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NEPHROPROTECTIVE EFFECT OF CARDILOPIN IN THE CASE OF PATIENTS WITH CHRONIC PYELONEPHRITIS

Under our observation there were 32 patients with chronic pyelonephritis accompanied with AH in age from 18 to 23 years (mean age was 20,5±1,7); there were 11 male and 21 female. Result of using Cardilopin during 3 month in the case of patients with chronic pyelonephritis and arterial hypertension give grounds to assert that preparation don't reduce blood supply in kidney and has positive effect on renal functions.
Keywords: *chronic pyelonephritis, arterial hypertension, nephroprotective effect*

On the opinion of many scientists, arterial hypertension (AH) is a risk factor in renal insuffiency development. Frequency of the AH in the case of terminal CRI according of the observation data of one group of the authors 85-90 percents, of another author's group approximate to 100 percent.

Chronic pyelonephritis (ChP) occupies one of the first places among the renal diseases that were accompanied by hypertonia. Frequency of arterial hypertension in adult with ChP amounts 50-70 percent: on the early stages it amounts 15-25 percent and 70 percent on the late stages [1].

Violation of the renal hemodynamics in the case of CP connected with interstice infiltration, hypostasis of renal tissue, its vessels compression that explained reversibility of AH on the early stages of disease development. As soon as fibrous processes in the renal interstice and perivascular sclerosis processes has been developed thickening and sclerosis of internal rare middle arterial coat takes place as well as hyalinosis of the arterioles. In V.V. Serov's opinion, these changes are the direct results of pyelonephritic process.

In healthy kidney glomerular filtration rate has been maintained on the relatively constant level due to vascular tension of the afferent arterioles that has been keeping up the blood circulation in wide rang of blood pressure values.

In the case of renal pathology, blood circulation self-regulation in kidneys brakes up in such way that even small increasing of the systemic pressure is passing to glomerule. They have been damaged by hydraulic force as soon as the glomerular pressure increases. This process accompanies with proteinuria and glomerulosclerosis aggravation and renal functions loss. On the top of it all mitogenic influence of the angitensin II, endotelin and other fibrogenic cytokines stimulates the proliferation of the mesangial cells. It provokes cirrhosis of the kidney, which worsen the renal function still more.

Arterial hypertension accelerates the process of renal functions loosing in the view of the last few decades investigations. Glomerular filtration rate in the case of renal disease decreases faster at patients with hypertension than with normal arterial pressure. Decreasing systemic blood pressure promoted glomerular damage limitation and renal functions loss delay in the case of simulated kidney pathology on animals. At the later time in multitudinous clinical researches was discovered that direct control of arterial pressure inhibits the renal pathology processes progressing in human organism too.

It becomes evidently that plasmatic proteins that had passed through glomerular membrane obtained the ability for active injuring of renal tissue, extend the inflammation and induce the renal fibrogenesis. "Nephrotoxic action of the proteinuria" is the term that may be used for description of this phenomenon [3, 8]. Nowadays proteinuria has been considered not only as the symptom of the chronic nephropaties but also as the progressing factor. Conception of the nephrotoxic influence of the proteinuria presumes direct participation of the some proteins fractions (albumin), which has been excreted with urine, in fibrogenesis processes induction in renal tissue particularly in tubular and interstice structures. Nephrotoxic effect of proteinuria revealed in influence to proximal canals epithelium cells acquired the ability for synthesis of inflammation hemokines, cytokines, proactive molecules and growth factors. Therefore, epithelium cell has been transforming into cell-inductor of tubular and interstice inflammation and fibrosis.

Remodeling of tubular interstice implies progressing of the interstice inflammation and fibrosis as one of the factors, which determines irreversible loss of the renal functions in the case of chronic pyelonephritis. Extent of the remodeling of tubular interstice correlates with rate of renal function's worsening and so this factor may be considered as independent herald of CRI progressing.

It makes no doubt that persistent and high AH and proteinuria is the factors of high risk in forming of renal insufficiency.

In connection with this fact, nephroprotective strategy anticipates the antihypertensional therapy that has been regarded as preventive measure against progressing of renal insufficiency. As a rule, compensation of the increased AP had entailed decreasing the level of excretion proteins with urine consequently it reduced nephrotoxic proteinuria.

Nowadays in nephrologic clinical practice RAAS effect's blocking drugs. Among them angitensin-converting enzyme inhibitors and angitensin II receptor's blockers and also calcium channels blockers. Experimental and clinical data verified that ACE inhibitors and calcium channels blockers retarded renal disease progressing to the greater extent than other groups of anthihypertensional medicine [5,6,9].

Nephroprotective effect of calcium antagonist's based on removal of the vasoconstriction of renal vessels and increasing of the renal blood circulation. Except it, calcium antagonists enlarged glomerular filtration rate; because of intrarenal reallocation of blood natriuresis increases, which supplements hypotensive effect. It is of importance that calcium antagonists were effective even in the case of patients with starting manifestation of the nephrosclerosis due to ability to suppressing of mesangium cell proliferation. There are other nephroprotective mechanisms of calcium antagonists. They are inhibition of renal hypertrophy and avoiding nephrocalcinosis due to decreasing of the overcharging of the renal parenchyma by calcium ions. It makes no doubt that CCB block vessel constrictive effect of endothelial cells' hormone – endotheline.

