2009
Scientific achievement of Ukraine
Due to its scientific discoveries, Ukraine has earned the reputation of the state with high intellectual potential. About 15 years ago, the team of researchers working in the Institute of Blood Pathology and Transfusion Medicine of the Academy of Medical Sciences of Ukraine (the city of Lviv) started to develop innovative medicinal product, which has become a real discovery in the modern infusion therapy. Reosorbilact is a scientific heritage of Ukraine, the drug product, without which it is impossible to imagine the modern therapeutic process.

More than 200 articles containing materials of reosorbilact clinical trials that were conducted in more than 20 scientific and clinical institutions in Ukraine and CIS countries with the participation of more than 6000 patients have been published over 10-year period of this drug product existence. This collection of articles is only a brief review of the clinical studies conducted over the recent years.
The main objectives of non-intensive infusion therapy are as follows:
- detoxification;
- improvement of microcirculation and tissue perfusion;
- correction of abnormalities in rheological and coagulation properties of blood;
- correction of metabolic disorders;
- improvement of the delivery of drugs to the pathological focus;
- compensating the circulating blood volume (circulatory volume) and the correction of hypovolemia;
- correction of water-electrolytic and acid-base balance.

The authors suggested a number of detailed classifications of drug products for infusion therapy: a functional (therapeutic) and syndrome-based ones. It has been concluded that non-intensive infusion therapy can be used based on the clinical and pathogenetic syndromes, depending on the severity of organ disorder and the mechanism of pathogenic effects of the drug product.

Table 1

<table>
<thead>
<tr>
<th>Group</th>
<th>Subgroup</th>
<th>The drug product</th>
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<tr>
<td></td>
<td>1.2 Dextran drug products</td>
<td>Polyglucinum Tensiton Rheopolyglucinum</td>
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<td></td>
<td>1.3 Drugs of polyatomic alcohols</td>
<td>Sorbilact Xylatum Reosorbilact Lactoxyl Gluxyl Lactasolum</td>
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<td></td>
<td>1.4 Other</td>
<td>Ringer's solution Neohaemodesum Albumin Perftoran Ionosteril Polyoxidinum</td>
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<td>2. The drug products correcting acid-base state</td>
<td>2.1. Sodium lactate products</td>
<td>Reosorbilact Sorbilact Lactoxyl Lactasolum Lactated Ringer's solution</td>
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<td>2.2. Bicarbonates</td>
<td>Sodium hydrocarbonate</td>
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<td>2.3. L-arginine</td>
<td>Tivortin</td>
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<td>2.4. Buffer products</td>
<td>Soda-bufer THAM Trisamine</td>
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<td>Group</td>
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<td>2. The drug products correcting acid-base state</td>
<td>2.5. Sodium acetate products</td>
<td>Xylatum</td>
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<td>Gluxyl</td>
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<td>2.6. Other</td>
<td>Mafusol</td>
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<td>Reamberin</td>
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<td>3. The drug products correcting rheological properties of blood</td>
<td>3.1. The drug products of the polyatomic alcohols</td>
<td>Reosorbilact</td>
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<td>Sorbilact</td>
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<td>Xylatum</td>
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<td>Latren</td>
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<td>Tivortin</td>
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<td>3.2. Dextran drug products</td>
<td>Rheopolyglucinum</td>
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<td>4. The drug products correcting water-electrolytic balance</td>
<td>4.1. Potassium drug products</td>
<td>GIK (glucose and potassium)</td>
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<td></td>
<td></td>
<td>Kamaginat</td>
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<td>Potassium and magnesium asparaginate</td>
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<td>Hamburger’s solution</td>
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<td>4.2. Balanced electrolyte solutions</td>
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<td>Ringer’s solution</td>
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<td>Hartmann’s solution</td>
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<td>Lactoxyl</td>
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<td>4.3. Other</td>
<td>Disolum</td>
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<td>Sodium chloride solution</td>
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<td>Chlosolum</td>
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<td>Acesolum</td>
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<td>Trisolum</td>
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<td>5. The drug product for parenteral nutrition</td>
<td>5.1. The drug products which are the energy sources</td>
<td>Gluxyl</td>
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<td></td>
<td></td>
<td>Sorbilact</td>
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<tr>
<td></td>
<td></td>
<td>Glucose</td>
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<td></td>
<td></td>
<td>Lactosol</td>
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<td>5.2. Amino acid (plastic) products</td>
<td>Aminol</td>
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<td>Infezol</td>
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<td>Aminosteril</td>
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<td>Polyaminum</td>
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<td>5.3. Fat emulsions</td>
<td>Lipofundin</td>
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<td>7. Solvents for infusion of drugs</td>
<td>7.1. Basic</td>
<td>Isotonic sodium chloride solution</td>
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<tr>
<td></td>
<td></td>
<td>Ringer’s solution</td>
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<td></td>
<td></td>
<td>Lactated Ringer’s solution</td>
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<td></td>
<td>7.2. Additional</td>
<td>Glucose</td>
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<tr>
<td></td>
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<td>GIK</td>
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<td>Lactated Ringer’s solution</td>
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<td></td>
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<td>Kamaginat</td>
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<tr>
<td>Group</td>
<td>Subgroup</td>
<td>The drug product</td>
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</table>
| 8. Complex infusion solutions |                  | Reosorilact  
Sorbilact  
Xylatum  
Latren  
Lactosol  
Gluxyl |
| 9. Detoxification solutions |                  | Reosorilact  
Sorbilact  
Xylatum  
Lactoxyl  
Ionosteril  
Haecodesum  
Ringer's solution  
Polyoxidin  
Gluxyl  
Neohaemodesum |
| 10. Infusion solutions of special action | Infusion antibiotics | Moxifloxacin (Maxicin, Avelox)  
Levofloxacin (Leflocin, Tavanic, Levofox)  
Ofloxacin (Tarivid, Zanocin)  
Ciprofloxacin (Ciprobay, Ciprinol, Cifran, Cipro)  
Imipinem (Tienam)  
PAS (PASKONAT),  
Gatifloxacin (Bigaflon) |
| 10.2. Antifungal agents     |                  | Fluconazole (Diflucan, Medoflucon, FCN-200) |
| 10.3. Inhibitors of proteolysis |                  | Aminocaproic acid |
| 10.4. Solutions for hemodialysis |                  | Solution No. 153 |
| 10.5. Cardioplegics         |                  | Cardiological solution No. 1 |
| 10.6. Solutions, stimulating intestinal peristalsis |                  | Sorbilact |
| 10.7. Drugs increasing the oncotic blood pressure |                  | Albumin |
| 10.8. Hemostatic products   |                  | Fibrinogen |
| 10.9. Hepatotropic products |                  | Aminoplasmal-Hepa  
Glutargin Hepa-Aminosol |
| 10.10. Peripheral vasodilators |                  | Latren |
### Table 2

#### Therapeutic effects of the basic intravenous fluids

<table>
<thead>
<tr>
<th>Therapeutic effect</th>
<th>NaCl(0.9% solution)</th>
<th>Reosorbilact</th>
<th>Glucose (5% solution)</th>
<th>Ringer’s solution</th>
<th>Sorbilact</th>
<th>Xylatum</th>
<th>Lactated Ringer’s solution</th>
<th>Dextran-70 (6% solution)</th>
<th>Dextran-40 (10% solution)</th>
<th>Dextran-40 (10% solution)</th>
<th>Hydroxyethyl starch</th>
<th>Gelatin</th>
<th>Sodium hydrocarbonate</th>
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</thead>
<tbody>
<tr>
<td>Diuretic</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
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<tr>
<td>Detoxifying</td>
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<td>+++</td>
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<td>+++</td>
<td>++</td>
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<tr>
<td>Increasing circulatory volume (or plasma volume)</td>
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<td>++</td>
<td>+</td>
<td>+</td>
<td>+++</td>
<td>++</td>
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<td>Antishock</td>
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<td>-</td>
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<td>Acid-base balance normalization</td>
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<tr>
<td>Improvement of blood rheology</td>
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<td>+++</td>
<td>+++</td>
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<td>Improvement of microcirculation</td>
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<td>+++</td>
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<td>Normalization of mineral metabolism</td>
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<td>Vehicle for i/v administration of drugs</td>
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<tr>
<td>Allergic or pseudoallergic</td>
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<tr>
<td>Stimulation of intestinal peristalsis</td>
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</table>

#### Notes:

- the drug effect is insignificant;
- the drug does not have this therapeutic effect.

