INSTRUCTION FOR USE OF THE PHARMACEUTICAL PRODUCT

HARTMANN

isotonic, balanced electrolyte solution

Composition:

<table>
<thead>
<tr>
<th>Ion</th>
<th>Concentration (mval/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na⁺</td>
<td>131</td>
</tr>
<tr>
<td>K⁺</td>
<td>5</td>
</tr>
<tr>
<td>Ca²⁺</td>
<td>4</td>
</tr>
<tr>
<td>Cl⁻</td>
<td>111</td>
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<tr>
<td>Lactate⁻</td>
<td>29</td>
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</tbody>
</table>

Action:

The electrolyte composition of the solution is close to that of plasma and extracellular fluids, being isoionic with them. The lactate added binds the free H⁺ ions, after metabolization, and has an alkalizing action.

Pharmacodynamics:

The preparation is used for replacement of big losses of water and electrolytes in the organism and it is being composed in such a way that causes the least deviations in the electrolyte composition of ECL. Approximately 60% of the body weight of adults consist of water. Water guarantees the normal course of the main physico-chemical and biological processes in the 10S⁰ to the O-atom, hence it is oriented in the electric field.

Sodium has an exceptional significance for the organism. It determines to the greatest degree the volume and the osmolarity of ECL, the charging of the cell membrane, the transportation of some organic substances through the cell membranes, the base-acid equilibrium of the blood and the enzyme activity. The reabsorption of the sodium cations is the most considerable process in terms of volume and use of energy in the kidney. About 80% of the oxygen consumed in the kidneys is used for sodium transportation to the different parts of the nephron. A part of the sodium passively carries away with itself the chlorine anions, another part is exchanged against H⁺ passively pumped out of the cell. Sodium which has penetrated the cell reaches the intracellular and interstitial sector of the cell membrane and activates the pump mechanisms localized there, which carry it away into the intercellular and interstitial...
space. This pumping out of sodium occurs against the penetration of potassium into the cells (sodium-potassium pump), after which sodium moves to the peritubular capillary net, passively accompanied by chlorine and carbonate anions and water.

The dynamics of chlorine anions depends on the dynamic properties of sodium when they are connected with the action of the kidneys and the sweat glands. The sodium cations and chlorine anions of sodium chloride have a specific pharmacological action.

Potassium ensures a constant pH of the cell and regulates its electrical activity (membrane and action potential). Micropuncture examinations in different parts of the nephron suggest that a specific pump mechanism acts along the whole tubule from the luminary surface of the epithelial cells, and that this mechanism ensures the potassium reabsorption in them and subsequently in the direction of the interstitial space.

Calcium regulates membrane permeability, neuromuscular excitability, blood coagulation and the activation of some enzyme systems.

Administered intravenously, sodium lactate releases sodium cations, and in this way, binds and neutralizes the acid ions and radicals, while the lactate ion metabolizes, a part of it being accumulated in the form of glycogen and another part being disintegrated to carbonic acid and hydrocarbonates.

Considering of the pharmacologic activity of the active substances, introduced in Hartmann isotonic solution, and that the preparation is well balanced, the preparation is indicated in case of great losses of water and electrolytes from the organisms, which is leading to deviation in electrolytic composition of extracellular fluid.

**Pharmacokinetics:**

The daily sodium need is about 5 g. Sodium is constantly eliminated from the organism, which occurs through the sweat and urine. After abundant perspiration, the loss of Na+ may reach 20 g daily. The reabsorption of Na+ is most substantial in the nephron, because 4/5 of the substances dissolved in the primary urine are sodium salts. About 70 % of the filtered sodium are reabsorbed in the proximal tubules. The concentration capacity of the kidney and the active transport of glucose and amino acids depend on it. Only 10 - 15 % of the filtered sodium reaches the distal and collecting tubules and it is subjected there to additional reabsorption. The sodium reabsorption is subjected to hormonal regulation and more particularly to the action of aldosterone.
The total quantity of the chlorine anions is about 100 g. Normally the chlorine anions in the organism are supplied in the form of sodium and potassium chloride. The chlorine anions have the highest concentration in ECL, compared to all other anions in the organism. The reabsorption of chlorine follows passively that of sodium.

