

The influence of arbidol on lipid peroxidation in diabetic patients

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The important role of free radical lipid peroxidation (LPO) on the pathogenesis of diabetes and angiopathy has already been established. In patients with types I and II diabetes, an increase of LPO has been seen [1, 3, 4, 11, 14, 17]. The breakdown of antioxidant defenses which diabetes causes can play a large role in diabetes complications [13]. Even in the early stages of the disease a rise in LPO occurs from a compensatory rise in the enzyme chain of the antioxidant defense system [10].

The “LPO/antioxidant system” is normally balanced and functions on the principle of negative feedback; a constant level of antioxidant activity is one of the main indicators of homeostasis [12]. Diabetes-related deficits in the antioxidant defense system lead to induction of LPO, the toxic products of which bring about changes in the lipid/protein complexes and in enzyme and macromolecule membrane stability, and interference with cell metabolism [16].

The administration of drugs with antioxidant action in the course of therapy for diabetes and its complications has a protective effect, limiting the intensity of LPO. A number of pharmacological preparations, such as anti-inflammatory drugs [5], spasmolytics [26], antiseptics, antihistamines, vitamins [22], as well as several antiviral drugs [20], have this capability.

There has been increased interest in a highly effective antiviral preparation (arbidol 1 – methyl – 2 – phenylmethyl – 3 – carboethoxyl – 4 – dimetilaminomethyl – 5 – oxy – 6 – bromo-hydrochloride monohydrate), which also has immuno-modulating properties [30]. Arbidol’s antioxidant properties [7] can act as a sort of trap against the peroxidation mechanism [24].

The goal of the present study was to examine the influence of arbidol on LPO, and the effects of antioxidant defense for type II diabetes patients.

Research methods

The study included 31 people from 39 to 70 years of age – 21 women and 10 men. Their length of illness with diabetes ranged from 1 to 20 years. All of the patients were undergoing treatment with blood-sugar lowering medications; these dosages were not changed during the course of the experiments. All of the patients had shown symptoms of peripheral neuropathy without trophic changes. Six patients had manifested microalbuminuria, and five had stage I retinopathy; one had stage II retinopathy. The patients received arbidol 0.1 gram (one tablet) per day for six weeks. Research was conducted before and after the arbidol therapy.

The following factors were measured: body mass index (BMI); glycosylated hemoglobin level (HbA1C); sensitivity to vibration, total cholesterol level (TC); triglycerides (TRG); high density lipoproteins (HDL) and low density lipoproteins (LDL); blood-activated recalcification time (BART); partial thromboplastin time (PTT); prothrombin index (PT/INR) and thrombin time (TT); thrombo-elastography; fibrinogen level; and fibrinolytic activity. LPO intensity was assessed by measuring the amount of malonyl dialdehyde (MDA), superoxide dismutase activity (SOD), and glutathione peroxidase (GP). We also worked under the consultation of an oculist-endocrinologist.

Determination of biochemical indicators in blood serum was conducted on Abbot Spectrum equipment (“Abbot Laboratories,” USA) in the Russian Academy of Medical Science endocrinology laboratories; determination of hemostatic indicators was done on a coagulometer from “Schnitger und Gross” (Germany) and thromboelastograph from “Hellige” (Germany). MDA concentration was determined according to thiobarbituric acid reaction [19]; SOD activity was measured by reaction formation of nitrogen tetrazole; erythrocyte GP activity was determined by the method of Paglia and Valentine [33].

Results and Discussion

In the diabetes patients who received arbidol, we observed a highly verifiable ($p < 0.001$) lowering of the MDA level in comparison with the initial data (Table 1), and a similarly accurate ($p < 0.001$) increase in SOD level. In earlier studies it was shown that arbidol’s coefficient of inhibition of chemiluminescence induced by bivalent iron ions in egg yolk lipoproteins is 54 times higher than the analogous coefficient of the antioxidant amoxipin [7]. The presence of antioxidant properties in arbidol is also confirmed by the drug’s metabolism in the body with corresponding primary and secondary oxidation products with sulfur atoms [24]. Taking into account the link of intracellular SOD to interferon defense, it is possible to speak of the importance of the connection of interferon-inducing and antioxidant activity within the active therapeutic mechanism of the drug [8, 32]. The initially lowered SOD activity in diabetic patients (normally 164-240 u/ml) normalizes after a course of arbidol. GP activity does not undergo changes that we have been able to establish conclusively. Arbidol has been shown to have a positive influence on markers of lipid exchange: an increase in HDL level, and a decrease in content of aggressive LDL’s and TRG (Table 2) and glycosylated hemoglobin.

Table 1: LPO and antioxidant system markers in diabetes type II patients receiving arbidol

Time of study	MDA, n mole/ml	SOD, u/ml	GP, u/l
Before the beginning of arbidol administration	6.08 +/- 0.20	148.74 +/- 8.04	6285.87 +/- 465.95
Six weeks after the beginning of arbidol administration	4.15 +/- 0.25	184.66 +/- 6.83	6012.90 +/- 326.32

Of specific interest is the lowering of the prothrombin index by 4%, and also the statistically significant ($p < 0.05$) increase of thrombin time and decrease of fibrinogen level. Activation of the LPO process and lowering of antioxidant activity enables the destruction of vasculo-thrombocytic, coagulant, and fibrinolytic links of hemostasis, and an increased aggregation of formed elements of the blood [15, 25, 26, 28, 6], which in turn leads to an increase of blood viscosity, thickening of the base membranes of vessel walls, destruction of rheological blood properties, and worsening of microcirculation [18, 23, 26, 29, 30].

Table 2: Arbidol's effects on basic biochemical markers in blood of diabetes type II patients

Time of study	TC, mmol/ml	TRG, mmol/l	HDL, mmol/l	LDL, mmol/l	HbA1c, %
Before beginning of arbidol administration	6.14 +/- 0.21	2.96 +/- 0.35	1.12 +/- 0.04	3.76 +/- 0.18	7.89 +/- 0.26
6 weeks after beginning of administration	6.03 +/- 0.32	2.32 +/- 0.35	1.26 +/- 0.05	3.43 +/- 0.20	7.34 +/- 0.21

Analysis of the effects of arbidol on the dynamics of vascular changes in five patients with nonproliferative-stage retinopathy showed a stabilization of the process, and normalization of capillary caliber. 87% of the patients displayed an improvement in sensitivity to vibration; and many of the patients noted a lessening of leg pains and parasthesias. One patient out of the 31 experienced epigastric discomfort, possibly not related to taking the drug [9]. At present, arbidol is not noted to have contraindications to administration [2, 21, 23].

Conclusions

1. In diabetes type II patients who took arbidol 0.1 g per day for 6 weeks, there was shown a lowering of activation of the LPO process and a strengthening of the antioxidant defense system.
2. On the basis of arbidol administration, a tendency has been shown toward normalization of lipid exchange markers and the system of homeostasis.