+++ the drug effect is pronounced;
++ the drug effect is moderate;
"Intoxication" is one of the most frequently used terms in the clinical practice. Medical staff has to deal with intoxication in many various fields of medical practice. The background of intoxication, which is understood as a dynamic process, is the dominance of the processes of the flow of toxins from the outside or their forming inside the body over the capabilities of the detoxification systems to eliminate them. Depending on the sources of incoming toxins, intoxications can be divided into exogenous, endogenous and the ones caused by endotoxin.

Mechanisms of physiological detoxification:
- metabolic (utilization of ketone bodies);
- excretory (urinary excretion, excretion with the exhaled air and the contents of digestive tract);
- immune (absorption of toxins by cells of monocytic-macrophage system, their binding by neutralizing antibodies, etc.).

Taking into account the potentially fatal results of progressing intoxication, detoxification has been and remains a major focus of intensive therapy. Most clinicians bear strong conviction about the detoxification capabilities of infusion therapy, which, in contrast to the methods of extracorporeal detoxification, can be easily used and is therefore used in all hospitals and medical institutions. Meanwhile, the infusion detoxification can only be effective if its capabilities are properly used, which requires knowledge of the pharmacodynamics of infusion drugs. There are several "myths" associated with infusion therapy, and it is essential to understand what is imaginary, and what is real about it.

The first myth. Infusion therapy always has a detoxification effect. It is clear that the detoxification effect of infusion therapy can be reached only in cases where there is background for enhancing the natural ways of detoxification with the help of the administered infusion drug. This is possible only in cases where the toxin has no strong connection with the carrier proteins or receptor molecules and can cross the kidney barrier, i.e. it is excreted from the body with the increase of urine output (diuresis). In these very cases, the infusion detoxification, known as forced diuresis, is the most widely spread method in toxicological practice. In other cases, the only effects that can be expected during the infusion therapy are dilutional effect and resulting decrease of concentration of toxic compounds in blood.

However, bearing in mind the fact that the volume of interstitial sector in adults is 15-16% of body weight (about 10 liters), and the plasma volume is 4-5% of body weight (about 3 liters), it is necessary to administer and maintain about 13 liters of fluid in a patient's body in order to reduce the concentration of dissolved toxins twofold, which will inevitably result in the development of edemas. It is clear that the benefits of such “detoxification” is doubtful.

The second myth. There are special “detoxication solutions” available. In the Ukrainian and Russian literature on infusion therapy, there is usually a section concerning plasma substitutes with detoxifying action. These medicinal products include derivatives of polyvinyl pyrrolidone (haemodesum, neohaemodesum). These low-molecular solutions are able to bind various toxic compounds and eliminate them with urine (in accordance with existing instructions). Unfortunately, all the efforts aimed at identifying primary scientific sources that could provide information on the sorption capacity of these drugs did not lead us to the desired goal. Such data are simply not available. At the same time negative properties of these solutions are well-known. Rapid administration of haemodesum and neohaemodesum may be accompanied by lowering of blood pressure, tachycardia, retrosternal pain, shortness of breath, and hyperemia of the skin. Thus,
Thus, the toxic effects of polyvinyl pyrrolidone are obvious. Moreover, it is known that haemodesum inhibits the function of the reticuloendothelial system after its repeated administration; repeated infusions of haemodesum inevitably result in the development of iatrogenic (cutaneous) thesaurismosis (Dupont-Lachapelle disease). This phenomenon is particularly expressed in newborns and infants. It is not surprising that the use of polyvinyl pyrrolidone derivatives was banned in the U.S. in 1958, and since the second half of the 1970s, the polyvinyl pyrrolidone derivatives was not mentioned in the foreign medical literature.

The polyvinyl pyrrolidone solutions are essential in detoxication infusion therapy. We will try to refute this myth. Considering the detoxification mechanisms specified at the beginning of the article, the assumption seems logical that the infusion solution, which is able to have detoxification effect should:

- optimize tissue perfusion to improve conditions for the diffusion of toxic factors from the damaged cells, tissues and organs into the bloodstream;
- cause hemodilution, accompanied by the decrease in concentration of toxins in the blood plasma;
- force diuresis, resulting in elimination of toxins and metabolites (that can overcome the hemorenal barrier) from the body;
- support the functional state of hepatocytes, which are the most important element of the metabolic detoxification;
- eliminate the effects of intoxication syndrome (metabolic acidosis, electrolyte disturbances and metabolic disorders).

An innovative infusion drug reosorbilact, developed by Lviv Scientific Research Institute of Pathology and Blood Transfusion Medicine of the AMS of Ukraine in 1998, introduced new opportunities for intensive care in patients with intoxication syndrome. This solution is characterized with a balanced composition of potassium, calcium and magnesium, containing an excess of sodium in the form of two salts - chloride and lactate. It is obvious that only the sodium component in the composition of this drug product provides osmolarity of about 600 mOsm/l, which makes reosorbilact very similar to the hypertonic lactated Ringer’s solution, which was used to control burn shock in 1970-1980-ies.

The main difference lies in the fact that it has much greater alkalizing ability due to sodium lactate, containing it almost 6 times more than lactated Ringer’s solution. Sodium lactate, metabolizing in the liver and kidneys, forms bicarbonate ion, increases the level of actual (available) bicarbonate in the blood plasma, and corrects the metabolic acidosis.

The second characteristic feature of reosorbilact is the inclusion of magnesium ions in its composition, due to which the positive impact of this electrolyte on neuromuscular excitability and smooth muscle tone can be expected.

Due to its high osmolarity reosorbilact causes fluid intake from the intercellular space in the bloodstream, facilitating improvement of microcirculation and tissue perfusion and thus solving the first problem of detoxification therapy. Movement of fluid from the intercellular sector in the intravascular space leads to an increase in circulating blood volume due to the increase in plasma volume, which is accompanied by hemodilution. Thus, the “drainage” of the interstitial space is carried out this way, as well as elimination of the toxic factors. The expressed diuretic properties of the drug product are observed thanks to the powerful osmodiuretic effect. It is essential that reosorbilact has nephroprotective action as well, and it also enhances diuresis even in patients with acute renal failure.

Therefore, toxins that are able to overcome the renal barrier are intensively eliminated from the body. In addition, reosorbilact normalizes carbohydrate and energy metabolism, which favorably affects the functional state of hepatocytes, where glycogen content is restored, which is an obvious contribution to the intensification of the natural detoxification processes.

Sodium lactate contributes to the correction of acid-base balance, as well as restores and stimulates reticuloendothelial system cell function of the liver and kidneys taking part in the reactions of carbohydrate and energy metabolism.

In summary, it should be emphasized that the clinical practice requires reconsideration of existing attitudes toward detoxification infusion therapy. It is obvious that the rejection of stereotypes regarding the detoxification solution only as a drug that binds and removes some toxic substances with urine, will help to expand our knowledge concerning the pathogenetic mechanisms and methods of detoxification, as well as the introduction of other, more justified and multifunctional means of infusion detoxification into clinical practice.

Mystetstvo Likuvannya (Art of Treatment) [040]
Acidosis is an important link in the pathogenesis of various diseases. It is the most frequent type of acid-base balance disturbances. It is well known that acid-base balance is an important component of homeostasis and includes a set of mechanisms aimed at maintaining a constant pH level of the internal environment of the body (the normal pH of blood and body fluids is 7.40 ± 0.03, the maximum allowable interval is 6.8-7.7).

What is associated with the need for development of mechanisms for maintaining the pH stability of the internal environment of the body during the evolution? The main factor in the acid-base homeostasis destabilizing is a natural biochemical activity of cells. The protons (H+) are continuously released in the tissues in the process of life. They are formed as a result of the intracellular oxidation-reduction reactions. The most important reactions are the intramitochondrial respiratory chain reactions. The synthesis of high-energy compounds (such as ATP) takes place due to chemical energy released during oxidation. Oxidative transformations of the abovementioned substrates end with forming of carbon dioxide, which is then eliminated. However, CO2 is transported in the dissolved state from the tissues to the lungs; and carbonic acid is formed while dissolving dioxide in water, which dissociates to the base and the proton:

\[
\text{CO}_2 + H_2O \leftrightarrow H_2\text{CO}_3 \leftrightarrow HCO_3^- + H^+
\]

Approximately 13000 mM of CO2 is formed in the respiratory chain per day, and 13 000 mM of protons are formed during its dissolving, respectively. Such acidic products of cellular metabolism as phosphoric acid and sulfuric acid, the daily amount of which is equivalent to 70 mM of protons, belong to the other sources of H+. Lactic acid formed during anaerobic glycolysis in the muscles, and ketone bodies (acetoacetic acid and p-hydroxy butyric acid) produced by hepatocytes are also endogenous sources of H+. Exogenous sources of protons are organic acids derived from food (for example, citric, ascorbic, phosphoric acids, etc.).

