at 0.5-1 mg / kg.

### ***Sodium hydroxybutyrate***

It has a hypnotic and analgesic effect negligible, the elements of nootropic activity, increases resistance to hypoxia well potentiates the action of sedative and narcotic drugs. It is considered a neurotransmitter, although not quite meet all the requirements of this class of substances. Is a precursor of gamma-aminobutyric acid (GABA), but directly on its receptors are not affected.

Pharmacokinetics. Effective with the intravenous, intramuscular, rectal and oral application, readily crosses the blood-brain barrier, like GABA inhibits the release of excitatory neurotransmitters from presynaptic terminals and causes postsynaptic inhibition. Readily metabolized to carbon dioxide and water, leaving behind a toxic metabolites. Metabolism is so effective that after 4-5 hours after injection drug was not detected in the blood. Small amount is excreted in the urine. Duration - 1 - 3 hours

### Pharmacodynamics:

#### *CV system*

causes slowing of heart rate, increased blood pressure and a significant increase in systemic vascular resistance;

#### *The respiratory system.*

during rapid intravenous administration may cause respiratory failure, up to

apnea.—

*System homeostasis.*

contains many Na<sup>+</sup>, which can develop sobstvovat hypernatremia;  
significantly reduces the level of cholesterol in the blood;  
contributes to the development of hypothermia.

*Central nervous system.*

is a pleasant, easy to fall asleep;  
has low analgesic activity;  
provides moderate central miorelaxation;  
antihypoxant is powerful;  
at the end of the action may be a motor and language stimulation.

*Contraindications.*

hypokalemia;  
myasthenia gravis;  
hypertension;  
preeclampsia.

*Dosage.* Induction dose of 75-100 mg / kg IV, the effect develops in 10-15 minutes and lasts for up to 1 hour. When IM administration dosage of 120-150 mg / kg, the effect is 30 minutes and last for about 1.5-2 hours with oral dose of 150 mg / kg, the effect occurs within 30-50 minutes, last for about 2 hours/

## ***Narcotic analgesics***

***Morphine*** - a reference preparation of the group.

Doses: premedication-in / m 1 mg/10 kg

induction - a / 1 mg / kg,

maintenance - in / 100-120 mg / kg / h.

Pharmacokinetics

duration of 4-6 hours;—

bound to plasma proteins at 26-36%;—

biotransformation mainly in the liver, derived mainly as metabolites in the urine and feces.—

Pharmacodynamics:

– therapeutic doses of morphine minimal hemodynamic effects, inhibits the heart rate and lowers blood pressure due to increased vagal tone (decrease in blood pressure may also be due to histamine release);  
can cause bronchospasm (due to histamine release);–  
promotes spasm of the sphincter of Oddi;–  
ADH release and inhibition of release of ACTH, FSH and LH.

***Fentanyl*** - a synthetic narcotic analgesic. For analgesic activity in 100-130 times greater than morphine. Lipophilic and very easy cross the membranes.

Doses: induction – IV -0.1 -0.2 mg maintenance anesthesia -2-4 mg / kg every 30 minutes

***Pharmacokinetics:***

duration of 20-30 minutes;  
plasma protein binds to 79-87%;  
biotransformation occurs mainly in the liver;  
excreted by the kidneys and gastrointestinal tract as metabolites (10% excreted unchanged).

***Pharmacodynamics:***

readily crosses the blood-brain barrier;  
reduce blood pressure due to vasodilation, decreasing venous return and cardiac;–  
at high doses can accumulate in fat and muscle tissue, at high doses can cause prolonged respiratory depression;  
bolus can lead to rigidity of the chest.

***Promedol*** - an analgesic activity weaker in 2 times compare with morphine.

Doses: induction – IV- 0.4-0.6 mg / kg, and maintaining anesthesia -0,2-0,4 mg / kg / h

***Pharmacokinetics***

duration of 3-4 hours;–  
biotransformation occurs mainly in the liver;  
excreted by the kidneys and gastrointestinal tract in the form of metabolites.

