Drug intoxication (pediatrics)

Drug intoxication is the most common reason for consultation of the **Toxicology Information Center (TIS)** in children and adults. The usual cause of drug poisoning in children under 5 years of age is accidents and medical errors (mixing up of drugs, their inappropriate use or incorrect dosage), a serious course of poisoning is an exception. In adolescents, it is mainly **suicide attempts**, and mostly in girls. In recent years, serious drug poisonings have decreased, mainly due to the fact that a number of very dangerous pharmaceutical preparations have been replaced by more modern active substances with lower toxicity. However, the current problem is **extended-release preparations**, which usually contain a larger amount of the active substance in one dose and where, due to the prolonged release, the course of the poisoning is unpredictable.[1]

The most important thing is education and prevention (do not offer medicines under the pretext that they are treats, keep medicines in inaccessible places, do not throw leftover medicines in waste bins, watch children during visits,...). [1]

Intoxication according to the age of the child

The most critical period for acute intoxication is the **second year** of a child's age, when motor skills, dexterity and the way of learning about the environment by putting objects in the mouth are developing. The severity of intoxication often depends on the environment in which the child grows up. In the household of young and healthy parents, intoxications usually occur with pharmaceutical preparations that are not serious in nature. The risk is higher in households where there are chronically ill or elderly individuals with chronic diseases of the circulatory system, psychiatric diagnoses, diabetes, obstructive pulmonary disease or pain conditions requiring opioid analgesics. In many cases, the daily medicine dispenser is emptied by the toddler. It is often not clear whether the child has eaten the medicine or just scattered it around, however, it is necessary to calculate the maximum possible dose, which is why **observation** in the children's inpatient ward is often necessary.[1]

Medicines are often confused with newborns and infants, for example Kanavit(vitamin K1 - recommended 1 drop per week) and Vigantol(vitamin D3 - recommended 1 drop per day). In addition, there may be **incorrect use** of the medicine (for example, orally instead of nasally), **incorrect dosage** (number of milliliters instead of the number of drops) or **multiple administration** of the same dose by different members of the household. [1]

Frequent accidental ingestion of medicines by children

Contraceptive Pills

- NU (several pieces): nausea, possibly vomiting, sometimes several hours after ingestion.
- First aid: administration of several tablets (1–3–8) of activated carbon (e.g. *Carbosorb* or *Carbotox*), crushed into a favorite drink or into fruit pulp, puree or yogurt.

Tablets containing sodium fluoride to prevent tooth decay (***Zymafluor, Natrium fluoratum***)

- the active substance of these preparations is toxicologically very serious, but in tablets for children it is contained in such a small amount that intoxication does not occur even after eating several dozen pieces;
- first aid: giving milk or another liquid milk product - the calcium contained in it reacts with fluorine to form calcium fluoride, which protects the gastric mucosa from the irritating effects of sodium fluoride and at the same time prevents the same reaction with calcium ions in the blood, which would occur if large doses of the drug were ingested caused poisoning with tetanic convulsions and other changes that could be fatal in severe cases.

Expectorants containing ambroxol (***Mucosolvan, Ambrobene***)

- even emptying the contents of an entire bottle of syrup for children (120 ml/360 mg ambroxol) should not cause anything more serious than indigestion and increased mucus secretion. [1]

The most dangerous drug intoxication

- calcium channel blockers,
- beta blockers or digoxin,
- theophylline preparations,
- tricyclic antidepressants and carbamazepine,
- oral antidiabetic drugs,
- colchicine or preparations containing iron,
- paracetamol and others [1]

Clinical manifestations

Depression of breathing opiates, barbiturates, digoxin, benzodiazepines, tricyclic antidepressants.	**Attenuation of consciousness** benzodiazepines, barbiturates, opiates, tricyclic antidepressants, antihistamines, (amphetamines, alcohol).
Hypotension opiates, barbiturates, tricyclic antidepressants, calcium channel blockers.	**Psychosis** antihistamines (amphetamines, cocaine).
Malignant dysrhythmia tricyclic antidepressants, digoxin, antiarrhythmics, antihistamines, (cocaine)	**Agitation** cocaine, alcohol.
Arrhythmia fast tricyclic antidepressants, caffeine, theophylline (atropine, cocaine, amphetamines).	**Delirium** atropine.
Arrhythmia slow calcium channel blockers.	**Mydriasis** tricyclic antidepressants (atropine, scopolamine).
Miosis opiates, barbiturates, carbamazepine.	**Liver failure** paracetamol.