The concentration of H+ can be high on the way from the site of formation (within the cells) to neutralization (the lungs) or excretion from the body (kidneys), therefore, there must be ways to prevent their adverse effects. With this purpose, a number of blood buffer systems were created maintaining the pH of the internal environment of the body within the acceptable limits.

There are six basic buffer systems, distributed between erythrocytes and plasma. For simplicity, they are divided into two groups: the bicarbonate system (mainly in the plasma) and non-bicarbonate system (in plasma and erythrocytes). Disturbances of the acid-base balance, with both pH decreasing (acidosis), and increasing (alkalosis) can be caused by rather wide range of diseases. Respiratory and metabolic acidosis can be distinguished.

Respiratory acidosis is caused by increase of \( \text{PaCO}_2 \) in blood; it can be caused by metabolic increase in carbon dioxide production, but most frequently it is caused by respiratory failure of various origins. Metabolic acidosis is a primary decrease in bicarbonate buffer system capacity (mainly the decrease in HCO3-) in blood plasma, which may be caused by neutralization of buffer with the strong non-volatile acids or excessive loss of bicarbonate via the gastrointestinal tract or kidneys. For laboratory differentiation of these types of metabolic acidosis, the concept of anion gap was introduced, which is the difference between the concentrations of the major measured anions and cations, which is calculated by the formula:

\[
\text{AP} = [\text{Na}^+] - ([\text{CL}] + [\text{HCO}_3^-])
\]

The normal anion gap is equal to 12 (9 to 15 mM/l). Metabolic acidosis with increased anion gap is caused by the accumulation of nonvolatile acids (lactic acid, ketoacids): it is observed in patients with severe tissue hypoxia, diabetes, starvation, uremia, intoxication with alcohol, methanol, salicylates, etc. Metabolic acidosis with normal anion gap is associated with external loss of bicarbonate ions.
(fistula of the gall bladder and pancreas, ureterostomy, adrenal insufficiency, diabetes, renal tubular necrosis, excessive administration of chlorides etc.).

Pathophysiological effects of the developed acidosis are quite diverse. With reduction of pH below 7.1, its direct depressing effect on hemodynamics is observed: a decrease in inotropic cardiac function and vasodilation, which causes the decrease of perfusion blood pressure. Acidosis reduces the affinity of hemoglobin for oxygen, which greatly exacerbates the tissue hypoxia. Decrease in pH causes inactivation of some enzymes, which include Na/K-ATPase; inactivation of the latter plays an important role in the pathogenesis of hyperkalemia in the acidosis. In addition, we can not ignore metabolic activation of sympathoadrenal and endocrine systems and many other effects, aggravating the disease. In this context, many clinicians have long been paying close attention to the correction of acidosis, which is the subject of much debate. Infusion therapy of metabolic acidosis continues to be relevant therapeutic problem.

**Alkalizing therapy**

The easiest way to correct acidosis is the administration of substances that can bind a proton, i.e. having alkaline properties. In 1916, Howland et al. suggested sodium bicarbonate for the treatment of diarrhea in children, and since that time it has been widely used to correct the acidosis of different etiologies. Alkalizing effect develops quickly with use of soda, within 10-15 min after its intravenous injection. However, sodium bicarbonate has a number of side effects, greatly limiting its use. In the process of rapid alkalinization, a significant amount of carbonic acid, and, consequently, carbon dioxide is formed in the blood plasma, the elimination of which requires an increase in the volume of pulmonary ventilation, thus sodium bicarbonate is contraindicated in respiratory failure. Produced CO2 easily diffuses through cell membranes, leading to a decrease of cytoplasmic pH (intracellular acidosis).

Other adverse events include the following: the reduction of coronary pressure below critical values, increased intracranial pressure, reduced oxygen content in the brain, reduction of the intracellular pH in the brain, carbon dioxide penetration in the cerebrospinal fluid, reduction of the cerebrospinal fluid pH, shifting the oxyhemoglobin dissociation curve and decreased oxygen supply to the tissues, hypernatremia, an increase of cytoplasmic sodium content in the myocardium, hypokalemia, hypophosphatemia, etc.

With an overdose of sodium bicarbonate, a metabolic alkalosis may develop, which is much more dangerous than acidosis due to lack of effective mechanisms of its compensation. Less popular alkalizing agent is trisamine (trometanol, triolamine, Pehanorm, THAM, Trisaminol, Trisbuffer). Trisamine is a branched tetraatomic alcohol, in which one of the oxy groups is replaced by an amino group (-NH2). When the substances that have amino group are dissolved in water, they acquire alkalinity, since the nitrogen takes one hydrogen atom from the water molecule. The formed hydroxyl ions (OH-) bind the protons in the acidic environment to form water. Despite the advantages of trisamine associated mainly with the lack of CO2, effects, this drug has a number of other negative effects. Its rapid administration may cause respiratory depression, reduction in blood glucose, sodium and potassium ions. The maximum dose of the drug product should not exceed 1.5 g/kg per day. Trisamine can be repeatedly administered not earlier than 48-72 h after the last injection. The drug is contraindicated in patients with disruptions of renal excretory function; it should be used with care in patients with hepatic function disorders.

**Organic anions**

The abovementioned drawbacks of sodium bicarbonate solutions were found long ago, therefore, as early as in the 30-ies in the 20th century it was suggested to use organic anions to correct acidosis. By that time it became known that organic anions such as lactate and acetate are intermediate products of metabolism in the body, and then they are transformed into the corresponding acids (lactic and acetic acids).

This requires a hydrogen ion, the source of which is carbonic acid. By adding the proton, anions become acids with the formation of bicarbonate ion. These processes are intermediate in the conversion of glucose (via acetate and lactate) into acetyl-CoA. The total reactions are as follows for acetate and lactate, respectively:

CH₃COO⁻ + CO₂ + H₂O ↔ CH₃COOH + HCO³⁻
CH₃CH(OH)COO⁻ + CO₂ + H₂O ↔ CH₃CH(OH)COOH + HCO₃⁻

Thus, one ion of bicarbonate is formed during the metabolism of an organic anion, which can then participate in buffer reactions of the acid-alkaline balance. These reactions occur in the cytoplasm of any cells but primarily in the liver, myocardium and skeletal muscle cells.
Hydrogen carbonate readily diffuses from the intracellular space into the intercellular matrix, and then - in the blood. In this connection an unordinary idea arose to use the natural biochemical processes to enhance the capacity of hydrocarbonate buffer. For this purpose, it was proposed to administer lactate or acetate in blood in the form of corresponding salts. The advantage of this approach was seen in that fact that endogenous hydrogen carbonate formed in the tissues should have more smooth and more durable effect. The first experiments confirmed this assumption, which stimulated the development of a variety of infusion solutions containing one or other organic anion (the main ones are listed in the table). All these solutions have similar pharmacodynamics - they regulate the acid-base balance, normalize the water-electrolyte balance, have a detoxification effect, and increase diuresis. They have a quite broad range of application: acidosis, compensation of extracellular fluid volume during blood loss, shock, trauma, vomiting, diarrhea, burns, peritonitis, severe infections, microcirculatory disorders. As opposed to hypertonic solutions of hydrogen carbonate and trisamine solutions, organic anions showed an acceptable tolerability and almost complete absence of contraindications.

However, some differences have been found as a result of a comparative analysis of the drug products containing acetate and lactate. Administration of a significant amount of acetate into the bloodstream may be accompanied by such symptoms as hypotension, nausea and vomiting, which are explained by the effect of vasodilatation, which can be caused by the acetate alone and by the products of its metabolism. Absolute advantage of lactate compared to acetate is its less pronounced vasodilatation effect, and, consequently, its better tolerability. In addition, since the metabolism of lactate in the body lasts 4-5 times slower than that of the acetate, the correction of acidosis is more prolonged.

