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## Pharmacoeconomic evaluation of domestic original preparation "succinasol"

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### ABSTRACT

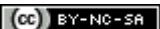
A new domestic preparation "Succinasol" is presented in this paper. According to its studied description it is the most appropriate agent for the purposes of detoxification, salt regulation, acid alkaline balance correction etc. Besides the above-mentioned properties, the preparation has an original energy producing effect. Succinic acid containing in the composition of preparation is able to be oxidized in the tissues when the oxygen content is reduced. "Succinasol" normalizes the acid-base status not due to passive neutralizing particularly oxidized products in the blood, and the normalization of metabolic processes in cells, relieves pain. The salt composition of the preparation is balanced with the composition of normal plasma. Large-scale implementation of measures on reducing the mortality rate in thermal burns requires large financial investments and adequate organizational resource involving State budget agents (investments) for the program.

**Keywords:** Succinasol, Reamberin, thermal injuries, burn disease, septicotoxemia, shock.

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## INTRODUCTION

Now our government has made significant arrangements for the timely provision of health care institutions and the population with effective medicines and medical devices. In the domestic pharmaceutical market in recent years is increasing a number of modern medicines. Nowadays, burn injuries are the actual medical and social problem due to the increasing of production, the development of vehicles, increased urbanization and the increase of natural disasters.

According to the World Health Organization data, burns currently occupy the third place in the overall structure of peacetime accidents. Despite some progress, the mortality of burnt with deep and extensive burns still remains high.

According to the Swiss statistics in peacetime worldwide die from burns 60,000 people annually. Mortality from burns a whole in recent years has considerably increased, ranging from 1.9-4.6% to 11-14%. Mortality among severe-burned patients (with critical injuries - 40-50% of the body surface and over critical - more than 50% deep burns) remains high even in the specialized agencies and varies according to different sources on the average from 33% to 82.2%. One of the main reasons for the high mortality rate among victims is the lack of the unified concept of treatment, a common approach to the prevention and treatment of life-threatening complications like multiple organ failure, burn sepsis, burn encephalopathy, leading to the death and disability of patients.

Despite its uniqueness, "Succinasol" has a foreign counterpart - "Reamberin" of Russian production. However, by comparison it has a number of advantages; firstly, it is a domestic production, therefore, much cheaper than the "Reamberin", the cost of which laid the customs, transport, etc. costs. Secondly, the base of "Succinasol" contains succinic acid - the substrate of the human body involved in the metabolic Krebs's cycle exchanges.

Available in Russian literature information on health-economic evaluation of the costs, quality and availability of hospital care is fragmented, which confirms the relevance of the study of the world experience of introduction of technologies and targeted programs within the framework of organizational models "end result", aimed at reducing the burden in burn injury. Thus, in short supply today preparations of complex action, especially poly-functional, the clinical introduction of new domestic drug "Succinasol" in common thermal burns is relevant and justified [1]. Taking into consideration the great importance of this problem, it is necessary to study the

pharmacoeconomic efficacy of "Succinasol" preparation that will allow to develop recommendations for its use in the correction and optimization of therapy in patients with critical conditions, justify the importance from the pharmacoeconomic point of view.

**The purpose of the study:** Comparative evaluation of pharmacoeconomic efficiency of "Succinasol" and "Reamberin" in critical conditions in terms of emergency medical aid. To study the duration of stay of the burn patients in a hospital in the conventional therapy with the addition to the protocol therapy "Reamberin". To evaluate pharmacoeconomic efficiency of "Succinasol."

**Scientific novelty:** complex evaluation of results of infusion therapy in case of emergency with "Succinasol" was first performed on the basis of the pathophysiological performance criteria of care and severity of metabolic disorders in patients. Conducting infusion therapy with the use of "Succinasol" contributes to the rapid cleansing of the body from the products of cellular and tissue metabolism in poisonings, reduce the severity of hemodynamic disorders, increase in urine output, reducing the severity of hypoxia and oxidative stress, and ultimately contributes to a fast recovery, and reduces the cost of treatment.

## MATERIALS AND METHODS

The conducted studies give reason to recommend the inclusion of "Succinasol" in complex therapy for the improvement of blood microcirculation, restoration of metabolism, detoxification and prevention of tissue hypoxia, which allows the fast exit of patients from the hospital, reducing deaths, which provide social and pharmacoeconomic efficiency for practical public health. Republican Scientific Center of emergency medical care for patients with burn disease. A comparative analysis of the prices of medicines, "the cost of treatment," "cost-effectiveness".

### Description of "Succinasol" preparation:

"Succinasol" - one of the new domestic medicines containing amber acid with antioxidant-antihypoxants and energoprotector and functions intended for infusion. "Succinasol" - as a substrate inhibitor of free radicals, membrane protectors, reducing lipid peroxidation peroxide. It has a wide spectrum of pharmacological action on the support system for the metabolic activity of cells, stimulates energosynthesis in mitochondria [2, 3]. New effective group of infusion remedies in metabolic correction of critical conditions in clinical practice are different solutions with transfer function of oxygen, increasing the oxygen capacity of the blood and normalizing the body's oxygen

regime and metabolism. Today, the preparation is produced on an industrial scale on the basis of domestic producer JV «REKA-MED-PHARM». It is also included in the list of essential medicines, which reflects its high quality and reliability of the therapeutic effect.