Paracetamol intoxication

1. Loss of appetite, nausea and vomiting, malaise (sometimes leads to further administration of paracetamol!)
2. first phase symptoms recede, pain or pressure in the right subcostal region may appear, hepatomegaly, oliguria ; increased bilirubin and liver enzymes, prolonged prothrombin time
3. 48–120 hours after ingestion, loss of appetite, nausea, vomiting, and malaise again, but with signs of liver failure(jaundice, hypoglycemia, coagulopathy, and encephalopathy); sometimes the development of renal failure and cardiomyopathy

- antidote: **N-acetylcysteine** - good efficacy demonstrated when administered within 10-12 hours of intoxication
- **within 6–8 hours after paracetamol ingestion, administration of activated charcoal** is effective, but reduces the effect of oral N-acetylcysteine
- other measures: rest, diet, vitamins, hepatoprotectants and ursodeoxycholic acid in the cholestatic form, corticoids in severe liver damage (uncertain effect), liver transplantation in fulminant liver failure. [2]

Intoxication calcium channel blockers

- *Verapamil, nifedipim, amlodipine, felodipine, isradipine,... ;*
- one of the most insidious and difficult to treat drug poisonings;
- small therapeutic range;
- bradycardia (slowing down of conduction of impulses through the myocardium, reduction of contractility) up to AV block or asystole;
- arterial hypotension on the basis of peripheral vasodilation;
- hyperglycemia caused by suppression of insulin release from the pancreas;
- unconsciousness and convulsions due to cerebral hypoperfusion;
- first aid: **activated carbon** (well absorbable);
- the necessity of ECG and blood pressure monitoring (preferably invasive);
- treatment: **bolus of crystalloids, calcium chloride** (an attempt to compensate for the blockage of calcium transport on cell membranes by administering preparations containing easily available calcium), **infusions of adrenaline or noradrenaline** (to reduce peripheral vasoconstriction, improve cardiac output), **glucose with insulin** (need to monitor potassium levels). [3][4]

Intoxication beta-blockers

- cardio-selective (beta-1-receptors in the myocardium, including the transmission system): *atonolol, metoprolol, acebutolol,...*
- cardio-non-selective (beta-2-receptors in the wall of blood vessels, bronchi and adipose tissue): *metipranolol, bopindolol, propranolol,...*
- alpha and beta-blockers: *labetalol, carvedilol*
- competence with catecholamines at beta-adrenergic receptor
- small therapeutic breadth and different individual receptivity
- bradycardia, reduced myocardial contractility, prolonged QRS and QT interval, varying degrees of AV blockade, arterial hypotension
- unconsciousness and convulsions(*metoprolol, propranolol, sotalol*)
- hypoglycemia, hyperkalemia, increased creatine kinase, thrombocytopenia

- first aid: **activated carbon** (well absorbable)
- the necessity of ECG and blood pressure monitoring
- treatment: **crystalloids**, **adrenaline infusion**, **atropine** (in case of significant bradycardia), **glucagon** (inotropic effect independent of beta receptors), **glucose with insulin, bicarbonate, calcium**. [3][4]

Intoxication with tricyclic antidepressants

- anticholinergic action – increased muscle tone, dryness of mucous membranes and circulatory symptoms (arterial hypotension);
- blocking of the so-called fast, voltage-dependent sodium channels in the CNS and in the myocardium and potassium channels;
- slowed conduction of the impulse, which is manifested by the widening of the QRS complexes;
- arterial hypotension;
- first aid: **activated carbon** (well absorbable);
- treatment: **bicarbonate, noradrenaline** (dobutamine contraindicated). [3]

Opioid intoxication

- codeine, slow-release morphine tablets, *buprenorphine* (Subutex);
- stimulation of specific opiate receptors in the CNS;
- first euphoria, then depression of consciousness and depression of the respiratory center with subsequent hypoventilation (hypoxia with cyanosis) up to apnea;
- significantly narrowed pupils; severe cerebral hypoxia is followed by mydriasis;
- bradycardia, hypotension due to peripheral vasodilatation;
- antidote: **naloxone** (quick application can cause a rise in catecholamine levels with risks of arrhythmia, pulmonary edema - "heroin lung", asystole, convulsions); the action of naloxone is shorter compared to other opiates (30-45 minutes), and therefore there is a risk of repeated depression of the respiratory center;
- adequate breathing support, monitoring of vital functions. [3][5]

Investigation

For a number of drugs, it is possible to determine the plasma level, and for drugs, it is also possible to detect it in the urine. For some drugs, the value of the plasma level and its dynamic development is crucial for deciding on the method of treatment (paracetamol, salicylates, digoxin, theophylline, barbiturates, carbamazepine, phenytoin).[6]

Treatment

Consultation with TIS on telephone lines **224 919 293** and **224 915 402**.

