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PATHOLOGICAL PHYSIOLOGY AND GENERAL PATHOLOGY

Effect of Cod-Liver Oil with a High Content of Polyunsaturated Fatty Acids (Eikonol) on Myogenic Tone and Vasoconstrictory and Vasodilatatory Responses of Isolated rat Caudal Artery

F. Z. Meerson and S. Yu. Mashina

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Recent studies have shown that a diet enriched with unsaturated fatty acids, eicosapentaenoic (20:5 *n*=3) and docosahexaenoic (22:6 *n*=3) possesses an antiarrhythmic effect and reduces the morbidity rate in acute myocardial infarction [3,8]. The antiatherogenic [5,10] and hypotensive [7,9] effects of this diet have been demonstrated. However, the influence of a diet enriched with polyunsaturated fatty acids (PUFA) and, in particular, with the nutritional supplement eikonol, containing a high concentration of the indicated PUFA, on the properties of resistive arteries, the tone and reactivity of which directly determine the blood pressure, has not yet been investigated.

The aim of the present study was to assess the influence of a PUFA-enriched diet (with the nutritional supplement eikonol added) on myogenic tone, α– and β –reactivity, and the extent of the endothelium-dependent dilatation of the isolated rat resistive artery.

MATERIALS AND METHODS

Male Wistar rats weighing 300 g were used for the experiments. The animals were fed standard

Research Institute of General Pathology and Pathophysiology, Russian Academy of Medical Sciences, Moscow
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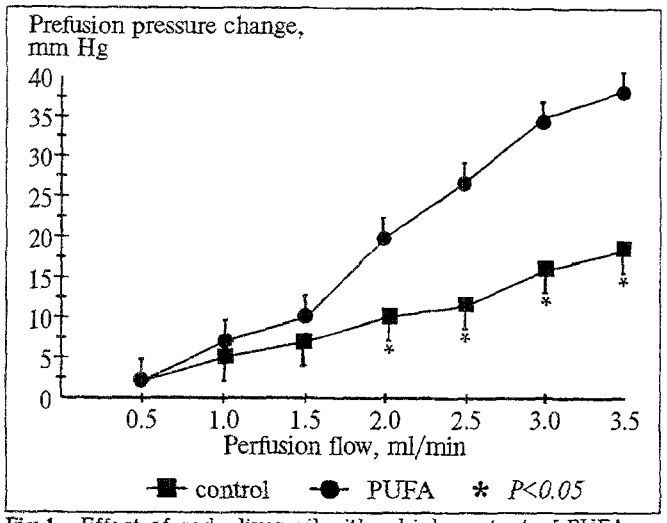

Fig.1. Effect of cod–liver oil with a high content of PUFA on myogenic tone of isolated rat caudal artery.

chow supplemented with 1.3 g/day eikonol for 25 days. Eikonol (TU 400 SP"A"–1145–118–90, Trinita, Moscow), according to Trinita information, contains up to 18.1% oleic, 18.2% linoleic, and 18.3% linolenoic acids together with saturated and monounsaturated fatty acids. The degree of unsaturation of eikonol (iodine number) reaches 190. A segment about 8 mm long obtained from the proximal part of the caudal artery of decapitated rats was cannulated at both ends and then placed in the incubation chamber. The segment was perfused with Krebs-Henseleit solution at a constant flow rate (2 ml/min) [1], the solution temperature being maintained at 37°C. The reaction of the perfused vessel was estimated by measuring the changes in perfusion pressure detected with a Statham transducer (USA) and recorded with a KSP-4 voltage meter. In a pharmacological study of the vascular segment's adrenergic reactivity the following agents were used: norepinephrine (Serva, Germany) in the concentrations 5×10^{-8}, 10^{-7}, 5×10^{-7}, 10^{-6} g/ml, phenylephrine (Serva, Germany) 10^{-7}, 5×10^{-7}, 10^{-6}, 5×10^{-6} g/ml, isoproterenol (Sigma, USA) 10^{-7} g/ml, and acetylcholine 10^{-7} g/ml. The vasodilatory responses to acetylcholine and isoproterenol were studied using norepinephrine-precontracted vessel segments. The norepinephrine concentration chosen was able to cause a constrictory reaction approximately to 100 mm Hg. The myogenic tone of the isolated caudal artery was estimated by the pressure–perfusion flow dependence curve and was expressed as mm Hg for the respective flow. In essence, this parameter reflected the dilatability of the resistive artery, removed from neuro-endocrinological influences of the integral organism. Rigidity of the artery at the given perfusion flow results in a pressure rise, whereas a high dilatability of the arterial wall produces the opposite result. The data were statistically analyzed using Student's t test.