**Medicament comprises:**

1. Sodium chloride - 6.20 gr;
1. Potassium chloride - 0.30 gr;
2. Calcium chloride - 0.16 gr;
3. Magnesium chloride, on the account of anhydrous - 0.10 gr;
4. Succinic acid - 2.0 gr;
5. Sodium bicarbonate - 3.0 gr;
6. Water for injection - up to 1 litre.

Succinic acid is a versatile intermediate metabolite formed during the interconversion of carbohydrates, proteins and fats in plant and animal cells [4, 5, 6]. Under physiological conditions, succinic acid is dissociated, so the name of its anion - succinate is often used as a synonym for the term "succinic acid". It is a product of the substrate in the fifth and sixth reaction of the Krebs cycle. The conversion of succinic acid in the body is associated with the production of energy necessary for life. When the load increases on any of the systems of the body, maintaining its operation is provided mainly by oxidation of succinic acid. The interesting thing is that the productivity of energosynthesis system using succinic acid, a hundred times superior to all other systems of the body's energy production. This is what provides a wide range of non-specific therapeutic action of succinic acid and its salts. In addition, succinic acid has other effects - antiviral and act-protective - providing the body's resistance to physical stress without increasing oxygen consumption and heat, thus enhancing efficiency. The experimental studies have shown that the biological activity of administered succinate depends on the dose, mode of administration, its chemical form (acid, salt, ester), and the functional condition of the organism.

In the application of physiological doses of succinic acid were identified two main groups of effects:

- The direct effect of succinic acid on cell metabolism;
- The effect of succinic acid on transport of free oxygen to the tissues.

In *in vitro* experiments, it was shown that the use of succinate leads to increase in oxygen consumption of tissues due to the oxidation of substrates added to the final products - carbonic acid, water and heat. One molecule added to the tissue dicarbonic acid provides oxidation of many endogenous substrates. In other words, the succinate oxidation

is a prerequisite for catalytic action of any other of the carboxylic acid to digest tissue oxygen [7, 8, 9]. Losing intermediates cycle increases in acute and chronic poisoning with ammonia. Replenishing acids of the Krebs's cycle is disturbed in alcoholism, hypo and vitamin B6 deficiency and poisoning with inhibitors of pyridoxal phosphate dependent enzymes. Therefore replenishment pool of Krebs cycle intermediates, including those from dietary sources, is a vital process. Succinic acid is a metabolite of the human organism, and its endogenous level in human plasma is normally 0.5 mg / 100 ml. Nature is also rich in the free succinic acid. A large number of (0.1-1.0 g / kg, or 0.8-8.0 mmol / kg) it is contained in the immature berries, juice of sugar beets, sugar cane, turnips, in rhubarb, aloe, hawthorn, strawberry, Kalanchoe, nettle, celandine, wormwood and other plants, as well as in products of alcoholic fermentation. An additional source of succinic acid directly in the tissue is lipolysis [10, 11].

For replenishment of organic acids of the Krebs's cycle in humans sufficient was exogenous administration of a single succinate, stimulating the synthesis of reducing equivalents in the cell. The biological significance of this phenomenon is the rapid resynthesis of cellular adenosine triphosphate and the increase of antioxidant resistance of cells.

The basis of therapeutic and prophylactic action of succinic acid and its compounds is a modifying influence on the processes of tissue metabolism - cellular respiration, ion transport, protein synthesis. The amplitude and direction of the modification depends on the initial functional state of the tissue, and its final result is expressed in the optimization of the parameters of their functioning. These properties allow to attribute succinic acid to the treatment and prevention preparations of new generation. Nevertheless, with the unique versatility of biological activity of succinic acid, it is still not enough demanded in the practice of medicine.

Succinic acid is a natural and completely non-toxic substance and does not accumulate in the body, which is confirmed by experimental data on the safety of the drug "Succinasol."

Summarizing the data, it can be concluded that the succinic acid containing blood substitute "Succinasol" restores hemodynamics, acid-base status, the energy potential of the organism. If antacidotic blood substitutes improve the pH by using alkalizing action in using "Succinasol" the normalization of acid-base status is due to the improvement of metabolic processes [12, 13].

**Clinical characteristics of examined patients:**

For the formation of experimental groups for observation of severe-burned patients in the acute period of burn disease use special selection criteria, including: the age (from 18 and older); total lesion area with burns (more than 20% of body surface area); time of admission to treatment after trauma (hospital admission in the first 3 h after injury, adequate antishock therapy before hospitalization). Exclusion criteria were burdened premorbid background, cancer; prior hormone therapy, chemotherapy, drug addiction, drug abuse, immunosuppression.

Total surveyed 75 patients with severe thermal injuries of various localization, treated in the burn intensive care unit of the Republican Scientific Center for Emergency Medical Aid.

To test the effectiveness of the developed method compared to the traditional method of treatment all the studied patients were divided into 3 groups:

- I (basic) group consisted of 25 patients treated with conventional therapy in combination with "Succinasol";
- II (basic) group consisted of 25 patients treated with conventional therapy in combination with Reambirin;
- III (control) group consisted of 25 patients who received conventional therapy.

Burn injury of basic amount of patients is due to the bulk of the flame resulting from ignition of easily flammable substances and gases (natural gas, gasoline, kerosene, etc.). These burns are characterized by a large area of injury often with lesions of the trunk, neck, face, upper and lower extremities.

