Pharmacodynamics of Kardos Administered as Monotherapy and in Combination with Hypothiazide and Enalapril in Grade I-II Arterial Hypertension

V. I. Petrov, O. I. Epshtein, S. A. Sergeeva, P. A. Bakumov, E. A. Zernyukova, Yu. A. Zabolotneva, M. V. Kachanova, and L. B. Sabanov

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 148, Suppl. 1, pp. 83-84, August, 2009
Original article submitted August 1, 2008

Therapy with kardos produced an antiihypertensve effect in patients with grade I-II arterial hypertension. This antiihypertensve effect was considerably potentiated, when kardos was administered in combination with enalapril.

Key Words: *arterial hypertension; kardos; pharmacodynamics*

Essential hypertension is one of the leading causes of morbidity, disability, and mortality in humans and is an important risk factor of myocardial infarction, stroke, and heart failure [5]. In the Russian Federation, the prevalence of this pathology in the general population is about 20% and in individuals above 65 years more than 50%; the incidence of this disease in men and women is 39.2 and 41.1%, respectively [3].

Despite a wide armory of antihypertensive preparations, effective control of arterial hypertension (AH) is still a pressing problem. For instance, the percentage of patients effectively treated for AH in USA, Finland, and Canada is 27.4, 20.5, and 16.0%, respectively [1], while in Russia only 5.7% men and 17.5% women receive effective antihypertensive therapy [2].

Low efficiency and poor tolerability of antihypertensive drugs are the main causes of inadequate blood pressure (BP) control. Treatment compliance is an important factor for improving the efficiency of antihypertensive therapy. The compliance is influenced by complex schemes of drug intake, their high price, and side effects [1].

The history of pharmacology showed that the search for principally new original approaches is required for the creation of effective and safe drugs [4]. In light of this, the use of ultralow doses in therapeutic practice is a promising trend. The use of antibodies to known markers with well-studied activity considerably facilitates the process of pharmacological screening. Ultralow doses of antibodies do not cause addiction. Antibodies to endogenous bioactive substances reproduce their activity in a modified form, which enables fine and integral regulation of the pathological condition [4]. In this context, it is reasonable to study the effect of preparations on the basis of ultralow doses of antibodies in the treatment of AH.

Here we evaluated the antihypertensive effect, safety, and tolerability of kardos, a preparation containing ultralow doses of antibodies to C-terminal fragment of AT_1 receptor of angiotensin II, in patients with grade I-II AH.

MATERIALS AND METHODS

The study included 63 patients with AH (34 men and 29 women) with AH with diastolic BP (DBP) 90-109

Department of Clinical Pharmacology and Allergology with a Course of Intensive Care, Faculty of Continuous Medical Education, Volgograd Medical University, Federal Agency for Health Care and Social Development

0007-4888/09/1482-0335

TABLE 1. Results of 24-h BP monitoring and Echocardiography in Groups of Patients before and after 6-Week Therapy (*M*±*m*)

Parameter		Initial	After 6-week therapy	% of initial
Group 1	SBP, mm Hg	150.1±2.9	139.3±2.3*	-7.1
	DBP, mm Hg	91.4±1.7	85.5±1.5	-6.5
	HR, bpm	74.0±0.8	69.5±1.5	-6.1
Group 2	SBP, mm Hg	151.2±4.5	136.0±3.8*	-10.1
	DBP, mm Hg	91.6±2.2	80.7±2.4*	-11.9
	HR, bpm	77.7±4.9	76.0±5.1	-2.2
Group 3	SBP, mm Hg	153.0±2.6	145.0±2.6	-5.3
	DBP, mm Hg	98.8±1.5	93.2±1.2^{+o}	-5.7
	HR, bpm	73.9±1.1	73.9±2.4	0

Note. *p<0.05 compared to: *initial values, $^{+}$group 1, ^{o}group 2.

mm Hg and systolic BP (SBP) <179 mm Hg, in whom 24-h BP monitoring revealed daily average BP>135/85 mm Hg. The mean age of patients was 52.1±3.6 years; mean history of the disease was 11.8±4.3 years.

Group 1 patients received kardos (1 tablet 3 times a day), group 2 patients received kardos (1 tablet 3 times a day) and enalapril (ednyt, Gedeon Richter) in a dose of 5 mg 2 times a day; group 3 patients received enalapril (ednyt, Gedeon Richter) in a dose of 5 mg 2 times a day. After 4 weeks, hypothiazide (Sanofi-Aventis) was prescribed to all patients in a dose of 25 mg after overnight fast. The observation and therapy was continued for 6 weeks.

The efficiency of preparations was evaluated by the results of 24-h BP monitoring after completion of the course. The safety of the treatment was evaluated by the incidence of undesirable effects, their severity, and relation with the prescribed treatment. The levels of glycemia, creatinine, and potassium in blood serum were measured before and after treatment. Routine laboratory tests were performed.

RESULTS

According to the results of 24-h BP monitoring (Table 1), daily average values of SBP and DBP significantly decreased in group 1, which led to a decrease in SBP and DBP area indexes (by 11.2 and 28.0%, respectively). In group 2, SBP and DBP also significantly decreased; SBP and DBP area indexes decreased by 20.1 and 32.4%, respectively. In group 3, the decrease in SBP and DBP was less pronounced. These changes led to a decrease in SBP area index by 10.9% and more significant decrease in DBP area index by 21.5%.

Biochemical parameters of the blood reflecting drug safety remained unchanged. No undesirable effects were noted in groups 1 and 2. In group 3, undesirable effects were observed in 2 patients (1 patient complained of dry cough and 1 patient had tickling in his throat); these undesirable events required no changes in the therapy.

Thus, kardos therapy in AH is effective and absolutely safe. Combined administration of kardos and enalapril led to significant potentiation of the antihypertensive effect, which probably attests to a synergism between these preparations. Kardos can be used in the treatment of patients with grade I-II AH in the form of monotherapy and in combination with diuretics and angiotensin-converting enzyme inhibitors.

REFERENCES

1. M. V. Leonova and M. V. Myasoedova, *Ros. Kardiol. Zh*., No. 2, 66-71 (2003).
2. R. G. Oganov, *Kachestvo Zhizni. Meditsina,* No. 2, 10-15 (2003).
3. *Prophylactics, Diagnostics, and Therapy of Essential Arterial Hypertension in the Russian Federation.* First Expert Report of Scientific Society for Arterial Hypertension, All-Russian Cardiological Society and Interdepartmental Council on Cardiovalcular Diseases (DAH 1). *Klin. Farmakol. Ter.,* **9**, No. 3, 5-30 (2000).
4. O. I. Epshtein, A. V. Martyushev, D. R. Kudryashova*, et al., Byull. Eksp. Biol. Med*., Suppl. 4, 69-72 (2002).
5. A. V. Chobanian, G. L. Barkis, H. R. Black, *et al., JAMA*, **289**, No. 19, 2560-2572 (2003).