***Pharmacodynamics:***

has a mild antispasmodic effect on smooth muscles of internal organs and increases uterine contractions (unlike morphine);

less than morphine depresses the respiratory center;  
less exciting center of the vagus nerve and the vomiting center.

**Sufentanil** - has 5-10 times more analgesic activity in comparison with fentanyl.  
Doses: induction 10.2 mg / kg, and maintaining anesthesia 0.6-3.0 mg / kg every 30-60 minutes

*Pharmacokinetics*

duration of 20-45 minutes;—  
plasma protein binds about 92%.—

*Pharmacodynamics:*

with bolus possible bradycardia—  
not release histamine;  
less than fentanyl is respiratory depression;

**Remifentanyl** - narcotic analgesic of the latest generation of ultrashort action.  
Doses: induction IV- 0.5-1.0 mg / kg, maintenance - 0.05-2.0 mcg / kg / min continuously.

*Pharmacokinetics*

70% of the drug bound to plasma proteins;  
— when entering the bloodstream undergoes extensive extrahepatic hydrolysis nonspecific esterases in blood and tissues (the main pathway); duration of 2-5 minutes; 90% of the drug is excreted as metabolites in the urine.

*Pharmacodynamics:*

causes a moderate decrease in blood pressure, decrease in heart rate and a decrease in cardiac output;  
causes dose-dependent respiratory depression;  
not affect intracranial pressure;  
does not cause histamine release.

**Droperidol** - antipsychotic used extensively by anesthesiologists for sedation, potentiation of general and regional anesthesia.

The dose is determined individually, based on the age, body weight, general physical condition, the nature of the disease, while drugs used, the type of anesthesia forthcoming. Scheme of droperidol determined by the specific clinical

situation. The average dose for the induction of droperidol is 0.25-0.5 mg / kg.

#### *Pharmacokinetics*

bound to plasma proteins by 85-90%;

metabolized by the liver, shows - 75% of the kidneys as metabolites, 11% of the bowel.

#### *Pharmacodynamics*

causes mild transient hypotension with tachycardia;

has antiarrhythmic activity in ectopic arrhythmias.

in large doses can disrupt thermobalance in the body and causes mild hypothermia.

#### ***Muscle relaxants***

Muscle relaxants - drugs that can alter the action of acetylcholine by binding to postsynaptic nicotinic acetylcholine receptors. These drugs cause skeletal muscle relaxation, allowing for abdominal surgery, in addition, they are also used to prevent muscle spasms in diseases such as tetanus, rabies, status epilepticus and nekupiruyuschiesya seizures of any etiology.

#### ***Classification of muscle relaxants***

*Depending on the mechanism of action of muscle relaxants are divided into:*

1. depolarizing:

succinylcholine (listenone, ditilin)–

2. nondepolarizing:

atracurium (trakrium)–

rokuronium (esmerone)–

tsisatrakurium (nimbeks)–

pipekuronium (arduan)–

pancuronium (pavulon)–

*Depending on the duration of neuromuscular blockade:*

1. short action - 5-7 minutes:

succinylcholine;–

2. average duration - up to 40 m:

atracurium (trakrium)–

rokuronium (esmerone)–

tsisatrakurium (nimbeks)–

3. duration - more than 40 minutes:

- pipekuronium (arduan)–
- pancuronium (pavulon)–

***The mechanism of action of depolarizing muscle relaxant.***

Depolarizing muscle relaxant structurally resemble acetylcholine, interact with n-acetylcholine receptors (acting as cholinergic agonists) and cause depolarization of the motor end plate just before the development of neuromuscular blockade.

Depolarizing muscle relaxants are not destroyed acetylcholinesterase. From the field of neuro - muscular synapse they enter the bloodstream, and then subjected to hydrolysis in plasma and in the liver under the influence of another enzyme - pseudocholinesterase (plasma cholinesterase). This process is very fast, which is a favorable character: no specific antidote.