Currently available products, containing lactate.

In recent years, the Institute of Blood Pathology and Transfusion Medicine of the AMS of Ukraine created fundamentally new combined infusion drug products containing lactate. These include reosorbilact.

<table>
<thead>
<tr>
<th>The drug product</th>
<th>Molar concentration (mM)</th>
<th>Osmolarity (Osm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Na⁺</td>
<td>K⁺</td>
</tr>
<tr>
<td>Lactated Ringer’s solution</td>
<td>130</td>
<td>4</td>
</tr>
<tr>
<td>Reosorbilact</td>
<td>279</td>
<td>4</td>
</tr>
<tr>
<td>Sorbilact</td>
<td>278</td>
<td>4</td>
</tr>
<tr>
<td>Reosorbilact with xylitol</td>
<td>143</td>
<td>4</td>
</tr>
<tr>
<td>Complex lactate</td>
<td>132</td>
<td>5</td>
</tr>
<tr>
<td>Lactosol</td>
<td>140</td>
<td>4</td>
</tr>
<tr>
<td>Disolum</td>
<td>127</td>
<td>-</td>
</tr>
<tr>
<td>Acesolum</td>
<td>109</td>
<td>13</td>
</tr>
<tr>
<td>Chlosolum</td>
<td>125</td>
<td>20</td>
</tr>
<tr>
<td>Quar tasolum</td>
<td>125</td>
<td>20</td>
</tr>
<tr>
<td>Ionosteril</td>
<td>137</td>
<td>4</td>
</tr>
<tr>
<td>Xylatum</td>
<td>134</td>
<td>4</td>
</tr>
<tr>
<td>Gluxyl</td>
<td>86</td>
<td>6</td>
</tr>
</tbody>
</table>

Table

The main characteristics of the infusion solutions containing organic anions
The high content of lactate - 330 mM – is many times higher than that in the well-known solutions like lactated Ringer’s solution or lactosol (27-30 mM), contributes to a noticeable increase of alkaline reserve of blood plasma carbonate buffer and provides high efficacy of the drug product in the prevention and treatment of metabolic acidosis. The unique composition of reosorbilact provides its broad indications for use. It has rheological, antishock and detoxication effects. The drug is used as a means to reduce intoxication, improve microcirculation and blood rheology, to correct acid-base balance and improve hemodynamics in traumatic, operative, hemolytic and burn shocks, acute blood loss, burn disease, prolonged purulent processes, various infectious diseases, acute and chronic hepatitis, trombotic obliterating diseases of blood vessels, as well as in preoperative preparative period and in postoperative period. Contraindications include alkalois, cases where the injection of fluid is contraindicated (cerebral hemorrhage, thromboembolism, severe cardiovascular decompensation, stage III hypertension).

Clinical experience of reosorbilact use in cases involving the development of metabolic acidosis, has shown its high efficiency.

Conclusions

1. Metabolic acidosis is an important link in the pathogenesis of various diseases. It is the most common type of acid-base balance disturbances and it exacerbates the diseases through disruption of hemodynamics, increased tissue hypoxia, inactivation of some key enzymes, and metabolic activation of sympathoadrenal system.

2. The use of direct alkalizing agents (sodium bicarbonate, trisamine) does not solve the problem of metabolic acidosis due to the availability of a wide range of contraindications for use and a high risk of side effects and complications associated with the peculiarities of their effects. Only the use of sodium hydrocarbonate buffer solutions (soda-bufer) is justified.

3. The most effective medicinal products to correct metabolic acidosis include compounds containing organic anions in high concentration (more than 300 mmol/L). Complex infusion solutions containing sodium lactate (reosorbilact) and sodium acetate (xylatum) are the most effective and safe among them.

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SURGERY

Local and systemic inflammatory responses as a response to surgical trauma in severe chronic critical lower limb ischemia (CLI), combined with multifocal atherosclerosis

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The purpose of the study
A study of the inflammatory response occurring in patients with severe chronic critical lower limb ischemia in combination with multifocal atherosclerosis that develops in the course of the operation, as well as justification of drug prevention methods of inadequate inflammatory responses.

Materials and methods
The study included 123 subjects: 63 patients with CLI and combined lesions of arteries of aorto-iliac and femoral-popliteal segments, which had 136 combined sequential reconstructive surgeries during the period from 1997 till April 2005, as well as two groups, each of which included 30 patients with CLI and occlusive arterial and femoral-popliteal segment without lesions of the iliac arteries and with reverse version of the lesion. The patients were divided into 2 groups with 30 subjects in each group: Reosorbilact was used in group A, and the conventional treatment was used in group B. Groups were comparable in age, duration and severity of vascular history. The dynamics of the chemokine production was assessed by repeated sampling of serum from peripheral artery and femoral vein.
Conclusions

1. Changing levels of chemokines and cytokines in the blood serum is a predictor of systemic inflammatory response (SIR) in the postoperative period.
2. Taking into account that the IL-8, IL-10 and other cytokines and chemokines are involved in the pathogenesis of ischemia-reperfusion disorders in chronic critical lower limb ischemia, their concentrations can be identified to estimate the severity of the inflammatory response, which is leading in the pathogenesis of infectious complications.
3. The normalization of the levels of chemokines and cytokines makes it possible to interrupt the chain of the pathogenesis of chronic critical lower limb ischemia.
4. Use of reosorbilact in preoperative and the postoperative period can combat the negative consequences of the systemic inflammatory response: the concentration of pro-inflammatory factors IL-8 and IL-10 reduced by 60% on the average compared with that in the control group.
5. Reosorbilact reduces the aggregation ability of platelets, plasma viscosity, and it has hemodilution effect, and therefore can be used not only to improve the rheological properties of blood, but also to prevent formation of microthrombs, which positively affects the postreperfusion period.

Mystetstvo Likuvannya (Art of Treatment) [032]

INFECTIOUS DISEASES

Desintoxication therapy with Reosorbilact as a part of combination therapy in patients with leptospirosis

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Kyiv Medical Academy of Postgraduate Education named after P.L. Shupyk, Department of Infectious Diseases.

Actualization of the problem

Leptospirosis is an urgent problem in practical healthcare, which is associated with the wide prevalence of this zoonotic infection, the severe character of this disease with the development of multiple organ dysfunction syndrome and its relatively high mortality. Thus, almost 70% of patients have severe leptospirosis, with the rapid development of infectious and toxic shock syndrome, dysregulation of the aggregation state of blood, development of panangitis with the multiple organ failure syndrome. The drugs that can bind and eliminate the exo-and endotoxins of pathogens, as well as toxic metabolites that accumulate in patients with the dysfunction of kidneys, liver and other organs, are extremely important in the treatment of patients with leptospirosis.

The purpose of the study was to study the detoxification effects of reosorbilact in the treatment of adult patients with severe and moderate leptospirosis.

Materials and methods

The study included 50 adult patients with leptospirosis caused by Leptospira Icterohaemorrhagiae (38), Grippotyphosa (7), Canicola (3) and Pomona (2).

Results

In the group of patients with leptospirosis who received reosorbilact, the following parameters improved 2-4 days earlier compared to the control group: body temperature returned to normal values; headaches, myalgia, vomiting, and meningeal signs disappeared; appetite, intestinal peristalsis, renal, liver and heart functions improved, which was accompanied by normalization of the daily diuresis urea and creatinine content, a decrease in yellowness of the skin, reduction in bilirubin level in the blood. In addition, haematological and biochemical parameters, in particular, the red blood cells, hemoglobin, white blood cells, platelets, erythrocyte sedimentation rate, bilirubin, urea, creatinine, alanine aminotransferase, alkaline phosphatase, the composition of circulating immune complexes, potassium, sodium and chlorine composition in the plasma, as well as other parameters normalized in the main group of patients 2-3 days earlier than in the control group. In the group of patients with leptospirosis treated with reosorbilact as a part of the
combined treatment, the signs of acute renal and hepatic failure, myocarditis, or serous meningitis did not progress. Such signs of endogenous intoxication, as leukocyte index of intoxication, hemodynamics, motor and evacuation function of the intestine normalized in the main group of patients 2-4 days earlier than in the control group.

