Fozinopril in the treatment of arterial hypertension

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The introduction of angiotensin-converting enzyme (ACE) inhibitors in the treatment of arterial hypertension (AH) was a significant milestone of the twentieth century. Pharmaceutical market has a large number of drugs belonging to this group, but, despite general mode of action, they differ in chemical structure, in prodrug nature, potency, pharmacokinetic profile, as well as additional pharmacological properties. For the clinicians, the inhibition strength of ACE in various organs and tissues is of great importance, which is related to their ability to inhibit ACE not only in plasma but also in tissues, primarily in the heart and kidneys, and in the vascular wall. One of the representatives of the last (third) generation and ACE is **fosinopril** (Fosicard) which is a prodrug and acts after absorption and transformation into the active metabolite–**fosinoprilat.**Exposure to transformation into an active metabolite not only in the liver, but also in the gastrointestinal mucosa makes the drug more rapid and “available to use” than other ACEI-metabolized drugs. In addition, due to the significant involvement of extrahepatic pathways of metabolic transformation, the pharmacokinetics of **fosinopril** are less dependent on the liver state, which is manifested in the stability of clinical effects from the first dose, regardless of associated gastrointestinal diseases, the patient's age, etc. Its great advantage is a balanced double way of excretion from the body: through the kidneys and through the gastrointestinal tract. Moreover, their involvement is approximately the same and they mutually compensate each other. Fosinoprilat has a high lipophilicity which facilitates the penetration of the drug through the cell membranes into all "interested" organs (heart, vessels, kidneys, lungs and adrenal glands) and allows effectively suppress the activity of not only the circulatory, but also tissue of renin-angiotensin-aldosterone system. The unique feature of fosinopril, which distinguishes it from other ACE inhibitors, is good tolerance. In this connection, it is widely used in the treatment of patients with metabolic syndrome [1,2].

The aim of our trial was to study the antihypertensive efficacy and safety of fosinopril in patients with AH.

Material and methods. Under our supervision there were 128 hypertensive patients between the ages of 47 and 71 years old (mean age 68.6 ± 1.3), of whom 68 were men (53.1%); women - 6 (46.9%). Inclusion criteria were primary arterial hypertension of 2 and 3 degrees, left ventricular hypertrophy on ECG, reduced ejection fraction of at least 40% according to Simpson on echocardiography, the absence of renal pathology (creatinine, urea) and liver (liver tests). Grade 2 AH was diagnosed in 94 (73.4%) and Grade 3 in 34 (26.6%). In 79 (61.7%) subjects AH combined with CAD, 17 (13.3%) observed patients was diagnosed with type 2 diabetes mellitus. Chronic heart failure (CHF) of I FC occurred in 38 (29.7%) and II FC in 90 (70.3%) cases according to NYHA. Fosinopril was administered in a dose of 10 mg and 20 mg. The initial dose was 10 mg 1 time per day, followed by an increase to 20 mg/day in case of insufficient antihypertensive efficacy. Duration of treatment was 8 weeks. All patients underwent 24-hour blood pressure monitoring (BPM). According to the BPM, the average systolic

blood pressure (SBP) and diastolic blood pressure (DBP) in day and night hours, heart rate (HR) were calculated. BP variability was assessed by the standard deviation of a varying value. To assess circadian variations of BP, the reduction degree of BP at night was calculated as the percentage ratio of the difference between the average daily and average night BP levels compared to the daily average. As indicators of pressure load, the percentage of hypertonic BP values was estimated at different times of the day (during wakefulness — more than 130/85 mm Hg., during sleep — more than 120/70 mm Hg.). The criteria for good antihypertensive efficacy of fosinopril was considered to be a reduction in DBP to 85 mm Hg and less and normalization of the average daily DBP according to the results of BPM; satisfactory – the reduction of DBP at 10 mm Hg and more, but not up to 89 mm Hg; unsatisfactory – a reduction in DBP of less than 10 mm Hg. Tolerability of the drug was considered good in the absence of side effects, satisfactory in the presence of side effects that did not require discontinuation of the drug, unsatisfactory if the side effects that arose necessitated discontinuation of the drug.

Exclusion criteria were: COPD, bronchial asthma, severe hepatic and renal insufficiency, pregnancy, lactation, solitary kidney, renal artery stenosis, allergic to ACE inhibitors, a history of angioedema.

Outcomes and discussion. All patients received complex therapy, which included antihypertensive therapy (fosinopril), lipid-lowering (statins), and, if necessary, diuretics, nitrates and cardioprotectors. The average dose of fosinopril was 16.5 ± 1.2 mg per day. During therapy with fosinopril, there is a significant decrease in BP of both systolic (152.6 ± 1.8 versus baseline 178.5 ± 2.3 mmHg) and diastolic (80.8 ± 1.5 versus baseline 95.2 ± 1.6). During therapy with fosinopril in 2 weeks, the antihypertensive effect was noted in 26 (20.3%) patients: in 15 (11.7%) BP returned to normal, in 11 (8.6%) BP decreased by more than 10% from baseline. Lack of antihypertensive therapy efficacy was observed in 102 (79.7%) patients, which was the reason for increasing the initial dose of fosinopril. After 8 weeks of fosinopril monotherapy, normalization of DBP was noted in 97 (75.8%) patients. The improvement of daily BP profile under the influence of treatment with ACEI is noted by most researchers. It has been proven that, overproduction of renin and related biologically active substances, primarily angiotensin II, leads not only to arterial hypertension, but also to end-organ damage not directly related to an increase in blood pressure, being a major factor in the progression of AH and its complications, remodeling of the heart and blood vessels. Fosinopril has a strong evidence base for efficacy and tolerability and is recommended as one of the front-line therapy for the treatment of CHF. According to the results of our observation, fosinopril demonstrated good clinical efficacy in patients with CHF. During treatment with fosinopril, the functional class of CHF significantly decreased, shortness of breath decreased, the frequency of hospitalizations for decompensated CHF decreased. Important additional characteristics of fosinopril are good tolerability, organoprotective properties allow recommending the earliest and wider prescription of fosinopril for the treatment of both AH and chronic HF.

Three patients at the maximum dose had a dry cough, which required discontinuation of the drug. Side effects of the drug at an average dose of 10 mg we did not noted. According to the literature, ACE inhibitors are not only effective antihypertensive agents, but also to the same extent as diuretics and β-adrenergic blocking agents, reduce cardiovascular morbidity and mortality in patients with AH.

Thus, the use of fosinopril (by Viva Pharm) in patients with AH and CHF, including with the metabolic syndrome, has a rather apparent antihypertensive effect, while demonstrating a high level of safety.

References:

1. Management algorithms for patients with arterial hypertension. All-Russian Public Organization “Assistance in the Prevention and Treatment of Arterial Hypertension. Antihypertensive League”. St. Petersburg, 2015. First edition. 29p.
2. Recommendations ESH / ESC 2013 for the treatment of arterial hypertension (translation from English into Russian by Russian Medical Society for Arterial Hypertension. 2013 //Journal of Hypertension 2013; 31(7):1281-1357