DEPENDENCE OF MYOCARDIAL CONTRACTILITY ON THE ENDOGENOUS PROSTAGLANDIN LEVEL IN THE HEART

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Prostaglandins (PG) are biologically active compounds. They do not accumulate in the tissues but are synthesized *de novo* in response to a definite stimulus [2]. Aortic stenosis is one of the most powerful factors known to activate PG synthesis in the heart [1, 7]. Meanwhile PG exert a positive inotropic and chronotropic effect on heart muscle [9] and take part in regulation of the coronary blood flow [8]; definite correlation is therefore possible between the level of endogenous PG synthesized in the heart and myocardial contractility.

EXPERIMENTAL METHOD

Experiments were carried out on 32 male Chinchilla rabbits (2.5-3 kg). The animals were anesthetized by intravenous injection of amobarbital (50 mg/kg). The experiments were carried out under open chest conditions with artificial ventilation of the lungs. Standard pressure overloading of the heart was produced by stenosis of the ascending part of the arch of the aorta so that the systolic pressure developed in the left ventricle (SPLV) was 80% of the maximal SPLV. In the course of the experiment SPLV and the end-diastolic pressure in the left ventricle were recorded, the rate of contraction and relaxation was determined, and the contractility index (dp/dt/p) was calculated. The myocardium of the left ventricle was excised quickly 15, 30, and 60 min after coarctation of the aorta and compressed by Wollenberger's forceps, cooled in liquid nitrogen. The frozen tissue was ground in liquid nitrogen to produce a homogeneous powder, after which the PG were extracted [3], divided into groups by column chromatography [4], and determined quantitatively by radioimmunoassay, using the reagents and the method suggested by Clinical Assay Inc., USA. The results were subjected to correlation and regression analysis. The statistical analysis was carried out on the HP 9825A computer.

EXPERIMENTAL RESULTS

During overloading due to coarctation, positive correlation was found between the contractility index (dp/dt/p) and the PG concentration in the heart, depending on the duration of stenosis. Correlation was strongest (statistically significant) at the 15th minute of stenosis ($r = 0.78$, $P < 0.01$ and $r = 0.86$, $P < 0.001$ for PGE and $PGF_{2\alpha}$, respectively), but became weaker as the duration of overloading increased, until the values of the coefficient of correlation did not differ significantly from zero. For instance, 30 min after coarctation of the aorta $r = 0.12$ and $r = 0.21$ ($P < 0.05$), and after 60 min $r = 0.08$ and $r = 0.03$ ($P < 0.05$) for PGE and $PGF_{2\alpha}$, respectively. Linear regression lines for dependence of the PG concentration on myocardial contractility after different periods of stenosis are illustrated in Fig. 1. The results thus not only agree with those of other investigations, when increased contractility of the myocardium was accompanied by increased production of PG [5] and hypodynamia by reduced production of PG [6] by the perfused heart, but they also confirm the existence of definite correlation between myocardial contractility and the endogenous PG level in the myocardium. As stated above, PG are synthesized *de novo* in response to a definite stimulus [2]; a significant increase in the PG concentration in the myocardium of adapted animals must therefore be attributed primarily to their local synthesis. According to data in the literature, PG play the role of intracellular transmitters

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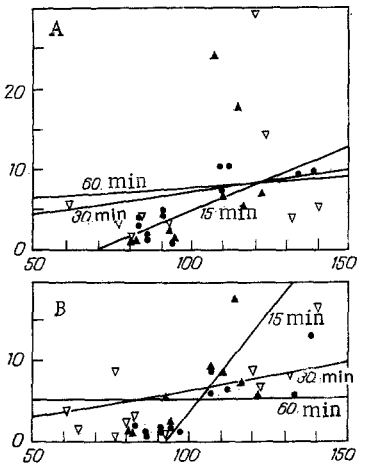

Fig. 1. Linear regression lines for dependence of PG concentration in heart tissue and myocardial contractility 15 min (filled circles), 30 min (filled triangles), and 60 min (empty triangles) after standard coarctation overloading of left ventricle in rabbits. A) Dependence of PGE on dp/dt/p; B) dependence of $PGF_{2\alpha}$ on dp/dt/p. Abscissa, dp/dt/p (in %); ordinate, C_X/C_0 (in %).

[2] and in the sequence of events they must occupy a position between the externally acting factor (pressure overloading of the heart) and the corresponding response of the organism (increased myocardial contractility). Limas et al. [7] demonstrated activation of the PG-synthetase system in the myocardium of rats as early as 5 min after aortic stenosis. On that basis they suggested that PG are one of the first links in the chain of biochemical reactions responsible for adaptation of the heart to pressure overloading [7]. On the basis of Limas' hypothesis, and considering the significant correlation observed between PG and myocardial contractility immediately after stenosis and also the subsequent weakening of this correlation depending on the duration of action of the coarctation overload, it can be tentatively suggested that a sharp rise in the PG concentration immediately after exposure to the stress factor is necessary to trigger the biochemical mechanisms of urgent adaptation of the heart to pressure overloading.

It can thus be postulated on the basis of data in the literature and the results described above that PG play a definite role in the system of biochemical reactions responsible for urgent adaptation of the heart to pressure overloading. If this is true, ultimately the endogenous PG level could serve as an indicator of the reserve powers of the myocardium.

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