**Conclusions**

Use of reosorbilact in combined treatment of patients with moderate or severe leptospirosis has a positive effect on the rate of regression of clinical manifestations of disease, as well as normalization of hemogram, parameters of water and electrolyte balance, acid-base balance, renal and hepatic function, as well as functions of other vital organs.

Mystetstvo Likuvannya (Art of Treatment) [014]

**MEDICINE OF EMERGENCIES**

**Use of Reosorbilact in the treatment of traumatic shock:**

A comparative study

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National Medical University named after O.O. Bogomolets. Ukrainian Military Medical Academy.

**Abstract:** The effect of infusion of 800 ml of reosorbilact, 500 ml of HES 130 and 800 ml of 0.9% NaCl with the infusion rate of 50-55 ml/min. on hemostasis, fluid content of the chest, hemodynamic parameters in patients with traumatic shock (n = 60) was studied.

**Actualization of the problem**

Pandemic nature of the injuries has long been considered as the accepted fact. The use of infusion products based on sodium lactate has become one component of solving the problem of post-traumatic liquid resuscitation.

**The objective of the study:** to improve the treatment outcomes in patients with traumatic shock via the scientific justification for reosorbilact use.

**Materials and methods**

The study was conducted on the basis of Anesthesiology and Intensive Care Division of the city clinical hospital No. 17 in Kyiv. 60 injured adult patients of both sexes with blood loss of III-IV classes, or episodes of reduction in systolic blood pressure <90 mm Hg. were randomized after hospitalization to conduct the planned clinical observations. The randomization was not carried out for the injured patients with heart injury, clinical signs of coagulopathy and expected mortality within 24 hours.

After the final arrest of the apparent (visible) bleeding or immediately after the establishment of the central venous access when it was impossible to conduct the single-step final hemostasis surgically, the infusion was started: 800 ml of reosorbilact with the rate of 50-55 ml/min. in the first group (n = 20); identical infusion of 0.9% NaCl in group II (p = 20); and 500 ml of HES 130 was infused in group III (n = 20).

After the infusion of the study drug, which lasted on average 13 min., liquid resuscitation was not stopped in all groups and it was continued with the infusion of 0.9% NaCl at a rate of 18-22 ml/min.

**Parameters of the central hemodynamics.**

After the start of the infusion, significant increase in the index of velocity (IV) was observed in all groups, but the maximum increase in preload in reosorbilact groups (+ 37% at the 15th min.) and HES 130 (+35% at the 25th min.) significantly (p <0.05) exceeded the maximum value in the 0.9% NaCl group (19% at the 10th min.). The effect of preload increase in reosorbilact and HES 130 groups was significantly more durable (p <0.05) than that after infusion of 0.9% NaCl.

Maximum increase in cardiac index (CI) in reosorbilact group was observed at the 25th min. and was 30% of the initial value (p <0.001).

In HES 130 group, the maximum increase was observed at the level of 18% (p <0.001) at the 45th min. of the experiment.

The authors emphasize that the effect of reosorbilact (compared to HES 130) should be recognized as faster and “more aggressive”, which is especially important in the so-called golden hour of shock - the first hour of the critical state development.
Coagulation system. Reosorbilact infusion was not accompanied by significant changes in any of the parameters of coagulation system, which may be a sign of lack of effect of the studied amount of the drug product on coagulation hemostasis in patients with trauma. In 0.9% NaCl group, the significant changes of all the parameters of coagulation hemostasis toward hypercoagulation were observed. Marked significant increase in aPTT (+18%), PT (+16%) and the value of INR (+16%) was observed after infusion of HES 130. The values of all the parameters of coagulation hemostasis were greater than normal, and in some cases the values of PT and INR increased by more than 1.5 times above the norm, which is theoretically considered as the threshold of coagulopathy.

Conclusions
Infusion of 800 ml reosorbilact in patients with traumatic shock is not accompanied by effects on hemostatic coagulation system, whereas infusion of equal volume of 0.9% NaCl is accompanied by a tendency to hypercoagulation and infusion of HES 130 in the amount of 500 ml – with hypocoagulation due to hemodilution.
Reosorbilact has pronounced hemodynamic effects and increases oxygen delivery, which makes its use justified in patients with traumatic shock.

Vrachebnoye delo (General Practice) 1-2-2009

TREATMENT OF INTERNAL DISEASES

Laser Doppler flowmetry as a method of controlling the correction of skin microcirculation disorders of the with the drug products reosorbilact and pentoxifylline

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Purpose of the study
Compare the effects of reosorbilact and pentoxifylline on the parameters of skin microcirculation in patients with diffuse liver disease (DLD) and chronic venous insufficiency (CVI).

Materials and methods
A total of 54 patients were examined: Group 1: 26 patients with II-III stage chronic venous insufficiency (CEAP, 1999) with deep vein thrombophlebitis of the lower extremities (CVI), Group 2: 28 patients with chronic diffuse liver diseases (DLDs): 5 patients had chronic viral hepatitis C (CHCV), 8 patients had chronic alcoholic hepatitis, 8 patients had nonalcoholic steatohepatitis (NASH), and 7 patients had chronic viral hepatitis B (CHBV). The control group included 30 healthy volunteers.

Laser Doppler flowmetry (LDF) was performed on the unit LAKK-02 (Russia). Common clinical and laboratory tests, duplex ultrasound investigation of the vessels lower extremities, organs of hepatobiliary zone and splanchnic blood flow were performed to verify the diagnosis. To correct the disorders in MC, reosorbilact was administered i/v at a dose of 6-8 ml/kg of body mass by drop infusion. In a day, 2% solution of 5 ml pentoxifylline at a dose of 7-8 mg/kg of body mass i/v with 200 ml of 5% glucose solution was used as a reference drug. The study of the microcirculation was conducted before the administration of the drug products and after their administration (for 25-40 min. infusion), due to the fact that the effect of drugs (in accordance with the pharmacodynamics) end in 24 hours.

Results of the study
According to the LDF findings, the main action of reosorbilact is directed at switching the regulation of the microcirculatory bloodstream system to the active mechanisms, primary – on endothelial and less - on neurogenic; this leads to vasodilatation of precapillary sphincters and improvement of regional microperfusion. When compared with the reference drug pentoxifylline in patients treated with reosorbilact, there is a marked statistically significant increase in the rate of microcirculation, i.e. reosorbilact can be recommended to correct the microcirculatory disorders in patients with chronic venous insufficiency and diffuse liver disease.
Pentoxifylline has shown the signficant corrective properties concerning microcirculation according to the LDF findings in the group with CVI, as had been
confirmed previously by other clinical and instrumental methods, mainly due to the effects on passive mechanisms of regulation.

Conclusions
1. Reosorbilact significantly improves the skin microcirculation, both in patients with chronic venous insufficiency and in patients with diffuse liver diseases, mostly with a favorable impact on the active mechanisms of regulation.
2. Pentoxifylline significantly improves the skin microcirculation in patients with chronic venous insufficiency, mainly under the influence (according to the LDF findings) on passive mechanisms of microcirculation regulation.
3. LDF of the skin, as a method of complex instrumental evaluation, with respect to all parameters of active and passive regulation of microcirculatory bloodstream allows using the selective approach based on the pharmacological tests in the choice of optimal treatment scheme in patients with chronic venous insufficiency and diffuse liver disease.

TREATMENT OF INTERNAL DISEASES

Experience of reosorbilact use in treatment of patients with hepatitis and liver cirrhosis with hepatocellular insufficiency

V.O. Moiseyenko, T.D. Nykula, N.S. Milovanova
National Medical University named after O.O. Bogomolets, Kyiv City Clinical Hospital No. 3

Materials and methods
36 patients with decompensated liver cirrhosis during exacerbation were examined, which were divided into two groups (the main group included 24 patients who received reosorbilact with the standard therapy).

General clinical methods of examination, sonography of the heart and blood vessels were used for verification of the diagnosis and monitoring of treatment. Parameters of intrahepatic hemodynamics were evaluated before treatment and after 3-4 weeks in the dynamics.

The following criteria of the treatment efficacy were considered: decrease in the severity of major clinical syndromes (asthenic-vegetative, pain, dyspeptic, jaundice syndromes), positive changes in laboratory parameters (bilirubin, aminotransferase, alkaline phosphatase levels, parameters of flocculation tests, coagulogram, urea and creatinine levels) and ultrasound investigation findings, reduction of the clinical manifestations of disease.