The aim of our investigation: was studying of the influence of the Cardilopin on teenager's renal functions with chronic pyelonephritis.

Materials and methods. Under our observation there were 32 patients with chronic pyelonephritis accompanied with AH in age from 18 to 23 years (mean age was 20,5±1,7); there were 11 male and 21 female.

Groups	Mean age	Sex		AH long standing	AH average
		male	female		
Control n-20	20,5±1,1	9	11	——	120,9±2,8

Experiment n-32	20,5±1,7	11	21	2,9	143,5±1,3

Diagnosis of HP had been verified on the clinical and laboratory information (general clinical analyses, biochemistry research that included blood creatinine, urine creatinine, urea investigation and Zymnicky and Reberg's probe) and instrumental investigation (excretory urography and USG of the kidneys).

As we know, the dihydropiridine derivates have tropism to vessels. They block the calcium channels in vessels heavily in 80 times in contrast to bensodiazepines and phenilalkilanimes.

Moreover they have selective tropism to defined sorts of the vessels. For example, Nisoldepine has tropism to coronary vessels and Nimodipine – to cerebral vessels. Such selective tropism inside the group determines difference of these effects.

There is scant information concerned Cardilopin in literature.

Cardilopin (Amlodipin) is the medication of the third generation of CCB produced Hungarian Pharmaceutical Company "EGIS". Cardilopin was prescribed in daily dose 5 mg during 3 month.

Evaluation criteria of nephroprotective effect were:

- influence on systemic AP,
- influence on the proteinuria,
- influence renal function's index (GFR by Cockloft-Golt formula)

$$GFR = \frac{(140 - \text{age, in years}) * \text{weight in kg}}{72 * \text{creatinine in blood serum, mg/dl} * 0.83 \text{ (for female)}}$$

Proteinuria had been determined using hemi quantitative methods of colorimetric analysis by test-bands and using sulfosalicylic acid. Then daily losses of protein were estimated. In single assay of the urine protein and creatinine content and their ratio were determined. Protein/creatinine ratio was near to daily excretion of protein with urine in g/daily on 1.73 square meter of the body surface. This ration is less than 0.2 in healthy people organism, in the case of renal pathology it hesitates within 0,2-3,5 [2, 11].

Results and discussions. CCB of the last generation are the prolonged medicals that's influence begins smooth and endures during 24 hours. Maximum effect the medical had on the second week. AP control has been carried out after 15 (I visiting), 30(II), 60 (III) and 90 (IV) days from the treatment beginning. Anthihypertensive effect of the Cardilopin is comparable with effect of the drugs from other groups but by the time of the second week and during the II and the III visiting AP level was reliable lower in the cases of the treatment by Cadilopin.

Proteinuria and GFR during the treatment process had reliable changed only to IV visiting (after 3 months). Taking under consideration that fact that AH not only damages kidneys but also steeply hastens renal insufficiency development. However, in clinical practice renal functions deterioration often passes unnoticed so that the efficient choice of the anthihypertensive therapy should be realized taking into consideration its influence on the renal functions. Fixed terminal points in case patients with renal functions insufficiency were mortality from CRI and necessitated haemodialysis and kidney transplantation. In order to value nephroprotective effect in brief space of time in the case of patients with the initial renal dysfunction's manifestation intermediate ("substitute") points had been used. They were microalbuminuria, proteinuria and glomerular filtration rate's decreasing [14]. CCB represent hypotensive drug group with high effectiveness.

In accordance of our investigation's results CCB of the last generation – Cardilopin not only decreases AP level but also decreasing proteinuria level without reducing GFR. The antihypertensive preparations, which preferred for treatment of the nephrogenic hypertension have to had the following properties:

- influence on the pathogenic mechanism of the AH development,
- don't decrease renal blood supply and oppress renal functions,
- to be able correct intraglomerular hypertension,
- don't impair the metabolism and have minimum of side effects.

ACE inhibitors and CCB satisfy these requirements largely.

Conclusions. As soon as AH is one of the progressing factors of the chronic renal insufficiency (CRI) of diverse etiology so that holding of efficient antihypertensive therapy in the case of patients with proteinuria and damaged renal functions is the most important problem of the treatment. At the same time, nephroprotective property of the preparations is the basic requirement to such therapy.

Alternative preparations are ACE inhibitors and CCB. In particular these two groups meet all requirements determined for antihypertensive preparations that intended for treatment of the nephrogenic arterial hypertension and all-important that they have nephroprotective characteristics. All CCB have nephroprotective effect, which determines by decreasing of the kidney hypertrophy, oppression of the metabolism and proliferation of the mesangium and therefore retards renal insufficiency progressing [12]. In according of literal finding Verapamil and Diltiazem decreases intrarenal hypertension while Nifedipine either don't influence on it or promote to increasing of the intraglomerular pressure [13]. There are no facts concerned Cardilopin on this point.

