Changes in the levels of glycoproteins and glycosaminoglycans in diabetes associated with myocardial infarction

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Abstract

Changes in the levels of glycoprotein (GP) and glycosaminoglycans (GAG) were studied in diabetes associated with myocardial infarction in rats. Diabetes was induced by alloxan while myocardial infarction was induced using isoproterenol. Most of the GAG fraction increased in the heart and aorta in diabetes superimposed with myocardial infarction. The carbohydrate of GP also increased in heart while in serum only sialic acid showed an increase. The activity of lysosomal enzymes showed an increase in the case of β-glucuronidase and β-hexosaminidase while in the case of β-galactosidase and β-fucosidase it showed a decrease in the heart.

Introduction

Glycosaminoglycans (GAG) and glycoprotein (GP) are major components of connective tissue matrix. The GAG heparan sulphate has antiproliferative properties (1), antithrombogenic and antilipemic effect (2) and also has important influence on the basement membrane permeability (3). GP along with proteoglycans and other structural proteins are directly involved in the precise alignment of cells within tissues and for the association of tissues in organs (4).

Studies have shown a close association of GAG metabolism to cardiovascular complications in diabetes (5). There are also changes in the density of heparan sulphate in the glomerular basement membrane in insulin dependent diabetic patients (6). Elevated levels of GAG fractions have been observed in heart at peak period of myocardial infarction (MI) (7).

Both quantitative and qualitative changes in GP has been observed in diabetes and MI. Wood et al (8) have shown a chronic depression in the concentration of serum sialic acid in diabetic rats. While elevated levels of total hexose, fucose and sialic acid have been observed in heart in MI (9).

Alterations in the activity of lysosomal enzymes have been observed in diabetes and MI. A significant decrease in activity of β-galactosidase in heart and serum has been reported in diabetes by Kutryk et al (10). Studies in this laboratory have also shown that the activity of lysosomal enzymes alter during isoproterenol induced MI (11).

Thus the studies so far carried out indicate alterations in the metabolism of GAG and GP in diabetes and MI. Since it is not clearly known what changes occur in the metabolism of these macromolecular components during diabetes associated with MI, we studied the metabolism of
these substances in diabetic animals superimposed with MI using isoproterenol as MI inducing agent. The results of this investigation is reported in this communication.

MATERIAL AND METHODS

Male albino rats (virgin) of Sprague-Dawley strain weighing 130-150g were used for the experiment. The rats were divided into two groups and fed normal laboratory diet.

Group I - Normal
Group II - Diabetic

Diabetes was induced by a single subcutaneous injection of alloxan 180 mgm per kilogram-bodyweight after forty eight hours fasting (5). Blood sugar and urine sugar were noted at regular intervals from the seventh day. After 3 weeks the animals with marked hyperglycemia were selected for the experiment. Each group were again divided into two.

Group I [a] Normal Control
   [b] Normal + Isoproterenol

Group II [a] Diabetic control
   [b] Diabetic + Isoporterenol

Isoproterenol was administered subcutaneously at a dose of 30 mg/100 g body weight twice twenty four hours apart (12). All the animals were sacrificed 36 hours after the first administration of Isoproterenol.

The heart and aorta were transferred to ice cold containers for various estimations and serum CPK (13) GOT and GPT (14) were estimated.

The tissues after defatting were dried and subjected to papain digestion for 48 hours at 65°C at pH 6.5. The individual glycosaminoglycans were determined as described by Jaya and Kurup (15).

For determining the activity of β-glucuronidase, β-hexosaminidase, fucosidase and galactosidase, heart tissue was homogenised in 0.1% Brij 35 and the supernatant was diluted suitably with appropriate buffer and enzyme activity was measured (16).

The carbohydrate components of glycoprotein, total hexose (17), sialic acid (18) and fucose (19) in serum and heart were determined after the papain digestion of dry defatted tissue. Statistical analysis was done by student's 't' test (20).

RESULT

The activity of serum GOT, GPT and CPK are given in the table. 1. All the enzymes showed elevated activity in MI, diabetes and DI. But the elevation was less in DI when compared to diabetes and the change in CPK level was not significant when comparing diabetes and DI.

Most of GAG fractions in the heart showed a significant alteration. HA,HS, DS and Ch4s + 6s were increased during MI, diabetes and DI. In aorta only DS increased significantly and the other