The second most common etiologic factor was boiling water or steam. In our study, burns with hot water and / or steam accounted for 25% of all burn injuries. These burns are characterized by superficial lesions.

In turn, burns with boiling oil are characterized by burns III AB degree abdomen and lower limbs, and more superficial burns.

Since the main factors affecting the duration of the treatment and determining its outcome, are the area and depth of the burn injury, the analysis of these indicators in all groups of patients was carried out. Observation of burned patients was carried out in course of the disease during treatment in a hospital. In diagnosing the classification has been used. The main criteria for diagnosis of the disease were agents (hot water, flames), the area and depth of the burn, the severity of burn shock, sowing flora from the blood, the results of biochemical and clinical laboratory testing of blood and urine.

Dynamic observation was conducted in patients with the presence of burn injury from 20 to 100% of the body surface in periods of burn disease (shock, toxemia, septicotoxemy, convalescence). All patients came to the hospital in a state of burn shock. Depending on the breadth, depth and location of the burn surface noted mild shock, severe and very severe. In 22 examined patients was light, 41 - a heavy and 12 patients had very severe burn shock.

In the course of the disease in patients underwent clinical and biochemical blood tests: level of hemoglobin, red blood cells, white blood cells, the activity of aspartate aminotransferase, alanine aminotransferase, total protein level of burn disease, bilirubin, indicators characterizing the severity of endogenous intoxication were defined on molecules content of medium and low weight, values of hematological indexes of intoxication - leukocyte. The level of energy production of the organism in the form of phosphate compounds was studied by the number of adenosinetriphosphate in serum by Boehringer Mannheim GmbH Diagnostica method. The results were evaluated using Student's t test.

**DETERMINATION METHODS OF PHARMACOECONOMIC EFFECTIVENESS**

Pharmacoeconomic efficiency is the main criterion by which is determined the best medicinal preparation having an acceptable ratio the cost pharmacological effect, among its analogues. In determining this indicator relatively the application of complex methods of treatment burns using hemocorrectors of the following factors:

1. The number of bed-days;
2. The number of treated patients;
3. The cost of medication per 1 bed-day;
4. The cost of one bed-day treatment;
5. The cost of one treated patient;
6. Consumption of "Succinasol" per 1 bed-day;
7. Cost of "Succinasol" per 1 bed-day;
8. The cost of "Succinasol";
9. Consumption of Reambirin per 1 bed-day;
10. Cost of Reambirin per 1 bed-day;
11. Cost of Reambirin.
12. The economic effect for health care associated with reduced duration of treatment was calculated using the formula:

$$E1 = (TTP - TH) * R * D$$

where, E1 - economic effect; TTP - the duration of treatment by conventional methods;  
 Tn - the duration of treatment of the proposed integrated methodology; K - number of patients;  
 D - the cost per 1 bed-day, respectively, or a clinic visit.

According to this formula, the economic effect is calculated separately for hospital and clinic, and then summed up.

The duration of treatment in the hospital is estimated in calendar days.

Interdisciplinary economic effect is associated with the payment of temporary disability benefits, reduction of terms of treatment, the release of the labor force, with an additional release of net output (R). Consequently, the overall economic effect in the national economy is given by:

$$E = D1 (TTP - TH) * K + D2 (TTP - Tn) * K * 0.75 + B (TTP - TH) * K + P (TTP - Tn) * K * 0.9$$

where, E - the economic effect in the national economy;

D1 - the cost per bed-day in the hospital;

D2 - the cost of clinic visits;

B - the average daily amount of the benefit for temporary disability;

P - the value of net production in monetary units produced by 1 working person per 1 day.

0.75 - coefficient of calculation the working days (determined by multiplying the duration of treatment in calendar days by 0.75).

0.9 - the number of patients that had started to work (estimated to be 90% of the patients returned to work) [1].

Economic efficiency costs are calculated according to the formula:

$$Ef = E / 3,$$

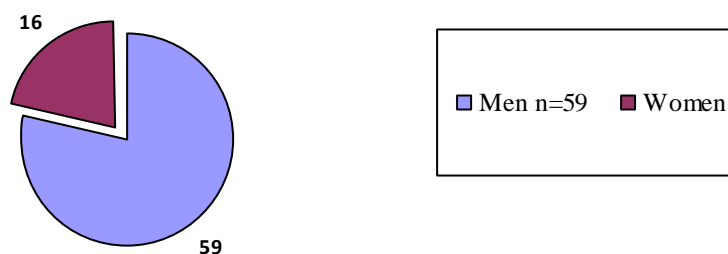
where, E - the overall economic effect in the national economy, 3 - additional costs associated with the introduction of a new method of treatment.

This method is for determination of socio-economic efficiency of the treatment. Statistical analysis of the results was performed in Microsoft Excel with the calculation of Student's t test. For statistically significant differences were accepted, those for which the value is  $p < 0.05$ .

Comparative analysis of conducted complex intensive therapies with the use of metabolic correctors "Succinasol" and "Reambirin" showed the significant superiority in all parameters of the first correcting action and completeness of the recovery of energy metabolism, reducing the intensity of lipid peroxidation and increase antioxidant capacity of the organism. Driving intensive care with "Succinasol" is pathogenetically substantiated and highly effective, can significantly improve the results of treatment of patients with severe burn injury.