Features of action of ***succinylcholine***:

- Full neuro - muscular blockade occurs within 30-40 seconds.
- The duration of the block is sufficiently short, usually 4-6 minutes. So it used for endotracheal intubation, followed by the transition to non-depolarizing relaxants.
- Cause muscle twitching. This phenomenon is associated with the simultaneous depolarization of most of the neuromuscular synapse. Muscle fibrillation can cause a number of adverse effects (postoperative muscle pain, release of potassium).
- Increased intraocular pressure (must be used with caution in patients with glaucoma, and in patients with penetrating eye injury they should be avoided).
- Is the trigger malignant hyperthermia syndrome.
- Stimulates the n-cholinergic parasympathetic and sympathetic ganglia, as well as m-cholinergic receptors sinoatrial node of the heart, leading to bradycardia.
- Causes hyperkalemia. When succinylcholine depolarization leads to that of healthy muscles is released potassium. At normal concentrations of potassium this phenomenon has no clinical significance, but in some conditions (burns, major trauma, certain neurological diseases, etc.) arising hyperkalemia can be life-threatening.
- Some patients succinylcholine causes activation of the EEG, a moderate increase in cerebral blood flow and intracranial pressure.

***The mechanism of action of non-depolarizing muscle relaxant.***

The mechanism is related to the competition between non-depolarizing muscle

relaxants and acetylcholine at specific receptors. As a result of relaxants on the neuro - muscular synapse postsynaptic membrane loses its ability to move into a state of depolarization, and muscle fiber loses its ability to contract. Non-depolarizing muscle relaxants act as competitive antagonists. Neuromuscular blockade caused by nondepolarizing relaxants may be terminated by using anticholinesterase drugs (Neostigmine): The usual process of biodegradation of acetylcholine concentration in the synapse increases, and eventually displaces relaxant of its association with the receptor. Non-depolarizing muscle relaxants are not hydrolyzed or acetylcholinesterase or pseudocholinesterase. When nondepolarizing block repair of nerve - muscle conduction due to redistribution, partial metabolic degradation and excretion of non-depolarizing neuromuscular blocking agents, or may be due to the influence of specific antidotes - acetylcholinesterase inhibitors.

### ***Atracurium (trakrium)***

Dosage. Dose required for intubation is 0.5 mg / kg, and it is administered within 30-60 with supporting - 0.1 mg / kg every 10-20 minutes.

#### ***Side effects:***

causes the release of histamine;—  
— possible hypotension and tachycardia: adverse effects on the cardiovascular system are rare, provided that the dose should not exceed 0.5 mg / kg. Atracurium can cause a transient decrease in PR and increase in cardiac index and bronchospasm independent of histamine release. Atracurium should not be used in bronchial asthma. Moreover, atracurium may cause severe bronchospasm, even when no history of asthma.

### ***Tsisatrakury***

Tsisatrakury unlike atracurium does not cause persistent dose-dependent increase in plasma histamine content. Tsisatrakury no effect on heart rate, blood pressure and autonomic nervous system.

### ***Rocuronium***

It is the only non-depolarizing muscle relaxant, which is effective as quickly as succinylcholine, making it the drug of choice for rapid sequence induction. The average duration of rocuronium is similar to that atracurium. Rocuronium provides somewhat more pronounced vagolytic effect than pancuronium.



*Dosage.* Dose required for intubation is 0,45-0,6 mg / kg. To maintain intraoperative muscle relaxation drug is administered in a bolus dose of 0.15 mg / kg. Infusion doses ranging from 5 to 12 mg /kg /min).

### ***Pancuronium (pavulon)***

Pharmacodynamics:

- Hypertension and tachycardia: Effect of pancuronium on the blood circulation due to blockade of the vagus nerve and the release of catecholamines from adrenergic nerve endings. Pancuronium should be used with caution in cases where the development of tachycardia are at risk (ischemic heart disease, hypertrophic cardiomyopathy).
- Arrhythmias: atrioventricular conduction and increase the release of catecholamines increase the likelihood of ventricular arrhythmias in patients at risk. Particularly high risk for arrhythmias in conjunction pancuronium, tricyclic antidepressants, and halothane.