Results
An overall positive clinical effect of 82.46 ± 2.43% (P <0.05) was observed as a result of three-week combination therapy in patients with hepatitis and liver cirrhosis. The decreases in cytolytic syndrome manifestations (transaminase activity), a syndrome of immune inflammation (levels of gamma globulins and thymol test indicators), cholestasis (concentration of bilirubin in blood and alkaline phosphatase activity), coagulopathy (prothrombin index) were observed in subjects. Reduced activity of the pathological process in the laboratory parameters was manifested as the stable decrease in daily proteinuria, ESR, and uremia. Changes in hepatic blood flow were characterized by an increase in the value of the linear velocity of blood flow in the hepatic artery by 28.2% as soon as after the first infusion of reosorbilact; the diameter of the artery during the study remained unchanged. Dynamics of clinical signs intensity was indicative of improved well-being of patients, which was probably caused by the detoxication effect.

Conclusions
Pathogenetic therapy with inclusion of reosorbilact reduces ammonia levels in the blood, provides positive dynamics of cytolytic, cholestatic, hemorrhagic and astheno-vegetative syndromes, reduces signs of hepatic encephalopathy.
TREATMENT OF INTERNAL DISEASES

Effect of reosorbilact on blood rheology in patients with ischemic heart disease and chronic obstructive bronchitis

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F.G. Yanovsky Institute of Tuberculosis and Pulmonology of the AMS of Ukraine, Institute of Gerontology of the AMS of Ukraine

Actualization of the problem
One of the most important pathogenetic factors in the development of tissue and organ hypoxia in patients with respiratory and cardiovascular disorders are the microcirculation disorders, which in turn are caused by impaired blood rheology. In patients with chronic inflammatory lung diseases in response to arterial hypoxia, compensatory increase in erythropoiesis is observed, as well as the development of polycythemia with increased levels of hematocrit. Hyperaggregation of blood cells, and as a consequence — microcirculatory disorders — are often observed in patients with pulmonary diseases. Data, collected over the past decades, suggest that increased blood viscosity is an independent risk factor for many diseases, including ischemic heart disease. In seven large epidemiological studies involving more than 1000 subjects, it was found that the risk of developing cardiovascular diseases is increased 3-fold in the patients with the hematocrit above 50%, and mortality from these diseases in this group of patients increases 6-fold, compared to the persons with normal hematocrit. Numerous reports show that high blood viscosity is typical for angina pectoris; it precedes the acute myocardial infarction and determines the clinical course of ischemic heart disease. Internal resistance to the flow of fluid is called viscosity. The principal factors that create the phenomenon of blood viscosity are hematocrit, plasma properties, cell aggregation and deformability of blood cells, mainly erythrocytes. Despite the importance of hemorheological disorders in the pathogenesis of a large number of diseases, the arsenal of drugs that can affect the rheological properties of blood, is extremely limited.

The purpose of the study
Compare the effects of infusion of reosorbilact and the mixture of glucose, insulin and potassium on hemorheological parameters in elderly patients with ischemic heart disease and chronic obstructive bronchitis.

Materials and methods
11 patients with ischemic heart disease in the form of stable FC II-III stenocardia without signs of heart failure and 4 patients with stage II chronic obstructive bronchitis in remission phase were examined. The examined patients were aged 60-79 years. The viscosity of the whole blood and plasma was determined using the rotation viscometer, the functional state of the erythrocytes was determined using a rotation viscometer with the calculation of the erythrocyte deformability index (EDI) and erythrocyte aggregation index (EAI). Rheological properties of blood were studied before the infusion, as well as 2 hours after infusion of 200 ml of reosorbilact. The study was repeated the next day using 200 ml of glucose-insulin-potassium mixture (GIP) as the comparator.

Results of the studies
The significant differences were obtained in studying the effect of drugs on the hemorheological parameters. GIP had no influence on blood rheology, whereas reosorbilact infusion resulted in a decrease in blood viscosity at all shear rates. Erythrocyte aggregation also decreased as a result of reosorbilact use. The change of rheological properties of blood under the influence of reosorbilact were unidirectional both in patients with the ischemic heart disease and in patients with chronic obstructive bronchitis.

Ukrainian Pulmonological Journal, 2003, No.3
TREATMENT OF INTERNAL DISEASES

Pathogenetic rationale and experience of reosorbilact use in the treatment of allergic diseases

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Kyiv Medical Academy of Postgraduate Education named after P.L. Shupik

Actualization of the problem
The use of infusion drugs that are able to normalize several types of disorders of homeostasis simultaneously, remains an urgent problem. Thus, asthmatic status is accompanied by respiratory and metabolic acidosis, disturbance of water-electrolytic balance in the body, which manifests itself as hypertonic dehydration, hypokalemia, and hypocalcaemia. Anaphylactic shock, toxic-allergic reactions for use of drug products and urticaria are accompanied by metabolic acidosis, hypertonic dehydration, hypokalemia, and hypocalcaemia.

The purpose of the study was to explore the possibilities of increasing the efficacy of treatment of the patients with allergic diseases by including reosorbilact solution in the combination therapy.

Materials and methods
The study involved 54 patients with exacerbation of bronchial asthma and asthmatic condition in the combination therapy of which was included reosorbilact at a dose of 200-400 ml intravenously by drop infusion (40-60 drops per minute) at a dose of 3.5 ml /kg of body weight every day or every second day No. 5.

The efficacy of treatment was estimated by the general condition of patients, the clinical course of disease, and laboratory parameters. The pulse rate, respiratory rate, systolic and diastolic blood pressure, and temperature reaction were measured in patients, as well as laboratory investigations were carried out, which included a study of total bilirubin concentration in blood, aminotransferase activity (ALT and AST), thymol test, urea concentration in blood, creatinine concentration, the function of external respiration before and after infusion therapy.

Results
Dynamics of the parameters of laboratory investigations in patients with bronchial asthma during their treatment with reosorbilact is shown in table.

Conclusions
As a result of clinical and laboratory studies it was found that reosorbilact normalizes the clinical and biochemical parameters, improves liver and kidney function, has detoxification effect, so it is recommended for use in the treatment of allergic diseases.

---

**Table**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Normal values</th>
<th>Before infusion</th>
<th>After infusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total bilirubin, mmol/l</td>
<td>4.3–20.5</td>
<td>29.4±2.9*</td>
<td>14.6±2.4**</td>
</tr>
<tr>
<td>ALT, mmol/l</td>
<td>0.10–0.45</td>
<td>0.62±0.04*</td>
<td>0.28±0.03**</td>
</tr>
<tr>
<td>AST, mmol/l</td>
<td>0.10–0.68</td>
<td>0.72±0.03*</td>
<td>0.46±0.04**</td>
</tr>
<tr>
<td>Thymol test, SH</td>
<td>5.0</td>
<td>7.6±0.4*</td>
<td>4.5±0.3**</td>
</tr>
<tr>
<td>Creatinine, mmol/l</td>
<td>0.07–0.17</td>
<td>0.22±0.02*</td>
<td>0.13±0.02**</td>
</tr>
</tbody>
</table>

Notes:
* difference in parameters compared with normal values is significant (p <0.05)
** difference in the parameters before and after treatment is significant (p <0.05)
Impact of reosorbilact on cardiohemodynamic and microcirculatory parameters in patients with chronic renal disease


National Medical University named after O.O. Bogomolets, Kyiv
Kyiv City Clinical Hospital No. 3

The goal of the work
To study the impact of reosorbilact on cardiohemodynamic and microcirculatory parameters in patients with chronic renal disease at different stages of the disease according to the data of clinical, laboratory and instrumental methods of investigations.

Materials and methods
A retrospective analysis of 234 case histories of the patients who were administered with intravenous reosorbilact infusions during their hospital treatment in the therapeutic clinic of the National Medical University. In addition, 34 nephrological patients with the process activity in I and II stage CRD (first group) and III-IV stage CRD (second group) were examined. This approach of the assigning the patients into the groups allowed to assess the ability of reosorbilact to affect hemodynamics and microcirculation at different stages of the disease. The drug was injected intravenously by drop infusion (30-40 drops per minute, 200-400 ml every second day, the treatment course included 5-10 infusions).