### THE RESULTS OF PERSONAL ANALYSIS

To form monitoring groups of severe-burned patients in acute burn disease were used inclusion criteria: from the age of 18 and older; total area of lesion was more than 20% of body area; admission to hospital in the first 3 hours after injury, adequate antishock therapy before hospitalization. Exclusion criteria: burdened premorbid background, cancer diseases; prior hormone therapy, chemotherapy, drug addiction, drug abuse, immune-depression. The study included 75 patients with severe thermal injuries of various localization who were treated in the burn intensive care unit of the Republican Scientific Center for Emergency Medical Aid.



**Figure 1. Distribution of patients by age and sex**

To test the effectiveness of the proposed method compared to the traditional method of treatment studied patients were divided into 3 groups:

- I (control) group consisted of 25 patients (22 men and 3 women) who received conventional (traditional) therapy;

- II (control) group consisted of 25 patients (17 men and 8 women) received conventional therapy in combination with "Reamberin";

- III (basic) group consisted of 25 patients (20 men and 5 women) who received conventional therapy in combination with "Succinasol." Of the total number of patients 59 are men and 16 women. The distribution of patients by age and sex is shown in Table and Fig.1.

**General presentation and clinical manifestations of burn injuries in the studied patients:** Thermal injury leads to development of a number of

pathological changes in the majority of organs and systems that manifest clinical and laboratory parameters of burned, so you need to treat it not as an isolated local process. In this connection, naturally to talk about burn disease, including periods of shock, toxemia, septicemia and reconvalescence. The severity and course of these periods depends largely on the nature of the therapy.

In the control group I surveyed 25 burned receiving conventional therapy. From them came to the clinic in a state of mild burn shock 7, severe-14, extremely severe -3. In 10 patients the total affected area was from 20 to 40%, in 13 patients-over 40%. Stage of burn shock characterized by tachycardia, heart rate -  $132,4 \pm 0,08$  beats/min. Blood pressure in the first hours after the injury remained relatively high 110-60 mmHg, central venous pressure -  $21,4 \pm 0,28$  mm of water. From the hemodynamic parameters observed tachycardia, pulse on peripheral vessels of medium and weak filling, listened the deafness or muffled heart sounds. Hourly urine output remained at the lower limit of normal.

In the control group II were examined 25 burned patients receiving conventional therapy in combination with "Reamberin". From them came to the clinic in a state of mild burn shock 6, severe-16, extremely severe-3.

At 7 wounded total lesion area was from 20 to 40%, in 14 patients-over 40%. Stage burn shock was characterized by tachycardia, heart rate - 136,4

$\pm 0,06$  beats/min. Blood pressure in the first hours after the injury remained relatively high 110-60 mmHg, central venous pressure -  $22,4 \pm 0,24$  mm of water.

In the study group examined 25 burned patients receiving conventional therapy in combination with "Succinasol." From them came to the clinic in a state of mild burn shock- 9, severe-13, extremely severe - 4.

In 13 wounded total affected area was from 10 to 40%, in 12 patients-over 40%. Stage burn shock characterized by agitation, restlessness, disturbance of peripheral blood circulation, manifested with pallor of the skin, visible mucous membranes, lowering the temperature of the skin of limbs, tachycardia, pulse -  $127,4 \pm 0,08$  beats/min. Almost all of the patients complained of severe pain in burn wounds, marked fever, muscle tremors, limpness came later.

Despite all the frustrations of hemodynamics, blood pressure in the first hours after the injury remained relatively high 110.2/62.8 mm Hg. This is due to an increase in total peripheral resistance to blood flow. The reason for the growth of the peripheral resistance - a spasm of vessels caused by increased activity of the sympathetic-adrenal system and an increase in blood viscosity.

One of the clinical signs of burn shock in the examined patients was reduction in central venous pressure  $20,6 \pm 1,24$  mm of water.

Table 1: Dynamics of clinical parameters of patients with burn disease on conventional therapy background and in combination with "Reamberin" and "Succinasol" ( $M \pm m$ )

Periods of disease	Blood pressure, mmHg systolic	Heart rate, beats/min	Central venous pressure, cm.water.	Respiratory rate, per 1 min	Daily diuresis, ml
Healthy	118,5 / 58,4	$81,2 \pm 0,24$	40 – 60	$18,6 \pm 0,56$	1200 – 1500
Shock (I)	110 / 60,5	$132,4 \pm 0,08^*$	$21,4 \pm 0,28^*$	$30,7 \pm 1,44^*$	$1424 \pm 0,12$
Shock (II)	110,0 / 60,3	$126,2 \pm 0,18$	$22,4 \pm 0,24$	$27,4 \pm 1,14$	$1426 \pm 0,22$
Shock (III)	110,2 / 62,8	$127,4 \pm 0,04^*$	$20,6 \pm 1,24^*$	$27,8 \pm 1,06^*$	$1420 \pm 0,12$
Toxemia (I)	116,8 / 58,0*	$121,6 \pm 0,12^*$	$31,5 \pm 1,54$	$25,4 \pm 0,25^*$	$2120 \pm 0,75$
Toxemia (II)	114,8 / 56,0	$120,6 \pm 0,08$	$32,4 \pm 1,08$	$22,4 \pm 0,18$	$2380 \pm 0,55$
Toxemia (III)	114,6 / 55,2*	$116,5 \pm 0,12^*$	$32,8 \pm 1,68$	$23,0 \pm 0,44^*$	$2430 \pm 0,75$