Allergic reactions: hypersensitivity to bromides may be allergic to pancuronium (pancuronium bromide).

*Dosage* of pancuronium 0.08-0.12 mg / kg after 2-3 min can intubate the trachea. Loading dose for intraoperative muscle relaxation - 0.04 mg / kg maintenance dose - 0.01 mg / kg every 20-40 minutes.

### ***Pipekuronium (arduan)***

The main advantage over pancuronium pipekuronium - no side effects on blood circulation. Pipekuronium not cause histamine release. Beginning and duration of action of these drugs are similar.

*Dosage.* Pipekuronium slightly more powerful drug than pancuronium. Dose required for intubation is 0,06-0,1 mg / kg. Doses to maintain intraoperative muscle relaxation is 20% lower than that of pancuronium.

### ***Combined methods of anesthesia***

Under anesthesia began to understand the management of many features. It went far beyond the use of a narcotizing funds into a complex set of activities, which are rightly called "anesthetic". When short-term and low-traumatic interventions are acceptable simple methods of anesthesia. On the other hand, a prerequisite for success of complex, lengthy and traumatic operations is the use of combined methods of anesthesia with the use of complementing each other. The main

principle is to select pharmacological agents that have a selective effect on various parts of the reflex arc.

Under the combined influence of pharmacological effects on the body understands several drugs introduced at the same time or in a certain order and time sequence.

The more complex and diverse combination of drugs, the more complex relationships occur in the body when using it. Of the general laws are the most important synergy and antagonism. "Synergy" - a term derived from the Greek word «synergia» and means of joint action. Synergy is manifested in two forms - the summation and potentiation of effects. The summation is such a thing as a common pharmacological effect is the sum of the effects of individual ingredients combination. Potentiate (exponentiation) the overall effect of pharmacological combinations exceeds the amount of pharmacological effects, characteristic for each component separately. In the application of anesthetic synergy has the advantage that allows you to get the desired pharmacological effect with relatively low doses of several drugs acting in the same direction. In this case, the toxic side-effects and drug combination significantly reduced.

Antagonism. At the core of this concept is the complete elimination or inhibition of manifestation of the pharmacological effect of one drug with another. In anesthesiology phenomenon of antagonism drugs used to monitor the effectiveness of, or correction of the primary drug.

The variety of anesthetics, analgesics, tranquilizers and neuroleptics causes many combinations for use in clinical practice in combination with or without muscle relaxants.

Ataralgnesia is a form of combined general, involves the use of ataraktiks (eg, diazepam) and narcotic analgesic (eg, fentanyl), the result is a state of ataraxia and analgesia. These conditions are essential and indispensable for the anesthesia. The other components of general anesthesia (depression of consciousness, autonomic inhibition and muscle relaxation) as a complement to them, depending on the type, nature, duration, and trauma surgery.

Premedication: one hour before surgery, the patient gets into diazepam (20 mg). 30-40 minutes prior to surgery intramuscularly administered fentanyl (100 µg) and droperidol (5 mg) with atropine (0.25-0.5 mg).

Induction. When breathing patient with a gas mixture of nitrous oxide and oxygen in a ratio of 2:1 by slow intravenous injection is administered 20 mg of diazepam and a muscle relaxant in the endotracheal dose on 0,2-0,15 mg fentanyl. After 2-3

minutes come lethargy, drowsiness, state of ataraxia. Against the background of the action of these drugs, while maintaining contact with the patient, water the root of the tongue, nose and throat part 2% lidocaine. When respiratory depression begin assisted ventilation. Then perform tracheal intubation and mechanical ventilation starting mixture of nitrous oxide and oxygen (2:1). Additionally, before skin incision injected 100-200 mcg of fentanyl. While maintaining anesthesia ventilator continues mixture of nitrous oxide and oxygen (2:1). Analgesic component of anesthesia support a split of 150-200 micrograms of fentanyl on average every 25-30 minutes. During long operations in 40-60 minutes in addition administered 10-20 mg of diazepam intravenously. Next, muscle relaxants are not applied. 2-3 min before application of the latest skin sutures supply of nitrous oxide was stopped and the patient is transferred to spontaneous breathing. Adequate spontaneous breathing and consciousness recovered quickly, and analgesia lasts 40-60 minutes after surgery.