Results
The positive changes in cardiohemodynamics were seen in patients who received combination treatment. In patients with CRD I-II, the value of the stroke volume tended to increase in the dynamics of treatment (82.62 ± 6.23 ml - before treatment and 84.46 ± 5.48 ml - after treatment (P>0.1)), left ventricular ejection fraction - tended towards increase from 70.78 ± 2.29% to 70.88 ± 2.35%. In analysis of the left atrial dimension, a tendency towards its reduction was observed - from 37.60 ± 1.34 mm to 37.26 ± 1.26 mm (P>0.1).

In patients with CRD III-IV stages the significant decrease of end-systolic dimension was observed (from 34.52 ± 2.82 mm to 30.51 ± 1.52 mm) and left ventricular end-systolic volume (from 53.36 ± 7.44 ml to 39.26 ± 4.72 ml (P<0.05)). The comparative analysis of heart pumping function in the dynamics showed that there was an increase in ejection fraction by 4.4% (P<0.05) by reducing left ventricular end-diastolic volume and end-systolic volume. The stroke volume value tended to increase (81.83 ± 4.07 ml - before treatment and 85.92 ± 7.10 ml - after treatment (P>0.1)).

A significant reduction in the severity of spasticity and atonic syndrome vasculopathy, as well as improvement of rheological properties of blood and reduction of severity of the perivascular edema were observed in patients with CRD of stages I and II under the influence of therapy. Positive changes were found in the study of intravascular microcirculation - small- and large-granular flow was found by 20.9% more rarely (p<0.05), erythrocyte aggregation was observed significantly less often (2.1 times, p<0.05).

In patients with CRD stages III-IV after treatment with reosorbilact, the mean value of A/B ratio increased by 16.9% (p<0.001), arteriolar spasms were found almost 2 times less often. The frequency of detection of lowered number of functioning capillaries decreased by 32.4% (p<0.01). After treatment, the frequency of detection of erythrocyte aggregation decreased 3.3 times (from 56.9% to 18.4% of cases, p<0.05), rheological properties of blood improved, a tendency toward reduction of the frequency of detection of perivascular edema was observed (P>0.1).

After treatment, a tendency to reduction of the number of leukocytes in the blood, reduction of the ESR, the daily proteinuria of erythrocytes and leukocytes in urinalysis and urine test according to Nechyporenko method (p<0.05) were observed in both groups of patients.

Conclusions
Reosorbilact when used in patients with chronic renal failure stages I-IV, has a positive effect on the structural and functional state of the cardiovascular system and improves microcirculation in patients at different stages of chronic kidney failure.
Kidneys are the most important organ that regulates homeostasis. In patients with renal diseases, the water-electrolyte balance is disturbed, vascular tone and blood pressure are increased, and metabolic acidosis develops. These changes are the most pronounced in patients with chronic renal failure, reaching their maximum in patients with terminal uremia. Metabolic disorders develop also in patients with pulmonary diseases as well. Pneumonia, asthma, chronic obstructive bronchitis, pulmonary insufficiency are often complicated by respiratory and metabolic acidosis, hypertonic dehydration, hypocalcemia and hypokalemia. Metabolic changes result in disturbances of microcirculation, disorders of hemorheological properties of blood, which closes the "vicious circle" of pathogenesis of internal organ diseases.

It is essential for the nephrologist to correct fluid and electrolyte and acid-base balance in patients with chronic renal failure to reduce the symptoms of intoxication.

**Materials and methods**

Reosorbillact was used in 32 patients with chronic renal failure (CRF) of various origins. 18 females and 14 males aged from 26 to 48 years were examined. Chronic pyelonephritis was the cause of chronic renal failure in 14 patients, chronic glomerulonephritis was the cause of chronic renal failure in 18 patients. I st. CRF was diagnosed in 16 patients, II st. CRF – was diagnosed in 13 patients, and III st. CRF – was diagnosed in 3 patients. All patients were divided into groups. One group (16 patients) received reosorbillact at a dose of 200 ml every second day No. 5 (infusion rate - 40-60 drops per minute). The combination treatment in comparison group included infusion of 5% glucose solution at a dose of 200 ml every second day. The efficacy and safety of treatment was based on the monitoring of the general condition of the patients, the clinical course of the disease, and laboratory parameters.

**Results**

The severity of intoxication symptoms such as nausea, itchy skin, thirst, was significantly reduced in the group of patients administered with reosorbillact. The treatment had significant effect on the levels of urea, creatinine, rate of glomerular filtration, a significant decrease of urea and creatinine levels, and increase in GFR. The authors attribute the improvement in nitrogen-release renal function and GFR primarily to disintoxicational, diuretic effect of the drug, reduction in the degree of hypertension that is accompanied by increased function of the residual functioning nephrons.

**Conclusions**

Analysis of the abovementioned data shows a certain nephroprotective effect of reosorbillact, the admimstration of which was accompanied by a significant decrease in daily proteinuria, creatinine and blood urea levels, increased GFR and daily diuresis. The trend toward normalization of blood pressure is explained by its diuretic and nephroprotective effect, its detoxication and alkalinizing effects, as well as the potentiating effect of loop diuretics.
The slowing of diabetic nephropathy (DN) progression is one of the major issues in the current endocrinology. The development of renin-dependent systolic hypertension, urinary syndrome, which manifests itself at the early stages as microalbuminuria is one of the earliest clinical manifestations of DN. Glycosuria, polyuria, and in case of inflammatory process - leucocyturia increase in patients with decompensation of carbohydrate metabolism.

In addition to clear glycemic control, hemodynamic parameters in kidneys should be normalized – the factors that create the phenomenon of blood viscosity.

The purpose of the study was to improve efficacy of treatment of patients with diabetes complicated by DN, by eliminating the symptoms of intoxication and improvement of microcirculation with the use of the drug product reosorbilact.

Materials and methods
The study included 24 patients with type 1 diabetes (DM1) of young and middle age (WHO classification), complicated by DN.

The study group included patients with persistent microalbuminuria (MAU) - III stage of the DN (Mogensen SE, 1983) without marked inflammatory processes in the kidneys and urinary tract. The control group included 14 healthy donors.

In the absence of proteinuria, urine microalbumin test was carried out using ELISA.

The following parameters were determined: creatitine level, urea level in serum and glomerular filtration rate (GFR), prothrombin index (PTI), fibrinogen, total protein and protein fractions of blood serum, monitoring of carbohydrate metabolism, kidney ultrasound investigation. All parameters were evaluated in the dynamics of treatment within 16-18 days. Patients with DM-1 DN-III were divided into 2 groups: group 1 (11 patients) received conventionnal therapy (diet therapy, intensive insulin therapy, ACE inhibitors, antiplatelets, angioprotectors); 2nd group (13 patients) were additionally administered with reosorbilact in addition to conventional treatment (200 ml i/v by drop infusion daily for 10-12 days).

Results
At the end of treatment, polyuria and polydipsia persisted in the most patients in group 1, which reflected both the lack of compensation of carbohydrate metabolism and hyperfiltration and renal hyperfunction. These symptoms decreased significantly in group 2, showing a positive effect of reosorbilact on metabolic disorders and decrease of functional load on the kidneys (haemodynamic and metabolic components). Treatment with reosorbilact promoted both achieving a better compensation of carbohydrate balance and correction of hemodynamic parameters. Decline in GFR in patients in group 2 indicated a decrease in hemodynamic load on the kidneys and reduced renal adaptive hyperfunction associated with the excretion of excess glucose.

Conclusions
1. Use of reosorbilact in the combination treatment of patients with DM-1 DN III increased the efficacy of treatment: rheological parameters of blood and indicators of functional state of the kidneys improved, the severity of intoxication syndrome decreased.
2. Reosorbilact use in combination with ACE inhibitors improved microcirculation in the kidneys, ensured their functional unloading, provided renoprotective action, slowed the progression of DN.
3. Good tolerance, lack of side effects, multilateral action of reosorbilact make it possible to use it in the combined treatment of patients with diabetes 1 DN1.
Influence of reosorbilact on gas composition and acid-base balance of blood in patients with idiopathic fibrosing alveolitis

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Actualization of the problem

Increase in the degree of hemoconcentration (increased hematocrit) due to compensatory erythrocytosis, hyperaggregation of red blood cells and platelets and, consequently, the disorders of microcirculation with impaired gas exchange, formation of microthrombs in the pulmonary vessels play important role in the pathogenesis of pulmonary insufficiency and chronic pulmonary heart disease. In this regard, infusion therapy plays an important role in the treatment of patients, which is aimed at improving of the blood rheology and microcirculation in the lungs.

