ASSESSMENT OF RENAL FUNCTIONAL RESERVE AGAINST THE BACKGROUND OF ANTIAGGREGANT THERAPY IN STAGE II-III CHRONIC KIDNEY DISEASE

Yodgorova Sadoqat Uktamovna
1st year master's student
Tashkent Medical Academy, Tashkent, Uzbekistan
Azim Atakhanovich Zhabbarov
Head of Department "Faculty and Hospital Therapy ¹2".
Tashkent Medical Academy, Tashkent, Uzbekistan
Sultanboy Bahodorovich Zhumanazarov
Assistant of "Faculty and hospital therapy ¹2" department.
Tashkent Medical Academy, Tashkent, Uzbekistan
Tashkent Medical Academy Tashkent Uzbekistan

Abstract: *The article presents the results of a study to evaluate the comparative effectiveness of the antiaggregant drugs dipyridamole and alltrombosepine on the functional kidney reserve in 50 patients at the early stage of chronic kidney disease. The study showed that long-term use of alltrombosepine improves*

the functional reserve of the kidneys. Thus, our studies have once again confirmed that the widely used antiaggregant, made from local raw materials, alltrombosepine is not inferior to dipyridamole, which is used in chronic kidney disease.

Key words: *chronic kidney disease, functional kidney reserve, glomerular filtration rate, antiaggregant, alltrombosepine, dipyridamole*

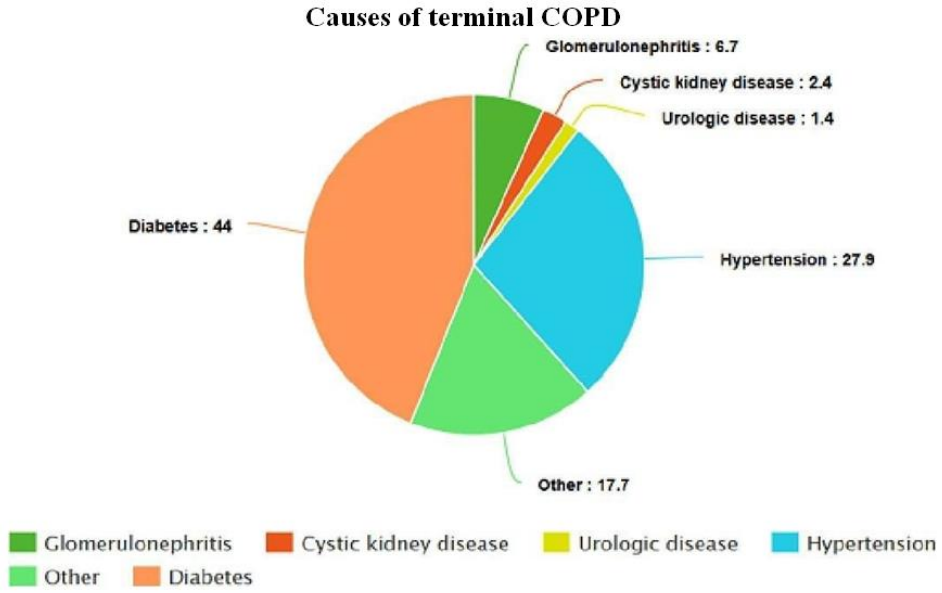
Chronic kidney failure (CKF) is currently considered to be one of the most important public health problems. NHANES studies have shown that the prevalence of chronic renal failure in the general population is about 5% [1].

The increase in the incidence of CKD is influenced by the aging of the population, typical for developed countries, which leads to an increase in the number of patients with vascular kidney damage [3]. A number of other factors also have a significant influence on the development and progression of CKD in the population, such as infectious diseases, taking a number of medications, alcohol, smoking, dietary habits and genetic characteristics of the population [2,4,5].

