EFFECT OF CHOLESTEROL AND MONOIODOACETATE ON HEXOSAMINE-SYNTHETASE ACTIVITY AND HEXOSAMINE AND HEXURONIC ACID CONTENT IN THE AORTIC WALL

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In experimental hypercholesteremia and during prolonged administration of monoiodoacetate the intensity of hexosamine biosynthesis and the concentration of hexosamines and hexuronic acids in the aortic wall of rabbits are increased, reflecting the connection between these changes and disturbances of carbohydrate metabolism.

In atherosclerosis there is a marked increase in the content of mucopolysaccharides in the vessel walls and a disturbance of their metabolism [1, 5]. The cause of these changes has not yet been established. It has been shown [4, 6, 7] that experimental atherosclerosis induced by cholesterol is accompanied by inhibition of glycolysis and, in particular, by the suppression of the activity of phosphoglyceraldehyde dehydrogenase (1.2.1.12). On the other hand, deliberate inhibition of this enzyme by monoiodoacetate causes pathological changes in the aortic wall characteristic of experimental atherosclerosis [1, 9]. Since the metabolism of hexosamines and hexuronic acids is closely linked with hexosphosphate metabolism it can be postulated that the decrease in glycolytic activity would promote the biosynthesis of the structural components of mucopolysaccharides.

It was accordingly decided to make a comparative study of the intensity of hexosamine biosynthesis and the concentrations of hexosamines and hexuronic acids in the aortic wall in rabbits with experimental hypercholesteremia or receiving prolonged injections of monoiodoacetate solution.

EXPERIMENTAL METHOD

Experiments were carried out on rabbits weighing 2.5-3 kg receiving cholesterol (0.5 g/kg) daily for 3 months with root vegetables (series I), or monoiodoacetic acid (7 mg/kg) as the neutralized solution

TABLE 1. Intensity of Hexosamine Biosynthesis and Concentrations of Hexosamines and Hexuronic Acids (in μg/mg protein) in Aortic Wall of Rabbits during Prolonged Administration of Cholesterol and Monoiodoacetate (M ± m)

Index studied	Control (n = 14)	Admin. of cholesterol (n = 10)	P	In % of control	Admin. of monoiodoacetate (n = 10)	P	In % of control
HASA . . .	0,264±0,01	0,361±0,02	<0,011	136,7	0,353±0,02	<0,001	133,6
HA	7,96±0,04	14,9±0,13	<0,001	187,1	14,1±0,20	<0,001	181,9
HU	6,98±0,05	12,7±0,11	<0,001	180,5	8,80±0,68	<0,012	126,1

Legend: HASA – hexosamine-synthetase activity expressed as the quantity of hexosamines; HA – hexosamines; HU – hexuronic acids; n – number of investigations.

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alternately by subcutaneous and intravenous injection (series II). The intensity of hexosamine biosynthesis was studied by the method of Haruki and Kirk [14] in aortic tissue extracts obtained by extracting homogenates with 0.067 M phosphate buffer, pH 7.4, for 30 min. Hexosamines were determined by the method of Elson and Morgan [12] in the modification of Gatt and Berman [13], and hexuronic acids by Dische's method [11] in Slutskii's modification [10]. The results were expressed in μg/mg aortic tissue protein.

EXPERIMENTAL RESULTS AND DISCUSSION

The investigations showed (Table 1) that the intensity of hexosamine biosynthesis in the aorta of the experimental rabbits was increased by 36.7% by the action of cholesterol and by 33.6% by that of monoiodoacetate.

Corresponding to the increased biosynthesis of the hexosamines an increase of 87.1% in their concentration in the aortic tissue was found as a result of the action of cholesterol and an increase of 81.9% by the action of monoiodoacetate. At the same time the concentration of hexuronic acids was increased in experimental hypercholesteremia and during administration of monoiodoacetate by 80.5 and 26.1%, respectively.

Both experimental hypercholesteremia and the action of monoiodoacetate are known to be accompanied by stimulation of the pentose phosphate cycle. On the other hand, the direct precursors for the biosynthesis of hexosamines and hexuronic acids, and also for the conversion of carbohydrates by the glycolytic and pentose phosphate pathways are hexose phosphates. This suggests that the inhibition of glycolysis by cholesterol and monoiodoacetate must lead by the feedback principle to the activation of biosynthesis of hexosamines and hexuronic acid, and this was in fact observed in the present experiments.

The results can thus be regarded as evidence of correlation between the inhibition of glycolysis and the increase in the mucopolysaccharide concentration in the aortic wall in experimental hypercholesteremia.

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