American Journal of Medicine and Medical Sciences 2022, 12(10): 1056-1058
DOI: 10.5923/j.ajmms.20221210.10

Evaluation of the Efficiency of Urinary Kallidinogenase (Kalgen 0.15 PNA) in Patients with Acute Ischemic Stroke

Avezova S. Yu.[1], Avakov V. E.[2]

[1]Tashkent Medical Academy, Tashkent, Uzbekistan
[2]Urgench Branch of the Tashkent Medical Academy, Urgench, Uzbekistan

Abstract Stroke is an extremely common disease worldwide. 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.

Keywords Ischemic stroke, Tissue kallikrein (kallidinogenase), MMSE, NIHSS, Rankin, Hemostasis

1. Introduction

Stroke is the second most common cause of death and the leading cause of disability in adults worldwide [2,6] Acute cerebral infarction is caused by a sharp decrease in blood and oxygen supply [1,4] Stroke is a heavy burden for the world due to inadequate traditional treatment available on today. [3] For stroke patients, improved cerebrovascular perfusion, such as thrombolysis, arteriolar expansion and new vessel formation in the ischemic penumbra remains a good option to salvage damaged tissue and alleviate neurological deficits [6,11]. The most severe form of stroke results from occlusion of large vessels of the main branches of the circle of Willis. Treatment strategies currently available in Western countries for large vessel occlusion include rapidly restoring blood flow by removing the problematic blood clot using mechanical or pharmacological means (e.g. tissue plasma activator).

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 cerebral vessels, as well as to a decrease or interruption of the blood supply to the nerve cells of the brain; thus appears hypoxic-ischemic necrosis. Inflammation at an early stage after cerebral infarction is one of the important mechanisms of neuronal damage in the areas of infarction and penumbra. [2,4]

Antithrombotic therapy is an important part of the current treatment of acute ischemic stroke (AIS) [6,7,8] During the onset of AIS, irreversible ischemia and hypoxic necrosis occur in the central region of the infarction due to reduced or intermittent blood supply. However, there are many surviving neurons in the ischemic penumbra of the marginal zone, which can restore their normal function if blood perfusion is restored in a short time. However, due to the short treatment period, most patients miss the best time for thrombolysis during treatment. [10] Angiogenesis plays a key role in the process of nerve repair, which mainly occurs in the border zone of ischemia. When blood flow in the local brain tissue is blocked, blood can enter the ischemic region through other collateral branches. The newly formed blood vessels can then promote neurorecovery processes, including neurogenesis and synaptogenesis, thereby improving functional recovery. [12]

Human urinary kallidinogenase (HUK), which is up-regulated via the kallikrein-kinin (KKS) system, catalyzing the hydrolysis of low molecular weight kininogens to vasoactive kinins, and thereby activates the bradykinin B1 and B2 receptors (B1R and B2R) and has a number of biological effects. Of these, activated B2 receptor can promote angiogenesis through Akt-GSK-3β-VEGF-VEGFR-2 and Akt-eNOS-NO signaling pathways. The protective mechanisms of kallikrein in ischemic brain damage include anti-inflammatory and anti-apoptotic effects, as well as stimulation of angiogenesis and neurogenesis in hind limb ischemia, myocardial infarction and renal ischemia. [14]

Objective: To improve the results of treatment of patients with acute ischemic stroke.

2. Clinical Materials and Research Methods

We examined 24 patients with acute ischemic stroke (18 men and 6 women) in the intensive care unit of the clinic of the Urgench branch of the TMA and in the emergency neurology department of emergency hospital, whose average age was 58.1 ± 4.4 years. We divided all patients into 2

Received: Sep. 7, 2022; Accepted: Oct. 12, 2022; Published: Oct. 14, 2022
Published online at http://journal.sapub.org/ajmms

groups: the control group, which included 12 patients, received standard therapy (antioxidants, neuroprotectors, detoxifications, anticoagulants (low molecular weight heparins), sedative and symptomatic therapy) and the study group, which included the remaining 12 who, in addition to the indicated therapy received Kalgen 0.15 PNA (urinary callidinogenase) once a day, diluted with saline intravenously, drip, slowly.

Both groups were randomized by us according to gender and age characteristics, the nature of the standard examination and according to MSCT data.

All patients underwent clinical and biochemical studies, computed tomography (CT), during therapy they monitored blood pressure (BP), mean arterial pressure MAP (according to the formula: SBP, mm Hg = (Syst. BP + 2 Diast. BP): 3), central venous pressure (CVP), blood glucose, thermometry and saturation of venous blood. We assessed the neurological status using the MMSE, NIHSS, Rankin.

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.

3. Results of Own Research

Average data for predicting the severity of functional disorders (MMSE scale, NIHSS, Rankin Scale) are shown in the table

Table 1. (M±m, n=24)

	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.