Only a small proportion of patients with CKD survive to replacement therapy, the cost of which is significant. At the same time, CKD is associated with a risk of increased cardiovascular mortality. One of the main links in this chain is the neurohumoral imbalance, which

is manifested by excessive activity of SAS, RAAS, endothelin (ET) system and other vasoconstrictor neurohumoral systems,

causing cell proliferation and remodeling of the heart, vessels, and kidneys [12].



CKD risk factors.

The main risk factors for CKD include diabetes mellitus and other metabolic disorders, presence of cardiovascular diseases, a number of autoimmune and infectious diseases, neoplasms, smoking and other bad habits, older age and male gender, presence of CKD in direct relatives, etc. (see figure). (see figure). Of particular importance are factors leading to the development of oligonephronia, i.e. the mismatch between the number of active nephrons and the needs of the body (see below): renal surgery, renal aplasia and hypoplasia on the one hand, and obesity on the other.[10]

Criteria for diagnosis of CKD:

1) presence of any markers of kidney damage:
   a) clinical and laboratory (primarily increased albuminuria/proteinuria), confirmed by repeat tests and **persisting for at least 3 months**;
   b) irreversible structural changes of the kidney detected by radiological examination (e.g., ultrasound) or morphological examination of a renal biopsy specimen;

and/or

2) **decrease in glomerular filtration rate** (GFR) to a level < 60 ml/min/1.73 m^2,persisting for three months or more.

Thus, the concept of CKD is composed of **two** components: signs kidney **damage** and **decreased GFR**.

of kidney condition at least once a year and active prophylaxis of CKD.

At the same time, a decrease in FFR to a level less than 60 ml/min/1.73 m² even in the complete absence of signs of renal damage and regardless of age not only indicates the presence of CKD, but also corresponds to its advanced stages (3-5). For example, a patient with a GFR of 55 ml/min/1.73 m² with absolutely normal urine tests and ultrasound picture of the kidneys will be diagnosed with stage 3A CKD.

Depending on the level of FFR, there are **5 stages** of CKD. Patients with stage 3 CKD are the most numerous in the population, at the same time this group is heterogeneous by the risk of cardiovascular complications, which increases with decreasing FFR. Therefore, it was proposed to divide stage 3 CKD into two sub-stages - A and B.

Table 1. Stages of chronic kidney disease.

Stage	Description	eGFR (mL/min)	Potential complications of reduced GFR (in alphabetical order)
1	Kidney damage with normal or ↑GFR	≥90	• Anemia, including functional iron deficiency • Blood pressure increases • Calcium absorption decreases • Dyslipidemia /heart failure/volume overload • Hyperkalemia • Hyperparathyroidism • Hyperphosphatemia • Left ventricular hypertrophy • Metabolic acidosis • Malnutrition potential (late)
2	Kidney damage with mild ↓GFR	60–89	
3	Moderate ↓GFR	30–59	
4	Severe ↓GFR	15–29	
5	Kidney failure	<15 or dialysis	

Source: Adapted from Identification, Evaluation and Management of Chronic Kidney Disease (www.health.gov.bc.ca/gpac/pdf/ckd.pdf)

Progression of CKD in the early stages is determined by the pathogenetic mechanism of the underlying kidney disease, further

Diagnosis of CKD depending on the state of renal function and the presence of damage markers

	Markers of kidney damage	
GFR ml/min /1.73m2	*There's*	*No*
≥ 90	HBP	Norm
60-89	HBP	Group risks
< 60	HBP	HBP

It is important to emphasize that at the beginning of CKD, renal function may remain intact for a long time, despite the presence of significant signs of damage. In normal or elevated GFR, as well as in patients with its initial decrease (60≤GFR<90 ml/min/1.73 m²), the presence of signs of renal damage is **a** prerequisite for the diagnosis of CKD.

GFR over 120 ml/min/1.73 m² is also considered an abnormality, since in diabetic and obese individuals it may reflect the phenomenon **of hyperfiltration**, i.e. impaired glomerular function caused by increased perfusion with the development of glomerular hypertension, which leads to their functional overload, damage with further sclerosis. However, to date, increased glomerular filtration is not included in the number of independent diagnostic criteria of CKD, but is considered a risk factor for its development. CKD in diabetes mellitus and obesity is said to be present only if there are markers of renal damage, primarily increased albuminuria.

