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Influence of a Hypotensive Agent Upon Coronary Blood Flow and Cardiac Metabolism¹

By STEVEN M. HORVATH, ENID A. FARRAND and R. FARRAND

There has been considerable doubt as to the direct relationship of coronary blood flow and the level of arterial or perfusing pressure forcing blood into the vessels of the heart muscle. Attempts to delineate clearly these relationships have been complicated by concomitant effects induced by circulating epinephrine. The drug dibenzylamine² makes it possible to evaluate the influence of hypotension on coronary blood flow. Dibenzylamine injection induces a fall in blood pressure while maintaining essentially unchanged the cardiac output and the cerebral blood flow (1).

METHODS

Ten experiments were conducted on 10 mongrel dogs ranging in weight from 10.8 to 22.8 kg. (mean body weight 17.7 kg.). The animals were anesthetized with sodium pentobarbital (30 mg./kg. body wt.) and heparinized (5 mg./kg. body wt.). Two single lumen cardiac catheters with bird's eye tips were inserted into two exposed branches of the external jugular veins and under fluoroscopic guidance positioned, one into the pulmonary artery and the other into the coronary sinus. A polyethylene cannula was inserted into a branch of the femoral artery. Blood pressures were recorded from the femoral artery, coronary sinus and pulmonary artery by means of Statham pressure transducers and appropriate amplifying and recording equipment. The point of zero reference was the right atrium. Oxygen consumption was determined by collection of expired air samples in a Tissot spirometer and analysis for oxygen content with a Beckman Oxygen Analyzer. Blood oxygen and carbon dioxide contents were determined by the method of Van Slyke and Neill (2). Coronary sinus and arterial blood were analyzed for nitrous oxide content by the procedure of Orcutt and Waters (3). Coronary blood flow was determined by a modification of the nitrous oxide technique of Kety and Schmidt (4). Cardiac output was calculated by the direct Fick principle.

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²Dibenzylamine is a beta-halo alkyl amino which is in a class of adrenergic blocking agents. The blockage produced by this compound is highly specific and of long duration (1).

Following the withdrawal of blood samples for the measurement of control levels, an injection of 2 mg./kg. body weight of dibenzyline was given into the pulmonary artery. The injection was given over a period of five minutes. Coronary blood flow and cardiac output measurements were made 30 minutes and 60 minutes after the administration of dibenzyline.

Upon completion of the experiment, the catheters were removed, the incisions sutured and each animal received 300,000 units of penicillin, intramuscularly. All animals were allowed at least three weeks to recover before being used for further experimentation.

Coronary vascular resistance was calculated by means of the formula:

$$\frac{\text{Mean arterial pressure} - \text{mean coronary sinus pressure}}{\text{coronary blood flow (ml./100 g. left vent./min.)}}$$

Peripheral vascular resistance was determined by the formula:

$$\frac{\text{Mean arterial pressure} \times 13.6 \times 60}{\text{cardiac output (cc./sec.)}}$$

The equations of Bing et al. (5) were used for the calculation of left ventricular oxygen consumption aerobic energy uptake of the left ventricle, left ventricular work and mechanical efficiency. All statistical analyses were carried out on paired samples and the level of significance was taken as 5 per cent or better.

RESULTS

The results obtained are summarized in Table 1. The mean arterial blood pressure decreased 46 mm. Hg 30 minutes after infusion of the dibenzyline and remained at this low level during the remainder of the period of observation. Cardiac output did not change during the course of the experiment. Arterial oxygen content had not changed 30 minutes post-infusion but had decreased 1.0 vols. per cent by the 60 minute measurement. Arterial-pulmonary arterial oxygen content did not change significantly 30 minutes after infusion; however, by one hour it had increased 1.04 vols. per cent. Systemic vascular resistance was decreased 30 minutes post-injection but returned to control levels by the end of the observation period.

Coronary blood flow decreased 37 ml./100 g. left ventricle/min. at the 30 minute post-injection measurement and returned to the control range by 60 minutes. As a consequence of the decreased coronary blood flow, a similar pattern of a decrease at 30 minutes and a return to control levels by 60 minutes, was noted in the coronary sinus oxygen content (-2.38 vols. %), oxygen consumption of the left ventricle (-2.5 ml./min.) and the aerobic energy uptake of the left ventricle.

The pattern of changes in the carbon dioxide content of the arterial blood, pulmonary artery and coronary sinus blood was similar, that of a decrease at 30 minutes post-injection and was followed by an even greater decrease at 60 minutes.

The work of the left ventricle did not change until the 60 minute measurement period, at which time a significant decrease (-1.3 Kg.M/min.) was observed.

