

COMPARATIVE EFFECTIVENESS OF LONG-TERM MANAGEMENT OF HYPERTENSIVES WITH FIXED COMBINATIONS OF ANTIHYPERTENSIVE MEDICINES

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Background. An application of fixed combinations of antihypertensive medicines (FCAMs) represents a viable alternative to usage of 2 or more antihypertensive drugs separately. In Ukraine FCAMs have been widely used for 40 years but it has not been the case in most Western countries. Three years ago we asked more than 100 Ukrainian specialists in internal diseases and cardiologists to indicate which antihypertensive drugs they prescribed most often. Forty six per cent of the interrogated answered that they preferred ACE inhibitors and only 11% of the physicians mentioned FCAMs. In some months we conducted an investigation entitled "Antihypertensive drugs in families at home". From all classes of antihypertensives FCAMs were found most often (21.5%) in families of hypertensive patients at home. In most cases FCAMs were the cheapest ones at Ukrainian pharmaceutical market.

The **aim** of the study was to estimate an effectiveness of management of patients with essential hypertension (EH) for 6 months' period with different FCAMs namely adelphane (reserpine 0.1 mg + dihydralazine 10 mg, Ciba-Geygi, India), tenoric (atenolol 100 mg + chlortalidone 25 mg, IPCA, India), enafrilum (enalapril 10 mg + hydrochlorothiazide 12.5 mg, Stirol, Ukraine).

We planned to randomise 144 patients using envelopes. During randomisation period some patients from different groups refused to take medicines just after opening envelopes, but they agreed to participate in the investigation (i.e. to fulfil probes with graded physical load, etc.). Randomisation was stopped prematurely because registration of adelphane in Ukraine came to an end and there were limited quantity of that drug in local drug store to fulfil the investigation. As a result, the study was conducted among 151 workers and employees of Kharkiv tractor factory aged 30-60 years with EH I-III grades and no comorbidities. Firstly adelphane, tenoric and enafrilum groups consisted of 39, 43 and 36 patients correspondingly. Control group was formed from 33 people refused from taking antihypertensive medicines or took them from time to time. Blood pressure (BP) was measured in office from 9 a.m. till 10 a.m. every day during first 14 days of treatment and after that in 1 month and 6 months after starting treatment. Within first month of treatment 8 patients from adelphane group, 5 patients from tenoric group and 7 patients from enafrilum group were excluded from the study due to adverse reactions and in cases of refusing to continue treatment (differences in amount of adverse reactions between groups were non significant). Finally, the 6 months' period of treatment/observation concluded 131 patients.

After 6 months' treatment/observation goal levels of blood pressure (BP) were achieved in 71, 89.5 and 86.2 % of people from adelphane, tenoric and enafrilum groups respectively and no person from control group. Mean decrease of systolic BP was $21.7 \pm 2.0\%$ in tenoric group, $22.1 \pm 2.2\%$ in enafrilum group and was significantly greater in both groups then in adelphane group ($15.3 \pm 1.8\%$, $p < 0.05$ in both cases). Similar results were obtained in relation to diastolic BP: $17.4 \pm 2.2\%$, $18.4 \pm 2.4\%$ and $13.6 \pm 2.0\%$ correspondingly ($p < 0.05$ as comparing with adelphane group).

Left ventricular mass index decreased only in tenoric and enafrilum groups (from 132.0 ± 9.2 to 111.3 ± 6.8 g/m² and from 131.6 ± 10.6 to 107.8 ± 6.8 g/m², respectively, $p < 0.05$ in both cases).

Results of detection of heart rate variability evidenced an increase of total power of heart rhythm spectrum in all groups of patients receiving FCAMs. In patients from tenoric group that was achieved predominantly due to an increase in parasympathetic tone whereas in patients from enafrilum group the same result was achieved predominantly due to an increase in sympathetic tone.

After 6 months' treatment with FCAMs there was an increase in tolerability of physical load in all groups of patients as evidenced by the method of graded physical load (veloergometry). Common work increased in all groups of patients receiving treatment and decreased in control group. Threshold load power increased in tenoric and enafrilum groups and decreased in control group.

In conclusion, if hypertensive patient refuses to take medicines, in 6 months it will lead to worsening in tolerability of physical load. From FCAMs tested the most effective ones were tenoric and enafrilum. Treatment with the least effective FCAM is better than no treatment.