The level of theSKF in the range of 60-89ml/min/1.73m² at **the absence of** signs of renal damage is referred to as "initial decrease in FFR," but **no** diagnosis of CKD **is made**. For those 65 years of age and older, this is considered a variant of the age norm. Individuals younger than this age are advised to monitor

Hemodynamic and metabolic factors begin to play an important role. The function impairment and infections, ureteral obstruction, pregnancy, allergic reactions aggravate.

Factors and mechanisms of progression:

I. Underlying kidney disease(inflammation, hyperglycemia, drug or other kidney damage).

II. Hemodynamic:

— arterial hypertension
— intracolumnar hypertension/hyperfiltration
— increased protein load
— anemia

III. Metabolic.

— proteinuria
— Hyperlipidemia
— hyperglycemia
— Hyperuricemia
— metabolic acidosis
— Hyperlipoperoxidation

IV. Intercurrent factors: infections, ureteral obstruction, pregnancy, allergic reactions, iatrogenic factors, hyponatremia, hypokalemia, hypovolemia, dehydration, blood loss.

The place of alltrombospine in the treatment of chronic kidney disease of nondiabetic etiology

The main goal of a nephroprotective strategy is to slow the progression or reverse the decline in renal function. This is the criterion used to evaluate the effectiveness of CKD treatment in clinical trials.

In practical nephrology, it is also possible to determine the effectiveness of therapy by slowing the rate of decline in GFR. A decrease in FFR by 5 ml/min/1.73 m2 per year or more is considered to be progressing. At the same time, the possibility of etiological treatment of CKD is very limited. In this regard, various schemes of pathogenetic treatment come to the fore,

of which antiplatelet therapy is an essential component. Such therapy improves blood coagulation properties, improves glomerular filtration and slows disease progression. Therefore, the search and development of new regimens with the use of modern antiplatelet agents, which include **alltrombosepine**, is an urgent need and constitutes the relevance of this study. [6,7,8]

Alltrombosepine is a highly selective antiaggregant. **Alltrombosepine** and its main metabolite GTB (2-hydroxy-4-trifluoromethylbenzoic acid) selectively inhibit platelet cyclooxygenase (COX-1), inhibit thromboxane A2 biosynthesis in platelets, preserving endothelial prostacyclin PGI2 biosynthesis. **Alltrombosepine** and GTB inhibit cAMP phosphodiesterase, increase the concentration of cAMP in platelets, inhibit calcium release and platelet aggregation, stimulate nitric oxide release by neutrophils, which enhances the anti-aggregant effect. The active metabolite **alltrombosepine has a** long half-life (35 hours).

Mechanism of action "**alltrombosepine**":

Enzyme	Role	The effect	ASK	Dipiridapier	Alltrom Bosepin
Vascular COX	Education just a little bit on the	Anti-Areagan	Iiti	—	No effect

Platelet COX	Education thromboxane A2	Aggregation	Inhibits	—	Inhibits
Platelet-associated cytoplasmic phosphodiesterase	Destruction of the cyAMP	Aggregation	No effect	Inhibits	Inhibits

Alltrombosepine when used does not increase the need for antihypertensive drugs in contrast to ASA. It does not decrease antihypertensive activity of ACE inhibitors, prescriptions in increasing dose do not cause allergic reactions in patients with asthma and primary ASA intolerance. Combination of **alltrombosepine** with moderate-acting anticoagulants leads to a 50% reduction of cardiovascular events, without increasing the risk of bleeding.

Recommended doses: 600mg once daily for AMI, Stroke/TIA, peripheral vascular disease including CKD stage III. 900mg (300 mg 3 times daily) after ACS, NS.

Taking all the above into account, we can conclude that to date there is not enough convincing data on the effectiveness of alltrombosepine as an aggregation component in therapy in stage III CKD patients, which requires further research in this direction.

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