In connection with a fact, our result of using Cardilopin during 3 month in the case of patients with chronic pyelonephritis and arterial hypertension give grounds to assert that preparation don't reduce blood supply in kidney and has positive effect on renal functions.

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СОЗЫЛМАЛЫ ПИЕЛОНЕФРИТПЕН НАУҚАСТАРДА КАРДИОЛИПИННІҢ НЕФРОПРОТЕКТИВТІК ӘСЕРІ

Түйін: Мақалада 18-ден 23 жас аралығындағы (орта жасы 20,5±1,7) созылмалы пиелонефрит және артериалдық гипертониямен 32 пациенттің, оның ішінде 11 ер және 21 әйел, үш ай мерзімінде Кардиолипинді қолданудың зерттеу нәтижелері келтірілген. Кардиолипин артериалдық қан қысымының мақсатты деңгейіне жетуде және жасөспірімдер мен жас адамдарда бүйрек қызметіне оң ықпал етеді.
Түйінді сөздер: созылмалы пиелонефрит, артериалдық гипертония, нефропротективтік әсер.

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НЕФРОПРОТЕКТИВНЫЙ ЭФФЕКТ КАРДИОЛОПИНА
У БОЛЬНЫХ ХРОНИЧЕСКИМ ПИЕЛОНЕФРИТОМ

Резюме: В статье представлены результаты исследования эффективности использования Кардилопина в течение трех месяцев у 32 пациентов с хроническим пиелонефритом и артериальной гипертонией в возрасте от 18 до 23 лет (средний возраст 20,5±1,7); из них 11 мужчин и 21 женщин. Кардилопин эффективен в достижении целевых уровней АД и позитивно влияет на функции почек в юношеском и молодом возрасте.
Ключевые слова: хронический пиелонефрит, артериальная гипертензия, нефропротективный эффект.

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ПАТОФИЗИОЛОГИЧЕСКИЕ АСПЕКТЫ НЕКОТОРЫХ ФУНКЦИОНАЛЬНЫХ ЗАБОЛЕВАНИЙ ОРГАНОВ ПИЩЕВАРЕНИЯ

В статье приведены современные сведения о патофизиологических аспектах функциональных заболеваний органов пищеварения. Патофизиологическим субстратом клинических проявлений функциональных заболеваний органов пищеварения являются, прежде всего, психоневрологические, нейрогормональные, иммуновоспалительные механизмы, дальнейшее изучение которых открывает перспективы разработки дифференцированной коррекции, а главное — профилактики данной патологии.
***Ключевые слова**: функциональные заболевания органов пищеварения, причины, патогенез.*

Функциональные заболевания органов пищеварения (ФЗОП) являются весьма распространенными в клинической практике и чаще всего наблюдаются такие функциональные нарушения, как функциональная диспепсия (ФД) у 19-70% населения земного шара, 10-20% отмечают наличие симптомов, свойственных синдрому раздраженного кишечника (СРК), а у 7,6-20,7% жителей планеты имеются признаки дисфункции желчного пузыря и сфинктера Одди (ДЖП, ДСО) [1, 2]. Причем, за медицинской помощью обращаются всего 20-25% пациентов. При ФЗОП ни эндоскопические, ни гистологические исследования не выявляют морфологических изменений пищеварительного тракта. Актуальностью проблема ФЗОП обязана, прежде всего, гетерогенности этиопатофизиологического механизма развития, и, как следствие, - чрезвычайному многообразию и многозначительности существующих методов диагностики, лечения и профилактики при их недостаточной эффективности [2, 3]. Это приводит к существенному снижению качества жизни пациентов, сравнимое с таковым при тяжелых органических заболеваниях соответствующей локализации, а зачастую и более выраженное, а также к социоэкономическим потерям [4].

Несмотря на широкое и всестороннее изучение ФЗОП в настоящее время все еще имеется множество неясных моментов в их патогенезе. В качестве основных факторов риска развития ФЗОП выделяют: возраст, пол, хронический стресс и психопатизацию личности, неблагоприятные социальные условия, вредные привычки, погрешности в питании, ожирение, некоторые виды медикаментозной терапии, инфицированность хеликобактерной инфекцией, наследственность и др. [5, 6, 7, 8, 9, 10, 11, 12].

В возрастном аспекте ФЗОП чаще развиваются у лиц молодого возраста, что связывают со свойственной этому периоду гормональной перестройкой, динамичностью нервных процессов, периодом активной общественной деятельности и наличием множества других социобиологических факторов риска ФЗОП [5, 8].

Многие исследователи приводят данные о более частом развитии ФЗОП у женщин, в то время как другие авторы не придают гендерному фактору большого значения [2, 6].

Очевидна негативная роль таких вредных привычек, как курение, злоупотребление алкоголем, психостимуляторами в развитии ФЗОП [7, 8].