RESULTS

The curves in Fig. 1 reflect the dynamics of the pressure rise for the increasing perfusion flow and clearly demonstrate that the pressure in the resistive artery of animals which received an excess of PUFA with eikonol supplement was more than twice as low as in the control. In other words, the artery became more dilatable as a result of the long–term treatment with PUFA (in the form of eikonol). This indicates a reduction of the resistive artery myogenic tone as a result of the long-term influence of a PUFA–enriched diet. The reduction may be connected with a decrease in the number of actin-myosin bridges remaining after dilatation due to the realization of two prerequisites:

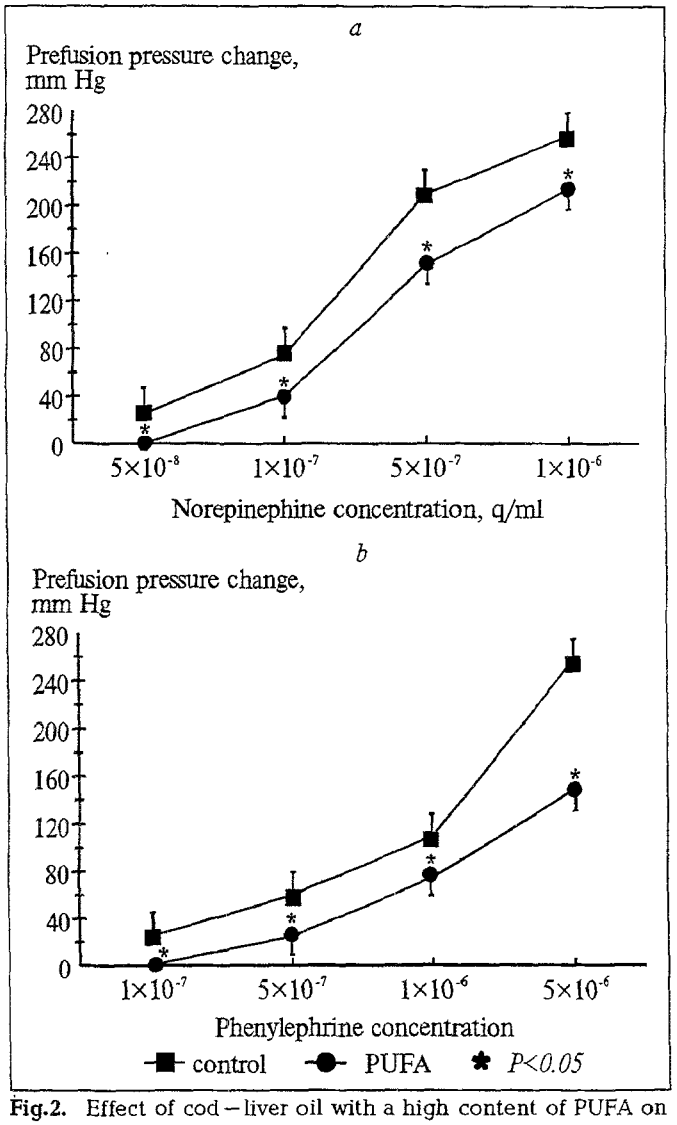

Fig.2. Effect of cod–liver oil with a high content of PUFA on constrictory reactions of isolated rat caudal artery induced by norepinephrine (*a*) and phenylephrine (*b*).