The total quantity of potassium in cells is about 250 g, while in ECL it is only 60 g. About 10% of the total cellular potassium is bound (mainly in the erythrocytes, the brain and bones), while the remaining 90% represent the so-called potassium which is metabolized. The daily needs of the organism are covered by the introduction of about 3 g KCl, mainly with vegetables and fruits. The tissues which regenerate and grow need more potassium. Conversely, during protein disintegration the cells lose potassium, which passes into ECL and is excreted with the urine. About 80% of the K+ in the organism is lost with the urine and 20% - with the feces. The K+ excretion from the organism occurs mainly through the kidneys (90%). Potassium from the primary urine is completely reabsorbed in the proximal tubule and is secreted in the distal tubule and in the collecting tubule, depending on the needs. Active K+ secretion occurs in the collecting tubule. Under normal conditions the most of the filtered potassium is reabsorbed. This occurs in the proximal tubule. If, however, a larger quantity is imported, the excreted potassium is more than the filtered one, which results from additional secretion. The potassium secretion towards the lumen occurs in the distal and collecting tubules. This transportation is considered to be a passive process, depending on the sodium in the tubular liquid and on the negative gradient created in the direction of the liminar cell membrane. Aldosterone increases the excretion of potassium.

The kidney plays a secondary part in calcium metabolism, but renal insufficiency of any origin is always accompanied by serious disturbances of calcium metabolism.

Only protein-bound calcium is filtered in the glomerules, which is almost fully reabsorbed in the proximal and distal tubule under the influence of parathyrin and actually only 1% of it is excreted. In the proximal tubule the reabsorption of Ca++. The movement of water in the organism, including through all parts of the nephron, is a passive process which depends on the differences in the osmotic pressure. In the proximal tubules the water permeability is maximal, which ensures a high water reabsorption (70% of the filtrate), corresponding to the movement of sodium and other osmotically active substances.
Water does not follow sodium and chlorine when they leave the ascendant part of the loop.

**Indications:**
Substitution for losses of extracellular fluids; intensive care in profuse blood loss, plasma loss, burns, intoxications, shock; correction of extracellular isotonic dehydration; correction of hyponatremia, hypochloremia and combination of water-electrolyte disturbances with metabolic acidosis.

**Contraindications:**
Hypertonic dehydration, injuries of liver cells, lactate acidosis.

**Special precautions and warnings:**
- To be administered cautiously to patients with cardiovascular, hepatic and renal insufficiency, when it is necessary to reduce considerably the quantity of the liquids intake and to control carefully the patient's condition.
- In case of infusion therapy, it is necessary to exercise control with strict monitoring of the amount of liquids introduced parenterally and orally, as well as of the amounts released mainly with diuresis. Parallel with that it is necessary to control regularly all hematological indices.
- Due to the presence of sodium lactate in the agent, the rapid infusion of the solution may result in inhibition of respiration, while the administration of larger quantities may result in disturbances in the water-electrolyte balance.
- **Use during pregnancy and breast-feeding**
  There is no evidence of embryotoxic or teratogenic effect of the solution used as a therapeutic agent.
- **Effects on ability to drive a motor vehicle or operate machinery**
  No data for a negative effect of the preparation on motor ability and CNS (central nerve system).

**Interactions with other medicaments and other forms of interaction:**
HARTMANN infusion solution should not be introduced simultaneously with tetracycline in the same application.

**Administration and dosage:**
Upon physician's prescription!
Up to 2500 ml daily with an infusion flow rate of 60 drops/minute or 2.5 cm$^3$/kg body weight/hour.
**Overdosage:**

The toxic dose of *sodium chloride* for human patients is 100-150 g. Due to the presence of sodium lactate in the agent, the rapid infusion of the solution may cause inhibition of respiration, while the administration of higher quantities may result in disturbances in the water-electrolyte balance.

**Undesirable effects:**

Symptoms referring to the volume of infused liquid in cardiovascular, liver and renal insufficiency.

**Pharmaceutical form:**

Infusion solution of 500 ml.

**Storage:**

Store in dry places, protected from light, at a temperature of 15 to 30°C.

**Expiry term:**

3 /three/ years of the manufacture date.