Treatment options: primary elimination of the drug from the body (before its absorption), symptomatic care, antidote and secondary elimination methods (after absorption of the drug into the circulation and tissues). Primary elimination from the body is achieved by removing the substance from the stomach by inducing vomiting, by suctioning the stomach contents or by washing the stomach and administering activated charcoal, or a combination of administration of activated charcoal and a laxative, the so-called gastrointestinal lavage. These interventions are most effective within an hour of ingestion, within 15 minutes for liquids. The exception is the ingestion of drug forms with prolonged release, drugs with anticholinergic effects and serious poisoning associated with atony of the stomach and intestines.

As part of supportive treatment, monitoring of basic vital functions and parameters of the internal environment is necessary. [6]

Vomiting

- Risk of aspiration of vomitus and injury in the oral cavity - the risks usually outweigh the possible benefits;
- indicated only in absolutely exceptional situations - after ingestion of substances and doses that threaten the child with very serious or fatal poisoning, especially when it is not possible to ensure rapid administration of activated charcoal, or when activated charcoal does not bind the ingested substance, or the child is allergic to activated charcoal. [1]

Gastric lavage

Indicated only after ingestion of toxicologically very serious drugs in doses that significantly threaten the patient's health or life.[1] The effectiveness of gastric lavage and the administration of emetics in eliminating the harmful substance from the stomach decreases significantly after 1 hour after ingestion of the toxic substance, while most patients arrive at the hospital after more than 3 hours after intoxication. [7] Based on experiments on animals and volunteers, the importance of the time factor on the effectiveness of the procedure was clearly demonstrated. When performed within 5 minutes of ingestion, up to 90% of the substance was removed, up to 45% within 10 minutes, 25% within 30 minutes and approx. 10% within 60 minutes..[6]

Procedure

- In a conscious patient, it is performed in a position on the left side, if possible with the head down to avoid

possible aspiration of vomit, or in a sitting position; immobilization by personnel is often required; prior intubation is required in an unconscious patient;
- a probe of the largest possible diameter (at least 9–11 mm) is introduced, the length from the root of the nose to *the xiphoid process* plus 10 cm;
- it is possible to make sure of the correct location by aspiration of the contents or, in case of doubt, by insufflation of air with simultaneous listening in the stomach area;
- gastric contents are aspirated, then tepid saline (5–10 ml/kg) is applied and again aspirated – this is repeated until clear gastric contents are obtained; a larger amount of liquid instilled at once can counterproductively accelerate the passage of gastric contents into the duodenum;
- at the end, a dose of activated carbon (up to 1 g/kg) is applied.[1][6]

Rare complications: laryngospasm, hypoxia, mechanical injury to the pharynx, esophagus or stomach, aspiration pneumonia, ion and water imbalance. [6]

Contraindications to lavage: unconsciousness with reactivity of the patient, ingestion of detergents, lyes and acids or kerosene - organic oils, kerosene, diesel, gasoline. [7]

Administration of activated carbon

As the most effective method of elimination, the administration of activated charcoal comes to the fore as a "universal antidote" (the recommended dose is governed by the amount of drug ingested; doses vary from 0.5-2.5 g/kg per dose, can be repeated indefinitely - repetition is appropriate if ingested drug undergoes enterohepatic circulation). Timely submission is important. It can also be administered at home, the condition for safe administration is the cooperation of the child (especially with sedatives). Contraindications are ileus and intestinal obstruction.[1]

Substances absorbable and non-absorbable on activated carbon

- Good absorption: acetaminophen (paracetamol), amitriptyline, amphetamine, acetylsalicylic acid and its salts, chlorpromazine, codeine, diazepam, digoxin, imipramine, morphine, pentobarbital, strychnine;
- poor absorption: boric acid, ethyl alcohol, methyl alcohol, ethylene glycol, Li, Fe, kerosene and other kerosenes, strong acids and bases. [7]