Note: \* - significant differences compared with healthy ( $P < 0.05$ )

From the hemodynamic parameters observed tachycardia, pulse on peripheral vessels of medium and weak filling, listened deafness or muffled heart sounds. Daily urine output was maintained in the range of  $1424 \pm 0,12$  ml. It should be noted that the severity of these parameters depend on the severity of burn shock. On the basis of complex multicomponent mechanism of burn shock, during antishock measures we worked on all of its

components. First of all, it held infusion-transfusion therapy, correction of disorders of the central and peripheral hemodynamics.

In this clinical picture of burn shock in the study group was somewhat different from the control group of patients who did not receive "Succinasol." The duration of severe burn shock in patients, from the first day of admission to hospital, went up to

2.5 days. The period of burn toxemia at examined burned patients was characterized by severe intoxication, the severity of which depended on the depth and location of the burn.

The initial symptoms of acute burn toxemia appeared since the elimination of shock as a result of absorption into the bloodstream with edema fluid formed in the wound burn toxins. As a result, in patients developed dysfunction of the central nervous system in the form of limpness, confusion, sleep disturbances.

One of the first manifestations of acute toxemia in examined patients was resorptive fever with the formation of wet and dry necrotic scabs. Fever was characterized by irregular waves, temperature curve ranged from 38-390 °C, in severe cases-up to 400° C and reduced with difficulties.

In 24.0% of patients in the control group and 17.2% of patients in the main group during the period of burn toxemia developed anemia it is 1.4 times less than in the control group ( $p < 0,05$ ).

From the wound process was observed acceleration of cleansing wounds, in deep burns areas the formation of necrotic scab, played an important role in reducing the absorption of the products of tissue decay.

Increasing intoxication accompanied by dysfunction of various organs and the occurrence of toxic pneumonia - in 13 (20.4%) patients in the control group and 8 (13.7%) patients of the main group, toxic hepatitis - 7 (12.8%) and 4 (6, 9%) of burned, which was also lower in 1.6 and 1.7 times than in patients of the control group. They manifested by increase of liver, hepatic manifestation of jaundice, vomiting, anorexia. Septic complications occurred in 10 (18.5%) and 7 (12.0%) patients, it is 1.4 times higher than in the control group.

To maintain the basic parameters of hemodynamics and improved laboratory parameters were transfused fluids, including native colloids. Thus, heart rate decreased and self-maintained between  $121,6 \pm 0,12$  and  $116,5 \pm 0,12$  min., suggesting more adaptive activity level regulation systems in the study group. It was also noted a decrease in respiratory rate up to  $25,4 \pm 0,25$  per minute and  $23,0 \pm 0,44$  per/min., increase of daily diuresis up to  $2150 \pm 0,75$  ml., central venous pressure could be maintained at the level of 40-60 mm of water.

Treatment of patients with concomitant diseases corrected after consultation with the experts and carried out symptomatic treatment as needed.

In 80.3% of patients the period of acute burn toxemia lasted from 7 to 10 days (in average 9

days), and in 7.2% this period reduced to 3-4 days due to the stratification of septic complications, which was confirmed by blood bacteriological tests.

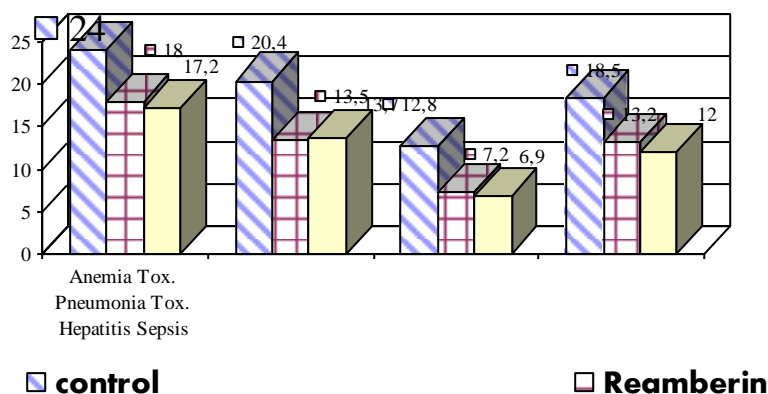
Septicotoxemia period lasted from the beginning of rejection of scab to complete wound healing. The initial phase of this period was characterized by symptoms that are characteristic for the stage of toxemia.

The condition of patients was severe, marked irritability, weakness, loss of appetite, sleep disturbances, all patients had purulent-resorptive fever, the duration of which depended on the severity of the wound healing process. This stage lasted in average 2-3 weeks, and in severe cases - in 58.4% of burned patients-1.5-2 months.