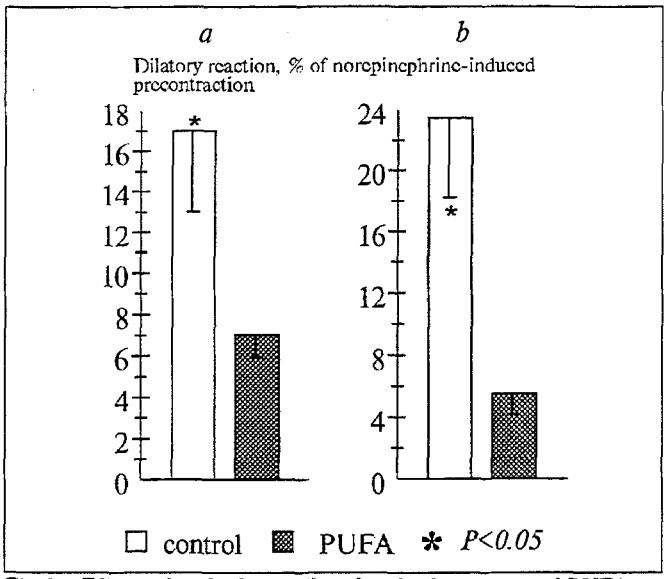

Fig.3. Effect of cod–liver oil with a high content of PUFA on dilatatory reactions of isolated rat caudal artery induced by isoproterenol (*a*) and acetylcholine (*b*).

first, a higher ATP concentration for elimination of actin-myosin bridges and, second, a more effective calcium removal by the membrane pump. A major role of both these factors in smooth muscle relaxation has been established [3,4]. However, this assumption needs to be verified regarding PUFA excess as a factor operating under our particular conditions.

An excess of PUFA in the diet and, consequently, in the cell membrane lipid bilayer, where both the oxidative phosphorylation and ion transport enzymes are located, made the resistive artery walls far more dilatable. Evidently, this factor may play a role in the antihypertensive effect of PUFA.

The curves illustrating the effect of PUFA excess on α– and β–reactivity are presented in Fig. 2, *a, b*. It follows from the figure that pressor responses to both the selective adrenoreceptor agonist norepinephrine and the α_1-agonist phenylephrine were decreased in the animals receiving PUFA excess. This might be related to a reduction of the myogenic tone of the isolated artery as well as to a decrease in adrenoreceptor affinity to agonists. This problem deserves special investigation, but regardless of any particular solution, the regulation of constrictory reactions should be considered as a possible component of the antihypertensive effect of PUFA.

The data shown in Fig.3 indicate that in the animals which received a PUFA excess the dilatatory effect of isoproterenol and the endothelium-dependent relaxation induced by acetylcholine are markedly increased. These effects should be considered highly significant, since in animals fed a PUFA–enriched diet they were exhibited against the background of a markedly reduced myogenic tone. For acetylcholine treatment, the dilatatory effect was increased threefold versus the control. This may indicate that the release of the endothelium–dependent relaxation factor (EDRF) is more pronounced in animals receiving a PUFA–enriched diet. This suggestion is consistent with the evidence that PUFA is a substrate for lipid peroxidation and, in turn, free–radical oxidation is an obligatory step in both EDRF and,ultimately, nitric oxide formation [2].

Generally, the data obtained suggest that a PUFA excess markedly decreases both the myogenic tone of resistive arteries and the constrictory effects of adrenergic agonists simultaneously with an increase in the dilatatory effects and, especially, endothelium-dependent relaxation. This complex of unidirectional shifts may play a significant role in the antihypertensive effect of a PUFA–enriched diet.

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