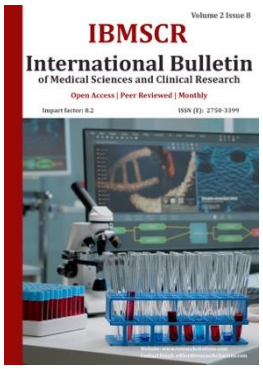

USE OF URINARY KALLIDINOGENASE IN PATIENTS WITH MALIGNANT ARTERIAL HYPERTENSION COMPLICATED BY BRAIN INFARCTION.

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Abstract: Stroke is a major burden worldwide due to unsatisfactory conventional treatments available today. Disability from a stroke ranks first among the causes of primary disability. [2.3] To date, the introduction of new methods of treatment contributes to the success of stroke treatment and greater patient survival. The use of urinary callidinogenase (Kalgen 0.15 PNA) as part of complex therapy for patients with cerebral infarction has an etiopathogenetically effective and rapid recovery of nervous function.

Key words: ischemic stroke, tissue kallikrein (kallidinogenase), MMSE, NIHSS, Rankin, hemostasis.

Introduction: Acute ischemic stroke (AIS) is the most common type of stroke caused by blockage of blood vessels supplying the brain, accounting for about 80% of all types of stroke [2.6]. Recanalization, especially thrombolysis, can significantly improve outcomes. However, hemorrhagic transformation, neurotoxicity and short treatment period are the main limitations of thrombolytic therapy [1.4].

Ischemic stroke is caused by hypertension, diabetes, heart disease, age, heredity and other risk factors [5.9]. This leads to stenosis and occlusion of the lumen of the brain vessels, as well as to a decrease or interruption of the blood supply to the nerve cells of the brain; thus, hypoxic-ischemic necrosis occurs. Inflammation at an early stage after cerebral infarction is one of the important mechanisms of neuronal damage in the infarct and penumbra regions [2.4].

Human urinary kallidinogenase (HUK) is a glycoprotein extracted from male urine. HUK belongs to the tissue kallikrein family, and tissue kallikreins exert their biological effects by activating the kallikrein/kinin system (KKS). Activated KKS will induce therapeutic angiogenesis and neovascularization, which may provide a new way to restore blood supply to the ischemic area [6,8,10,12].

KLK - is a group of serine proteases present in most body tissues and fluids, including plasma kallikrein (PK) and tissue kallikrein (TK). Tissue kallikrein is found in the tissues of the lungs, kidneys, blood vessels, brain and adrenal glands and plays a key role in the regulation of blood microcirculation, blood pressure and blood flow; acts as a necessary component for maintaining homeostasis and a response factor to diseases, and is also responsible for the production of kinins (bradykinin and kallidin), which promote local vasodilation and long-term vascularization, and also specifically increase blood flow in inflamed tissues by increasing the level and activation of BK2R (bradykinin receptor) [1,2,9].

Urinary Kallindinogenase - selectively expands capillaries in hypoxic and ischemic zones, and also promotes the function of the vascular endothelium and has an antioxidant effect, can reduce the volume of cerebral infarction foci and increase the perfusion of ischemic

brain tissue, and the mechanism of this is associated with the opening of collateral circulation in ischemic zone [2,4].

Objective: to evaluate the clinical effectiveness of urinary kallidinogenase (Kalgen 0.15 PNA) in patients with malignant arterial hypertension complicated by cerebral infarction.

Clinical materials and research methods:

In the intensive care unit of the clinic of the Urgench branch of the TMA, we examined 32 patients with acute ischemic stroke (20 men and 12 women), whose average age was 56.1 ± 6.4 years. We divided all the patients into 2 groups: a control group (retrospective), which included 16 patients, who received standard therapy, where we studied archival data, and a study group, which included the remaining 16, who, in addition to the specified therapy, received Kalgen 0.15 PNA (urinary kallidinogenase) once a day diluted with saline intravenously, drip, slowly. We measured ICP non-invasively using the Complexmed 1.2 device using m-Echo pulsation of the 3rd ventricle of the brain (normal, moderate and marked increase in ICP). All patients underwent clinical and biochemical studies, computed tomography; during therapy, coagulogram (PTT, fibrinogen, IPT), blood pressure, mean arterial pressure, blood glucose, thermometry and venous blood saturation were monitored. We assessed neurostatus using the Glasgow scale and NIHSS.

In addition to general clinical methods of blood and urine analysis, coagulogram parameters, biochemical parameters of blood, markers of kidney function (urea, creatinine) were monitored in all patients of the study and control groups.

The length of stay of patients in the ICU and in the multidisciplinary clinic of the Urgench branch of TMA as a whole was studied.

Study design: single center prospective study.

Results of own research:

In our studies, we included only those patients who had malignant arterial hypertension that was unresponsive to antihypertensive drugs.

Table №. 1 Monitoring of hemodynamic parameters

	B/P (mm. Hg.)	**Heart rate (b.pm)**	**MBP(mm.Hg.)**
"Kalgen" concentrate for preparing solution for infusions 0.15 PNA			
Before treatments	**180,3/100,6**	**110,33**	**126,63**
After treatments	**130,86/90,0**	**88,53**	**103,3**
Traditional therapy			
Before treatments	**180,6/100,2**	**108,13**	**126,7**
After treatments	**150,33/81,33**	**92,93**	**104,9**

Blood pressure indicators also showed positive changes - almost all patients in the study group experienced a decrease in blood pressure to normal levels without the use of any antihypertensive drugs. For patients in the control group, we selected antihypertensive drugs individually, together with a cardiologist.

The data presented in the table clearly demonstrate the effectiveness of complex therapy using urinary kallidinogenase (Kalgen 0.15 PNA) in the studied patients with cerebral infarction.

Table №2 Average data for predicting the severity of functional disorders (MMSE scale, NIHSS, Rankin Scale)

(M±m, n=32)

	MMSE (point)	**NIHSS** (point)	**Rankin scale (point)**
"Kalgen" concentrate for preparing solution for infusions 0.15 PNA			
Before treatment	**22,6**	**10,8**	**2,4**
After treatment	**25,8**	**7,6**	**1,8**
Traditional therapy			
Before treatment	**24,6**	**10,46**	**2,4**
After treatment	**25,4**	**9,53**	**2,0**

According to the data obtained, the Kalgen drug had a positive effect on the state of cognitive functions. This was confirmed by an increase in the total score when performing the MMSE technique on the 10th day of treatment. Thus, Kalgen had a significant positive effect on cognitive functions. The average improvement on the MMSE scale shows an improvement in the cognitive status of patients from a pre-dementia state to a slight decrease in cognitive functions.

The average statistical time of stay of the study patients of the main group in the intensive care unit was 10.3±1.1 days and in the control group 15.3±1.1.

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