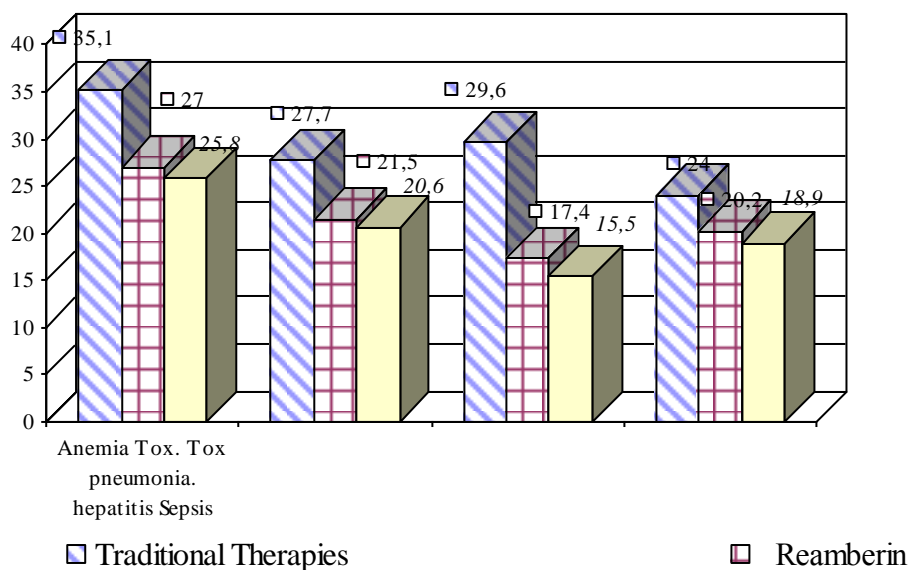
During septicotoxemia in 15 (27.7%) patients of the control group and 12 (20.6%) patients of the main group of burned developed toxic pneumonia. This manifested in 1.25 times less than in the main group. In 16 (29.6%) and 9 (15.5%) of patients allied toxic hepatitis, which was characterized by an increase in the blood levels of aminotransferases, increase of liver size. It is also 1.7 times less in the main group. Septic complications increased 1.3 times in the control group 13 (24.0%) and in the main group - 11 (18.9%).

Wound surface was purified by necrectomy method, followed by closing with autodermotransplantants. Postoperatively, in 12 (22.2%) patients in the control group and 8 (13.7%) patients of the main group was noted out a partial lysis of the transplanted grafts, and therefore prolonged wound healing time and hospital stay. (Figure 2). The duration process of septicotoxemy in 58.4% patients was directly related to the nature of the wound healing process.

Under the influence of ongoing intensive therapy we observed burned to the period of convalescence gradually started the improve of clinical and laboratory parameters characterized by the cessation of intoxication picture, better overall health, appetite, normalization of temperature curve. In group I of patients receiving traditional treatment, wounds were cleaned to an average of 22nd day from the date of injury, epithelialization started at the same time and later. Bed-day in average was 49 days. It should be noted that in the III group of patients under the influence of complex therapy with "Succinasol" accelerated the process of cleansing the wounds on the average to the 20th day, had improved engraftment of the transplanted skin grafts in the postoperative period. The phenomena of intoxication were eliminated in a short time, as evidenced by normalization of clinical data and blood test, which led to a reduction in hospital stay.



**Figure 2. Comparative characteristics of clinical indicators in toxemia, in%**



**Figure 3. Comparative characteristics of clinical indicators in septicotoxemia**

Analysis of the data showed the effectiveness of "Succinasol" in patients with thermal injury. Thus, in major clinical group in the result of the intensive therapy with "Succinasol" observed 1.5 times less than in the control group the number of pneumonias, 1.8 times less of toxic hepatitis, 1.4 times less of anemia and stay in a critical condition.

Application of pathogenetically substantiated therapy contributed to a more rapid regression of clinical symptoms, 1.2 times more likely continued the process of cleansing wounds from 22 to 18 days, reducing the number of complications,

shorter hospital stay by 4.7 (10%) days - from  $49,0 \pm 2,4$  day to  $44,3 \pm 1,6$  bed-days.

**Complications and mortality:** As it is known the mortality is one of the main integral parameters of overall treatment effectiveness and influence on the outcome of certain drugs in particular. Considering that the analyzed contingent totaled affected with severe and critical thermal injury, characterized by a high mortality rate, it seems appropriate to assess not only the overall mortality, but the timing and occurrence of deaths in the study and control groups. Overall mortality in the study group for the entire treatment period was 3 (12.0%) in the control



group 1-5 (20.0%), in the control group 2-4 (16.0%). In analyzing the distribution of deaths by maturity showed a significant reduction in their

frequency in the critical period of thermal injury in the affected of the main group (Table 2).

**Table 2: The distribution of deaths by maturity**

	Number of deaths%				lethality,%
	1-3 d.	4-7 d.	8-14 d.	15-60 d.	
Traditional n = 25	2 (8,0)	1 (4,0)	1 (4,0)	1 (4,0)	5 (20,0)
Traditional "Reamberin" N = 25	1 (4,0)	0	2 (8,0)	1 (4,0)	4 (16,0)
Traditional "Succinasol" N = 25	1 (4,0)	0	1 (4,0)	1 (4,0)	3 (12,0)

Main number of deaths occurred in the period from 16 to 60 hours, some of them were associated with chronic diseases became aggravated during the course of burn disease. In the control group, on the contrary, the principal amount of deaths was in the critical period of burn disease and caused the early onset of respiratory distress syndrome, acute renal and liver failure. Data of clinical effectiveness of

intensive therapy in patients of both clinical groups are presented in Table. 3. In assessing the effectiveness of different treatment options of burn disease found that the complex method of using "Succinasol" allowed significantly to reduce the mortality rate by 12.0% compared to 16.0% "Reamberin" and by 20.0% in the traditional method of treatment.