Leptoanalgesia - total intravenous anesthesia technique, in which the main pharmacological agents are powerful antipsychotic and strong central analgesic. Antipsychotics provide one of the necessary conditions of balanced anesthesia - neurovegetative protection. Of antipsychotics in clinical practice is used mainly droperidol, low toxicity, high antishock effect and antiemetic activity. Common and convenient analgesic is fentanyl, which has a high analgesic activity and relatively short-term effect. The practice is used and official mixture of fentanyl and droperidol in the ratio of 1:50, which has the name "talamonala." 1 ml contains 50 mg talamonala fentanyl and 2.5 mg droperidol. In such a mixture, the analgesic effect of fentanyl increases, but decreases its cholinergic action.

The classical method involves the use of droperidol, fentanyl, nitrous oxide, muscle relaxants and mechanical ventilation. Commonly used for sedation talamonal, given patient weight: at 41-50 kg - 1.5-2 ml and 61-80 ml kg -2-4. Usually drug GIVING intramuscularly 40-45 min before surgery. The average dose for the induction of droperidol is 0.25-0.5 mg / kg. Fentanyl is administered at the rate of 5 mg / kg. Administration of fentanyl prior to injection into the endotracheal dose of muscle relaxant, which prevents the formation of muscle rigidity after administration of the main dose of fentanyl. Induction is performed on the background of breathing mixture of nitrous oxide (70%) and oxygen (30%). While maintaining anesthesia breathing is similar to the gas mixture. Fentanyl administered fractionally on 50-100 mg 20-30 minutes, muscle relaxation in favor

of imposing a muscle relaxant in the usual dose, given the duration of surgery. 20-30 minutes before the end of the operation a split fentanyl is stopped. When applying the latest skin sutures stops supplying nitrous oxide and restore spontaneous respiration. 3-5 min after the patient regains consciousness. An overdose of fentanyl can hinder recovery of adequate spontaneous breathing. In these cases, use of analgesics morphine antidote (naloxone, etc.).

Schemes of different combinations of inhaled and intravenous anesthetics Barbiturates, and nitrous oxide. In this case, barbiturates act as fast-and short-hypnotic, allowing you to achieve the shutdown of consciousness, bypassing the stage of excitement. Nitrous oxide also adds cut consciousness analgesic effect. However, the analgesic effect of nitrous oxide is still weak, so the traumatic, painful and relatively long procedures in this combination adds fractional analgesics (promedol, fentanyl).

Premedication was performed using atropine in combination with the various components (diazepam, promedol or fentanyl). Induction exercise thiopental sodium. Tracheal intubation produced against muscle relaxation with succinylcholine. Then transferred to a ventilator with a mixture of nitrous oxide (70%) and oxygen (30%).

Downstream anesthesia is administered periodically by indications small doses of barbiturates (50-100 mg), potentiating the hypnotic effect of nitrous oxide, and analgesics (fentanyl), increasing analgesia. Miorelaxation support fractional succinylcholine at 0.5-1 mg / kg, approximately every 5-10 minutes. By the end of the interval between the introduction of anesthesia and muscle relaxant analgesic increase.

General anesthesia is based on the combined use of liquid inhalation anesthetic and analgesic. Method, which currently enjoys the world's most popular. He avoids excessive deepening anesthesia and at the same time provides sufficient depth, efficiency, manageability and security. Can be recommended as the primary method of anesthetic management of surgical interventions of any complexity and duration.

Barbiturates, nitrous oxide, halothane. This kind of combination anesthesia used in surgical interventions of varying duration.