Reosorbilact reduces the relative blood viscosity, increases the osmotic pressure of plasma, thereby providing additional influx in vascular interstitial fluid and lowering hematocrit (hemodilution effect), has antiaggregation properties. All this eventually results in improvement of microcirculation. Along with the rheological effect, reosorbilact affects the acid-base balance of blood, which is associated with the metabolism of sodium lactate. This component of reosorbilact has long been used to correct acid-base balance of blood during metabolic acidosis. The study the impact of reosorbilact infusions on acid-base balance of blood in patients with non-compensated respiratory acidosis showed high efficacy of the drug product. However, respiratory acidosis can develop in patients with severe chronic lung diseases.

The purpose of the study

The study of the possible negative impact of reosorbilact on gas composition and acid-base balance of blood in the patients with chronic pulmonary heart disease during hypercapnia.

It has been found that reosorbilact infusion (200 ml daily for one week) in patients with hypercapnia did not significantly affect the rate of carbon dioxide tension in blood. However, reosorbilact increases blood oxygenation, which is most likely associated with the rheological effect of the drug, improvement of microcirculation in the vessels of the lungs and gas exchange. The findings allow to recommend the use of reosorbilact in combination treatment of patients with chronic pulmonary heart disease, including the ones with the signs of hypercapnia and compensated respiratory acidosis.

Materials and methods

The study involved 13 patients with idiopathic fibrosing alveolitis. Respiratory failure of I degree was observed in 1 case, 11 patients had II degree respiratory failure, and 1 patient had III degree respiratory failure. One patient had I stage congestive circulatory failure. The control group included 18 healthy individuals.

The state of respiratory function was assessed by analyzing forced expiratory curve, parameters of gas composition and acid-base balance of capillary blood: pH, carbon dioxide tension (pCO2, mm Hg), actual plasma bicarbonate (HCO3, mmol / l), standard plasma bicarbonate (SBC, mmol/l), an excess of buffer bases (ABE, mmol/l), the standard excess of bases (SBE, mmol/l), oxygen tension (pO2, mm Hg, hemoglobin oxygen saturation (sO2, % ).

Choice of the duration of the course was based on literature data, according to which the maximum effect of reosorbilact on gas composition and acid-base balance of blood develops on average within 3-4 days after the start of the therapy.

Results

1. In patients with idiopathic fibrosing alveolitis, disorders of the gas composition and acid-base balance of blood are observed – hypoxemia in combination with hypocapnia, partially compensated respiratory alkalosis.
2. A significant decrease in the degree of hypocapnia and normalization of acid-base balance of blood were
observed 2 hours after infusion of 200 ml of reosorbilact. The positive effect of the drug product on the gas composition and acid-base balance of blood is observed on the 4th day of the study as well (1 day after the three-day course of reosorbilact injections), but the dynamics of parameters is expressed to a greater extent immediately after the infusion.

3. Decrease in the degree of hypoxemia observed after infusion of reosorbilact, which is most associated with the rheological effect of the drug, improvement of microcirculation in the lungs and gas exchange.

4. The obtained study results give grounds to recommend the use of reosorbilact to correct gas composition and acid-base balance of blood in patients with idiopathic fibrosing alveolitis.

**TREATMENT OF INTERNAL DISEASES**

**Reosorbilact as a component of neuroprotection in patients with acute cerebral insufficiency**

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In recent years, a number of concepts and directions of intensive therapy in acute cerebral insufficiency has been developed. These include: the concept of the role of structural and functional levels of vascular brain system in disease, revealing of molecular and biological and pathophysiological basis of ischemic stroke, including the concept of "penumbra", the phenomena of "luxury" and "poor" perfusion, phenomena of "cytoprotective window" and "reperfusion window", etc.

It has been found that, regardless of the etiology of cerebral insufficiency, key pathogenetic factors causing its development, are discirculation (ischemia), anoxia (hypoxia), toxemia.

One of the important aspects of intensive therapy (IT) in acute cerebral insufficiency is the timely restoration of adequate perfusion in the affected areas of the brain.

The purpose of the study was to develop the new protocols of infusion therapy in patients with acute cerebral insufficiency, and evaluate their neuroprotective effects on the restoration of adequate cerebral circulation.

Materials and methods

The study was conducted in patients Clinic of Neurosurgery of the Donetsk Regional Clinical Territorial Medical Association (DOKTMO), which were treated at the Department of Neuroresuscitation after various surgical procedures to remove intracranial hematomas and on the intensive care unit due to a severe brain injury. According to the latest developments, only adequate cerebral blood flow (CBF) can fundamentally solve the problem of acute death of neurons in the perifocal area. According to the opinion of the authors, adequate CBF can be reached primarily through the achievement of adequate parameters of central hemodynamics (cardiac output, total peripheral vascular resistance, pulmonary capillary-wedge pressure) and satisfactory rheological properties of blood. It must be remembered that the use of crystalloids in a large volume in craniocerebral injuries leads to increased edema-swelling of the brain. Therefore, reosorbilact at a dose of 3-5 to 7-10 ml/kg is included in the modern protocols for emergency care of patients with acute traumatic brain injury as a starting antishock therapy for prehospital stage, as well as at the stage of the specialized treatment, as the basis of infusion therapy both in the preoperative and in intra-and postoperative periods. Identified positive rheologic, hemodynamic and osmotic properties of reosorbilact in complex intensive therapy in patients with acute cerebral insufficiency can be considered as neuroprotective due to efficient recovery of blood supply in the affected areas of the brain, active removal of toxic metabolites and effective relief of edema of the brain.

Medicinal Products of Ukraine (Liky Ukrainy), February 2007
Experience of using reosorbilact in combination treatment of hyperbilirubinemia in newborns

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The study was conducted on the basis of the intensive care unit and neonatal intensive care of the Pediatric Clinical Hospital No. 1 in Kyiv.

Objective of the study: to study the efficacy of reosorbilact as a part of combination therapy in treatment of neonatal hyperbilirubinemia.

Materials and methods

28 children with hyperbilirubinemia were examined (18 children with conjugated jaundice, and 10 children – with the hemolytic disease of the newborns). Reosorbilact was administered intravenously at a dose of 5 ml/kg/day in a drop infusion, every 12 hours for 1-2 days.

Normalization of acid-base balance was observed after infusion of reosorbilact (acidosis before the infusion was changed into the normalization of the parameters hereafter), changes in laboratory parameters (see the table). Decrease in yellowness of the skin was noted on physical examination. The signs of cerebral edema in children were decreased according to neurosonography data in dynamics. No significant changes of blood electrolytes, glucose, creatinine and urea levels were observed. Reosorbilact infusions were well tolerated by the newborns – no side effects or adverse reactions were recorded during and after the transfusion.

Dynamics of changes in laboratory parameters in patients with jaundice (p < 0.05)

<table>
<thead>
<tr>
<th></th>
<th>Conjugated jaundice</th>
<th>Hemolyt. jaundice</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before infusion</td>
<td>After 2 days</td>
</tr>
<tr>
<td>Total bilirubin (mmol/l)</td>
<td>222±24,3</td>
<td>114±21,2</td>
</tr>
<tr>
<td>Unconjugated bilirubin (mmol/l)</td>
<td>198±23,6</td>
<td>86±16,7</td>
</tr>
<tr>
<td>ALT (u/L)</td>
<td>36,4±8,6</td>
<td>21±6,1</td>
</tr>
<tr>
<td>AST (u/L)</td>
<td>72±10,2</td>
<td>36±8,2</td>
</tr>
</tbody>
</table>
INFUSION DETOXIFICATION

Hyperosmolarity

- Increase of blood volume
- Rheological effect
- Improving microcirculation
- Increase of tissue perfusion, “washing off” toxins
- Fluid moving from interstitium
- Toxins concentration lowering

- Diuretic effect
- Toxins excretion
- Decrease of hematocrit and platelets and RBC aggregation
- Pre- and postcapillary sphincters dilation

- Acid-base imbalance (metabolic acidosis) correction
- Fluid-electrolyte imbalance correction