**Table 3: Clinical criteria of efficiency of complex intensive therapy in patients with thermal injury of the 1st and 2nd clinical groups**

Indicators	Group 1 (without "Succinasol")	Group 2 (with "Reamberin")	Group 3 (with "Succinasol")
Number of Patients	25	25	25
Age (s)	44,9 ± 3,8	43,7 ± 4,8	44,8 ± 4,5
The total area of burns (%)	52,0 ± 4,6%	54,2 ± 4,2%	55,0 ± 6,8%
ITP (units)	82,0 ± 6,8	86,6 ± 7,2	87,0 ± 5,7
The frequency of anemia	15 (60,0%)	10 (40,0%)	8 (32,0%)
The frequency of pneumonia	14 (56,0%)	9 (36,0%)	7 (28,0%)
The frequency of sepsis	13 (52,0%)	6(24,0%)	6 (24,0%)
The frequency of toxic hepatitis	13 (52,0%)	9 (36,0%)	7 (28,0%)
The incidence of delirium	15 (60,0%)	11 (44,0%)	11 (44,0%)
The duration of delirium (d)	5,2 ± 2,1	3,0 ± 1,5	2,2 ± 1,1
Time spent in HITD	26,2 ± 2,5	25,0 ± 2,4	23,5 ± 3,8
Length of stay in hospital bed days	49,3 ± 2,4	44,9 ± 1,5	43,7 ± 1,6
Died	5 (20,0%)	4 (16,0%)	3 (12,0%)

Results of treatment of patients of the control and main group are shown in table. 4. Thus, in the 2nd clinical group in the result of intensive therapy with "Succinasol" noted less in comparison with the 1st and 2nd group (without "Succinasol"), the number of pneumonia (respectively 56.0, 36.0 and 28.0%), sepsis (52.0; 24.0 and 24.0%) and delirium (60.0; 44.0 and 44.0%), the duration of delirium (5,2 ± 2,1; 3,0 ± 1,5 days and 2,2 ± 1,1 days) and staying in a critical condition (26,2 ± 2,5; 25,0 ± 2,4 and 23,5 ± 3,8 hours) reduction in mortality from 20.0% to 12.0%. Application of pathogenetically substantiated therapy contributed to a more rapid regression of clinical symptoms, reduce the number of complications and reduce of mortality.

**Pharmacoeconomic evaluation of the effectiveness of drugs used in the treatment of burn disease:** Combustiology is one of the most expensive areas of health care. Spending it make a long stay in hospital, repeated surgeries, expensive equipment and its operation. In economically developed countries, the costs associated with burn injury are higher than the costs of providing medical care for stroke and AIDS. The calculation of the exact cost of the treatment of burn patients is a very difficult task, but an analysis of the costs necessary for the budget planning and management of hospital expenditure. Implementation of the proposed method can significantly reduce hospital stay, overall treatment time, both in the hospital

and in outpatient clinics. In addition, the improvement in the results of plastic surgery and engraftment allows to avoid reoperation. Described in Chapter 2 of this paper method of determining the socio-economic effect of the introduction therapeutic techniques, makes it quite accurately to estimate the absolute numbers in terms of money

received from the introduction of new methods of treatment.

Initially was made calculation of the cost-effectiveness of this scheme. It is possible to calculate this result for a short period of time.

**Table 4: Evaluation of the effectiveness of the pharmacological treatment of patients**

The number of bed-days (I group)	49,3 ± 2,4
The number of bed-days (II group)	44,9 ± 1,5
The number of bed-days (II group)	43,7 ± 1,6
The number of treated patients (I group)	25
The number of treated patients (II group)	25
The number of treated patients (III group)	25
The total number of patients	75
The cost of medical treatment of the patient with the operations of stay in intensive care for one bed-day	100 316 sums
The cost of one bed-day treatment	106 286 sums
Diagnostic costs:	
Laboratory research	10 196,4 sums/day
Instrumental research	971,6 sums/day
Non-medical costs:	
Transportation costs-	16 000 sums
The costs of caring: nutrition	12 000 sums/day
The cost of one treated patient (I group)	5 790 482 sums
The cost of 1 treated patient (II group)	5 273 684
The cost of a single visit to clinic	5 132 739
The average amount of the allowance for temporary disability	14 560 sums
The net production in monetary units produced by 1 person per 1 day.	10 000 sums
Consumption of Succinasol or Reamberin per 1 bed-day ml.	0,09 l
The cost of "Succinasol" per 1 bed-day	1800 sums
The cost of "Reamberin" per 1 bed-day	6300 sums
The cost of "Succinasol" 1 l	20 000 sums
The cost of "Reamberin" 1 l	70 000 sums

The obtained results led to the conclusion that the treatment of burn patients need to use medications that contain the names of the international names Comb. drug (sodium chloride, sodium bicarbonate, calcium chloride, succinic acid foodgrade), pharmacotherapeutic groups of saline solution, a dosage form and the form of the solution for infusion 100 ml, 200 ml, 400 ml (glass bottles), companies and producing countries «Reka-Med Farm », JV, CLR. One of these medications is sold under the name "Succinasol- safe and highly effective therapy in patients of burn disease.