Premedication with atropine spend, the rest of its components (diazepam, promedol or fentanyl) is used as indicated. Induction of anesthesia performed with a solution of sodium thiopental. Intubation produce on the background of

succinylcholine in the usual dose. Followed by feeding a mixture of nitrous oxide and oxygen (2:1) and inhaled halothane (initial concentration of 0.5 vol.%). Allowable concentrations of halothane in a mixture of 0.5 to 2 vol.%. A gradual increase in concentration in the breathing gas flow of nitrous oxide is reduced to 50%. The concentration of halothane increase until there will come a surgical stage of general anesthesia. Maintenance of anesthesia is performed on the background of inhalation mixture of nitrous oxide and oxygen in a ratio of 1:1 or 2:1, regulating the supply of halothane (0.5 - 1.5% vol.). Analgesic effect of halothane weak, so during anesthesia add small doses of promedol (20-30 mg) or fentanyl (50-100 mcg). Miorelaxation maintained by tubocurarine or pipekuronium. Depending on the duration of the operation flow halothane stop for 5-10 minutes until it ends. 2-3 minutes before the end of the operation switch off nitrous oxide and increase the concentration of oxygen in the breathing mix.

Total intravenous anesthesia (TBA) - general anesthesia, in which all drugs administered intravenously. Anesthetics turn off consciousness, opioids prevent pain and muscle relaxants facilitate ventilation. The introduction of the modern practice of drug-acting intravenous anesthetic gives more character driven and in this respect closer to its inhalation, aided and technical design of infusion systems, providing the most accurate dosing of drugs. Example TBA - combined use of Diprivan (propofol) and fentanyl. Diprivan - strong hypnotics (ie, drug, providing loss of consciousness), can reduce the frequency of awakening intranarkoznogo and achieve sufficient depth in all phases of even the most traumatic operations. The absence of cumulative effects allows for propofol (Diprivan) for maintenance of anesthesia of any duration. The method was particularly common in surgery, "one day" because of the simplicity and comfort.

Ketamine, diazepam, fentanyl. The essence of this technique is the use of ketamine as a hypnotic, diazepam is used as proof of hypnotic effect of ketamine and drugs that cause autonomic inhibition. Analgesic fentanyl enhances the analgesic component of this combination. Induction produced by infusion of ketamine at a dose of 1-1.5 mg / kg followed by 10-20 mg of diazepam. After the loss of consciousness should be an injection of 0.2-0.3 mg of fentanyl and succinylcholine in a dose - 1.5-2 mg / kg. After tracheal intubation, during the period of anesthesia and surgery is carried out with a mixture of air ventilation with 40-50% oxygen. If necessary, you can increase the oxygen concentration is maximum. Anesthesia is maintained by a continuous infusion of ketamine, fentanyl, diazepam and muscle

relaxant. Most successfully used in the mixture used infusion systems.

### ***Non-pharmacological methods of general anesthesia***

#### *Galvanonarcosis*

In anesthetic practice in recent decades for the analgesic component of general anesthesia with mixed results using different methods of electro-effects on the CNS, under the general title "galvanonarcosis." Opinions of the authors on the parameters of electrical current for galvanonarcosis contradictory. According to most researchers, to choose the appropriate mode of electrical stimulation and the electrodes can significantly reduce the required dose for analgesia of general anesthetics and narcotic analgesics.

*Elektroanalgeziya (EA)* is particularly indicated in cases when you want to limit the use of drugs for general anesthesia: the liver and kidneys, various intoxications (peritonitis, burns, etc.), in patients with senile and debilitated. EA is the method of choice for infants, because it has a dampening effect on neuromuscular conductivity contributes to the rapid recovery of consciousness and muscle tone is complete.

#### *Electroacupunctural analgesia*

Electroacupunctural analgesia (EAPA) is the physical (electrical) method of exposure to certain dietary corporal and auricular points to achieve analgesia in the corresponding area of the body to be surgery or eliminate pain. EAPA is a variation of the ancient method of classical acupuncture (AP), which appeared in China more than 4,000 years ago.

## **VIII. Self-study**

### *Task number one*

Calculate the dose of rocuronium for intubation, as well as prolonged muscle relaxation in a patient weighing 80 kg.