Table 2. 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	**140,3/85,3**	**95,33**	**103,63**
After treatments	**122,86/79,0**	**80,53**	**93,62**
Traditional therapy			
Before treatments	**138,3/88,0**	**78,13**	**104,7**
After treatments	**128,33/81,33**	**79,93**	**96,9**

Table 3. Dynamics of changes in some indicators (M±m, n=24)

	Urea mmol/l	Creatinine mmol/l	ESR (mm/h)	Hb (g/l)	APTT (sec)	Fibrinogen (mg/l)	PTI (%)
	"Kalgen" concentrate for preparing solution for infusions 0.15 PNA						
Before treatments	7,6	84,7	**7,33**	**105,0**	**22,56**	**584,66**	**109,8**
After treatments	7,05	79,5	**6,73**	**112,13**	**27,52**	**304,0**	**92,93**
	Traditional therapy						
Before treatments	**8**,2	**90**,2	**8,4**	**112,4**	**23,73**	**322,0**	**96,86**
After treatments	**7**,8	**89**,6	**8,2**	**113,44**	**23,82**	**317,66**	**96,6**

Changes in the direction of improvement also wore an indicator of blood pressure - in many patients there was a significant restoration of pressure to normal levels.

The data presented in the table clearly demonstrate the effectiveness of the ongoing complex therapy using Kallidinogenase (Kalgen) in the studied patients with cerebral infarction.

The average time spent by the studied 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.

In the process of using the drug Kalgen, no allergic reactions and other complications were observed. Tolerability of the drug by patients is good.

4. Conclusions

1. Kalgen 0.15 PNA (urinary callidinogenase) etiopathogenetically provides an effective and rapid recovery of nervous function in cerebral infarction.
2. Kalgen in the complex therapy of patients with ischemic stroke, reducing plasma fibrinogen and PTI by 48.1% and 15.4%, respectively, and increasing

the APTT time by 21.9%, significantly improves hemostasis.

3. Kalgen (urinary callidinogenase) is well tolerated by patients and does not cause any complications.

REFERENCES

[1] WHO. The top 10 causes of death. 2018.

[2] Go AS, Mozaffarian D, Roger VL, et al. Heart disease and stroke statistics—2020 update: a report from the American Heart Association. Circulation 2020; 129: e28–92.

[3] Wang W, Jiang B, Sun H, et al. Prevalence, incidence, and mortality of stroke in china: results from a nationwide population-based survey of 480 687 adults. Circulation 2017; 135: 759–71.

[4] Amarenco P, Bogousslavsky J, Caplan LR, et al. The ASCOD phenotyping of ischemic stroke (Updated ASCO Phenotyping). Cerebrovasc Dis 2019; 36: 1–5.

[5] Grysiewicz RA, Thomas K, Pandey DK. Epidemiology of ischemic and hemorrhagic stroke: incidence, prevalence, mortality, and risk factors. Neurol Clin 2008; 26: 871–95. vii.

[6] El-Koussy M, Schroth G, Brekenfeld C, et al. Imaging of acute ischemic stroke. Eur Neurol 2014; 72: 309–16.

[7] Yew KS, Cheng EM. Diagnosis of acute stroke. Am Fam Physician 2015; 91: 528–36.

[8] Montecucco F, Mach F. Atherosclerosis is an inflammatory disease. Semin Immunopathol 2019; 31: 1–3.

[9] Tuttolomondo A, Di Sciacca R, Di Raimondo D, et al. Effects of clinical and laboratory variables and of pretreatment with cardiovascular drugs in acute ischaemic stroke: a retrospective chart review from the GIFA study. Int J Cardiol 2018; 151: 318–22.

[10] Di Raimondo D, Tuttolomondo A, Butta C, et al. Effects of ACEinhibitors and angiotensin receptor blockers on inflammation. Curr Pharm Des 2012; 18: 4385–413.

[11] Di Raimondo D, Tuttolomondo A, Butta C, et al. Metabolic and anti-inflammatory effects of a home-based programme of aerobic physical exercise. Int J Clin Pract 2020; 67: 1247–53.

[12] Reshi R, Streib C, Ezzeddine M, et al. Hyperglycemia in acute ischemic stroke: Is it time to re-evaluate our understanding? Med Hypotheses 2017; 107: 78–80.

[13] Gonzalez-Moreno EI, Camara-Lemarroy CR, Gonzalez-Gonzalez JG, et al. Glycemic variability and acute ischemic stroke: the missing link? Transl Stroke Res 2014; 5: 638–46.

[14] Licata G, Tuttolomondo A, Corrao S, et al. Immunoinflammatory activation during the acute phase of lacunar and non-lacunar ischemic stroke: association with time of onset and diabetic state. Int J Immunopathol Pharmacol 2019 19: 639–46.

[15] Kruyt ND, Biessels GJ, Devries JH, et al. Hyperglycemia in acute ischemic stroke: pathophysiology and clinical management. Nat Rev Neurol 2010; 6: 145–55.