Analyzed the direct and indirect costs of hospital treatment for an average of 43 days with "Succinasol" preparation (course of treatment). Analyzed the direct and indirect costs of hospital treatment for an average of 44 days with "Reamberin" preparation (course of treatment).

One of the objectives of the study was to estimate the cost of treatment in two ways: "Analysis of the

cost of the disease" and "cost effectiveness analysis." In the analysis of the cost of the disease was used the formula:

$$COI = DC + IC,$$

where: COI - cost index of disease;

DC - direct costs;

IC - indirect costs [14].

The cost of treatment "Reamberin" were as follows:

$$COI = DC + IC = 2743,60 + 91,66 = 2835,3 \text{ sum,}$$

and costs for treatment with "Succinasol" are:  $COI = DC + IC = 2581,6 + 85,6 = 2667,4 \text{ sum.}$

Economic efficiency was determined by using a "cost-benefit analysis." The ratio of cost - effectiveness for each alternative regimens were calculated using the formula:

$$CEA = (DC1 + IC1) - (DC2 + IC2) / Ef1 - Ef2,$$

where in: CEA - ratio cost - efficiency (shows cost efficiency per unit);

DC1 - direct costs of using the first method; IC1 - indirect costs when using the first method; DC2 - the direct costs of the second method of treatment;

IC2 - indirect costs for the second method of treatment; Ef1 and Ef2 - respectively the efficacy of treatment by using the first and second methods.  $CEA = (2743,4 + 91,7) - (2581,7 + 85,6) = 333\ 350$  sums.

"Succinasol" is efficient and cost effective: the economy is equal to 333 350 sums per 1 patient treatment with "Reamberin" is 167,9 sums more expensive. In particular, a comparison of cost-effectiveness of the two drugs "Succinasol" and "Reamberin" showed that the former has a clear advantage. For example, direct costs of patients in Group 1 averaged 5 447 552 sums, the indirect costs – 182 000 sums. In the 2nd group, these parameters were "respectively 5 126 202 and 170 000 sums. In Table. 4. the effect of the patients in Group 1 (Ef1), who received the "Succinasol" is much higher than in the 2nd (Ef2).

Republican Scientific Center for Emergency Medical Aid in 2012 has registered 200 patients in Uzbekistan treated for burn patients.

On our reasonable efficacy of medicinal preparation for one patient will be saved 333 350, and 200 patients – 66 670 000 sums.

Through the use of "Succinasol" managed to reduce direct and indirect costs of medical actions, which had a positive impact on the socio-economic situation of the patient, and that is very important for the economic condition of the clinic.

The drug "Succinasol" is more effective for the treatment of burn disease of severe form than "Reamberin" as the positive effect on the quality of life of patients.

## CONCLUSION

Thus, the use of "Succinasol" in the treatment of burn patients prevents the development of oxidative stress, and has a restorative effect in the early period after thermal injury. The data indicate the feasibility of targeting a metabolic change in burn disease drugs capable of eliminating not only changes in hemodynamics, acid-base status, but also to restore metabolic processes. Therefore, detoxification therapy with natural metabolites of an organism is more suitable for reducing the severity of endogenous intoxication, which necessitates their widespread use in clinical practice. "Succinasol" is well tolerated with burn disease. Reactions, complications and side effects when it is used during and after infusion of the medicinal preparation was not observed. This pharmacoeconomic efficiency of its use is obvious: "Succinasol" is a domestic drug, therefore it is much cheaper and therefore more accessible to the general population, so its use in the treatment of

not only burn patients, but also patients with other severe pathological conditions, guarantee a significant reduction in public expenditure for treatment of sick contingent, unlike "Reamberin" imported from the Russian Federation.

In recent decades, parameters of mortality and hospital mortality from burn injuries in Uzbekistan remain one of the highest that can be associated with a complex of factors, including socio-economic, institutional and etc. This therapy has contributed to the rapid regression of clinical symptoms, had a positive effect on hematologic parameters and has a good detoxification effect.

Combined therapy of severe-burned patients with the use of "Succinasol" in the acute period of burn disease leads to a significant reduction of hypoxia, the level of endogenous intoxication 1.3 times faster than the control group. The use of "Succinasol" in severe-burned patients have shown high clinical efficacy of the medicinal preparation, which showed a decrease 1.3 times the incidence of septic complications, reduction of the period of stay in the anesthetic and intensive care unit, a decrease in mortality compared to the control group, and III group of examined patients.

In burn disease "Succinasol" has a positive effect on hemodynamic parameters, acid-base status, it stimulates kidney function and restores the biochemical parameters and functionality of the liver. "Succinasol" effectively reimburse blood volume, corrects metabolic acidosis and 1.2 times increases the body's energy potential.

An integrated treatment of severe-burned patients with "Succinasol" preparation can significantly improve the effectiveness of treatment and socio-economic parameters and, thereby, resulting in savings of about 9,6% of the costs for hospital care.

Infusion solution "Succinasol", being a domestic preparation and possessing multifunctional properties, cheapness and availability compared to the "Reamberin" is quite applicable for the treatment of patients in critical situations.

## CONFLICT OF INTEREST

Authors declared that there is no any conflict of interest

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