### *Task number two*

Calculate the required dose of propofol intravenous induction and maintenance of anesthesia to the patient 18 with weight 72 kg.

## **IX. Clinical problems:**

### *Objective number one*

A young woman hypotonic postpartum bleeding. Anesthesia is necessary for uterine curettage. Select the method of anesthesia. What anesthetic will have

beneficial effects on hemodynamics in this situation?

*Objective number two*

The patient, 39 years old, was admitted to the surgical department with a diagnosis of peptic ulcer disease. For 7 years suffering from gastric ulcer, has never been treated with alcohol, smoking. When you receive a serious condition. The patient is restless, complaining of general weakness, rapid emaciation, epigastric pain, abruptly pale, heart rate - 100 beats per minute., Rhythmic, BP - 90/60 mm Hg Vomiting "stagnant" content with clots. Made fibrogastroscopy, found an old ulcer on the back of the duodenal bulb, hemorrhagic gastritis, pyloric stenosis. The patient was scheduled for laparotomy, resection of the stomach. Select the method of anesthesia, the components of anesthesia.

Test control:

1. When ketamine is noted:

- a) maintaining reflexes larynx and pharynx;
- b) improvement of atrioventricular conduction
- c) an increase in coronary blood flow and myocardial oxygen consumption;
- d) bronchiectasis.

2. Ketamine anesthesia is contraindicated in:

- a) intracranial hypertension;
- b) cases involving convulsive;
- c) hypotension of any etiology;
- d) the availability of surgical bleeding is not stopped.

3. The positive effects of barbiturates:

- a) sedation;
- b) pronounced depression of the cardiovascular system and respiratory
- c) hyperalgesia;
- d) the rare occurrence of nausea and vomiting.

4. Prolonged effect of succinylcholine may depend on:

- a) Low level of normal cholinesterase;
- b) from a low pseudocholinesterase;
- c) the presence of hereditary diseases;

g) the correct answer.

5. Remifentanyl feature is that it:

- a) is eliminated through the skin;
- b) has a maximum duration of action;
- c) does not cause respiratory depression when used with any dose;
- g) is metabolized extrahepatic, hydrolyzed nonspecific esterases in blood and tissues.

6. With an overdose of opioid use:

- a) nalbuphine;
- b) naloxone;
- c) Nialamide;
- d) Bemegride;
- e) kordiamin.

7. Drugs used for ataralgia:

- a) Halothane;
- b) droperidol;
- c) diazepam;
- d) Fentanyl.

8. Drugs used for neuroleptanalgesia:

- a) Halothane;
- b) droperidol;
- c) diazepam;
- d) Fentanyl.

9. Anesthetic during surgery are the least dependent on:

- a) an illness of the liver and kidneys;
- b) prior drug therapy;
- a) age;
- g) of childhood appendectomy.

10. The indications for an additional dose of fentanyl at neuroleptanalgesia are:



- a) sweating;
- b) hypertension;
- c) the tachycardia;
- d) bradycardia.

*Answers:*

*Objective number one*

Be optimal intravenous anesthesia with ketamine sedation against diazepam.

*Objective number two*

Required catheterization several peripheral veins and central veins for infusion therapy, bladder catheterization for hemodynamic monitoring and renal function, laboratory blood (group, Rh factor, complete blood count, biochemical analysis, clotting (coagulation)). As anesthesia - mnokomponents anesthesia, use of muscle relaxants and mechanical ventilation. Should be used for the induction of ketamine, it can be used for maintenance of anesthesia in combination with narcotic analgesics, or, under the control of hemodynamic and other parameters used for maintenance of anesthesia neyroleptoanalgesia (ataralgesia), in combination with N<sub>2</sub>O.

Test control:

- 1 a, b, c, d
- 2 - a. b, d
- 3 - a, d
- 4 - b,
- 5 - a, d
- 6 - b
- 7 - c, d
- 8 - b, d
- 9 - g
- 10 - b. in