Administration of the antidote

Ingested medicine	Indication	Antidote[7][1]	
opiates	coma, respiratory depression	naloxone	intubation, artificial lung ventilation, only then naloxone 0.01 – 0.03 mg/kg iv, repeat after 15 min. before regaining consciousness, no more than 1.2mg
acetaminophen – paracetamol	75 mg/kg and above	N-acetylcysteine**	intravenously in a 21-hour protocol or an initial dose of 140 mg/kg per person, then 70 mg/kg/4 hours.
benzodiazepines	coma, respiratory depression	flumazenil**	0.01 – 0.05 mg/kg in total. doses of 2 mg; contraindicated in combined poisoning with drugs that cause convulsions in toxic doses (especially in combination with tricyclic antidepressants and carbamazepine) – risk of status epilepticus
iron preparations	above 20 mg Fe/kg	deferoxamine	
antimyasthenics (reversible acetylcholinesterase inhibitors)	severe muscarinic symptoms	atropine	
aminoqinolones	methemoglobinemia	toluidine blue	
atropine		physostigmine salicylate	
digoxin; digitalis		DigiFab (sheep digoxin-specific antigen binding immunoglobulin fragments)	

(*) The antidote must be administered within 60 minutes of ingestion of the toxic substance.
(**) The antidote must be administered within 120 minutes.

Gastrointestinal lavage

When removing non-absorbable harmful substances and depot, retarded forms of drugs or contents of small batteries swallowed by the child with activated carbon.

- preparations containing sodium fluorate, highly ionized salts in the form of iron preparations for the treatment

of anemia or antidepressants containing lithium, preparations with borates, with ethanol, etc., or it is the ingestion of tablets with controlled release.

Application of an aqueous solution of macrogol (e.g. Fortrans) through a stomach tube at a dose of 35 ml/kg/h, or for children from 9 months to 5 years 500 ml/h, up to 12 years 1,000 ml/h.

In case of ingestion of delayed-release tablets, the active substance of which binds to activated charcoal, it is possible to administer a dose of activated charcoal of 0.5-1 g/kg at intervals of 2-3 hours.

The massive departure of stool occurs in 1-2 hours after the start of macrogol application. Its administration is terminated at the moment when clean intestinal contents or contents with the presence of activated carbon leave.[1]

Secondary elimination

Indicated after absorption of the drug into the circulation and tissues - methods: forced diuresis, peritoneal dialysis, extracorporeal methods such as hemodialysis and hemoperfusion. Forced diuresis has a questionable effect and a relatively high risk of water and ion imbalance. Substances with a low molecular weight, with a small distribution space and a small binding to plasma proteins (e.g. salicylates, methanol, ethylene glycol, lithium, isopropanol) are suitable for dialysis. Hemoperfusion is suitable for substances with low solubility in water and high affinity to absorbents and low affinity to plasma proteins (carbamazepine, barbiturates, theophylline). Hemofiltration removes substances with a larger molecular weight.

Methods of extracorporeal elimination and substances for which they have the greatest effect[7]

hemodialysis	hemoperfusion	forced diuresis
salicylates	barbiturates	barbituráty
barbiturates	chlorpromazine	benzodiazepiny
sulfonamides	cyclic antidepressants	paracetamol
alcohols	paracetamol	hydantoinates
(acetone, aniline, toluene)	theophylline	(heavy metals)

Lipid emulsions

Indicated for acute poisoning with cardiotoxic drugs, when severe cardiac symptoms cannot be managed in any other way. Fat solubility is a prerequisite. It is used in the therapy of poisoning with some beta-blockers, calcium channel blockers, but also with some cardiotoxic antidepressants, antiepileptics, antipsychotics.

Procedure

- Intravenous administration of 20% Intralipid (1.5 ml/kg as a bolus, followed by 0.25–0.5 ml/kg/min. for 30–60 **minutes** up to an initial maximum of 500 ml; the bolus can be repeated 1–2 times; speed administration is titrated according to clinical response).[1]

Lay first aid

General principles of lay first aid:

- Keep calm;
- never induce vomiting;
- if the child is symptom-free, he can be given water or tea to drink, not milk;
- find out what the child has ingested, in what quantity and how much time has passed since ingestion;
- contact the Toxicology Information Center (TIS) on telephone lines 224 91 92 93 or 224 91 54 02, or a pediatrician, emergency service or hospital;
- most often, the TIS doctor will recommend the administration of activated ("black" or "animal") charcoal tablets;
- if necessary, gentle transport to the hospital (risk of injury or aspiration of vomit), with a sample of what the child has ingested.

Links

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