DISCUSSION

The initial changes that occurred in the coronary circulation as a result of the injection of dibenzyline are due to the sharp decrease in arterial blood pressure. Eckenhoff et al. (6) reported that there was a direct relationship between arterial blood pressure and coronary blood flow; however, Alella et al. (7) stated that although mechanical factors are important in the changes in coronary blood flow, cardiac oxygen consumption has even more influence. Both the level of mean arterial blood pressure and the myocardial oxygen consumption influenced the coronary blood flow in the current experiments. Initially, the marked fall in arterial blood pressure led to a decrease in coronary blood flow and myocardial oxygen consumption. Later, although the arterial pressure remained low, the coronary blood flow and oxygen consumption increased, illustrating the influence of the oxygen uptake. A slight decrease in coronary vascular resistance was observed during this latter period. During the initial stages, the extraction of oxygen by the myocardial tissue increased, apparently to a maximum; however, this increase was not adequate to compensate for the decreased coronary blood flow and a decreased oxygen consumption was recorded. Therefore, an anoxic condition of the cardiac tissue occurred. This, in turn, probably induced the constriction of the coronary vessels (7, 8) and a return of the coronary blood flow and the oxygen consumption to normal levels. In agreement with previous investigations, cardiac output did not change appreciably as a result of the dibenzyline injection. Cardiac work decreased late in the experiment consequent to the decrease in arterial blood pressure and the unchanged cardiac output.

SUMMARY

Coronary blood flow is modified by both the level of the perfusing pressure and the degree of availability of oxygen to the myocardium. Although the precise contribution of each of these factors to the regulation of volume flow could not be determined, it would appear that the oxygen supply was the more important of the two.

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Table 1

The Changes in Cardiovascular Functions As a Consequence of an Infusion of 2 mg./kg. of Dibenzylamine into the Pulmonary Artery

Item	Control		Differences from Control					
	Mean	S.E.	30 minutes after drug			60 minutes after drug		
			Mean	S.E.	t	Mean	S.E.	t
Mean Arterial Pressure mm. Hg.	125	26.4	- 46	6.3	7.3 *	- 47	7.4	6.4 *
Arterial Oxygen Content vols. %	16.4	2.3	- 0.5	0.3	1.42	- 1.0	0.4	2.50*
Art.-Pul. Art. Oxygen Content vols. %	3.95	0.93	- 0.89	0.48	1.85	- 1.04	0.37	2.81*
Cardiac Output L./min.	2.44	1.08	0.36	0.42	0.86	0.01	0.12	0.00
Arterial Carbon Dioxide Content vols. %	41.9	5.9	- 5.1	0.8	6.07*	- 7.0	0.8	8.33*
Pul. Art. Carbon Dioxide Content vols. %	45.0	5.6	- 3.3	0.7	4.40*	- 5.0	0.7	6.66*
Cor. Sinus Carbon Dioxide Content vols. %	51.8	5.2	- 3.3	0.9	3.63*	- 6.7	1.0	6.5 *
Coronary Blood Flow ml./100 g. left vent./min.	33	29.7	- 37	8.6	4.30*	11	19.4	1.04
Coronary Blood Flow ml. left vent./min.	47	23.0	- 21	5.8	3.62*	15	17.7	0.85
Coronary Vascular Resistance units	1.64	0.52	0.0	0.2	0.0	- 0.51	0.30	1.70
Systemic Vascular Resistance dynes/cm ²	4435	2624	-2223	913	2.43*	-720	825	0.87
Cor. Sinus Oxygen Content vols. %	3.34	1.17	- 1.28	0.40	3.20*	- 0.83	0.53	1.60
Oxygen Consumption of Left Ventricle ml./min.	6.2	2.6	- 2.5	0.8	3.12*	1.7	2.4	0.70
Aerobic Energy Uptake of Left Ventricle KgM./min.	12.5	5.3	- 4.5	1.3	3.35*	2.8	4.0	0.69
Work of Left Ventricle Kg.M./min.	4.6	1.9	- 0.9	1.6	0.56	- 1.3	0.2	5.91*
Mechanical Efficiency %	34	21.0	1.0	7.8	0.13	- 15	14.3	1.05

*Significant at 5 per cent level or better

References

1. Nickerson, M. and L. S. Goodman. Pharmacological properties of a new adrenergic blocking agent: N, N-dibenzyl-B-chloroethylamine. *J. Pharm. & Exper. Therap.* 89: 167-185, 1947.
2. Van Slyke, D. D. and J. M. Neill. *J. Biol. Chem.* 61: 523, 1924.
3. Orcutt, F. S. and R. M. Waters. *J. Biol. Chem.* 117: 509, 1937.
4. Kety, S. S. and C. F. Schmidt. *Amer. J. Physiol.* 143: 53, 1945.
5. Bing, R. J., M. M. Hammond, J. C. Handelsman, S. R. Powers, F. C. Spenser, J. E. Eckenhoff, W. T. Goodale, J. H. Hafkenschiel, and S. S. Kety. *Amer. Heart J.* 38: 1, 1949.
6. Eckenhoff, J. E., J. H. Hafkenschiel, and C. M. Landmesser. *Amer. J. Physiol.* 148: 582, 1947.
7. Alella, A., F. L. Williams, C. Bolene-Williams and L. N. Katz. *Amer. J. Physiol.* 183: 570, 1955.
8. Eckenhoff, J. E., J. H. Hafkenschiel, C. M. Landmesser, and M. Hormel. *Am. J. Physiol.* 149: 634, 1947.

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