EFFECT OF ALTITUDE HYPOXIA ON MYOCARDIAL METABOLISM

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Hypoxia is one of the strongest stimuli affecting coronary blood flow[1]. Whereas acute hypoxia of short duration has been shown to increase coronary blood flow[2-5], the response of prolonged hypoxia has not been adequately studied. High altitude offers a unique model to study the effects of prolonged hypoxia. This communication deals with our observations on immediate and chronic effects of high altitude hypoxia on myocardial metabolism and coronary circulation in man.

MATERIAL AND METHODS

To study the immediate response, 19 healthy plainsmen with an average age of 21·4 years were studied at sea level and again within 24 to 96 hours of arrival at high altitude (3658 m above sea level) by air. To study the chronic response, 8 healthy high altitude natives with an average age of 20·6 years were studied at high altitude. Right heart catheterization was performed in all in a fasting state without any premedication. Cardiac output was determined by the Fick principle[6], coronary blood flow by the nitrous oxide desaturation method[7] and blood lactate content by the enzymatic technique (Kits supplied by M/s Boehringer, Germany). The various parameters were calculated as follows:—

1. $MVO_2 = \dfrac{CBF \times (A-CS)\ O_2}{100}$

2. $MO_2EC = \dfrac{AO_2 - CSO_2}{AO_2}$

3. $LVWi = \dfrac{CI \times BA\ m \times 13{\cdot}6}{1000}$

4. $MEILV = \dfrac{LVWi}{MVO_2 \times 2{\cdot}06}$

5. $MECL = \dfrac{A_L - CS_L}{A_L}$

Where

MVO_2	=	myocardial oxygen consumption ml/100 g LV/min;
CBF	=	coronary blood flow ml/100 g LV/min;
A	=	arterial;
CS	=	coronary sinus;
MO_2EC	=	Myocardial oxygen extraction coefficient;
LVWi	=	External left ventricular work index KgM/min/m^2;
CI	=	Cardiac index l/min/m^2;
BAm	=	Brachial artery systolic mean pressure mm Hg;
MEILV	=	Calculated external mechanical efficiency index of the left ventricle%;
MECL	=	Myocardial extraction coefficient of lactate;
L	=	Lactate mg%

RESULTS (Table I)

The coronary blood flow and myocardial oxygen consumption per 100 g of left ventricle decreased significantly at high altitude. The myocardial oxygen extraction coefficient was not altered. The external left ventricular pressure work did not significantly change but the calculated external mechanical efficiency index of the left ventricle was increased at high altitude. Though the arterial and coronary sinus lactate contents were increased at high altitude, the myocardial extraction of lactate was reduced. The data obtained in the plainsmen at high altitude and high altitude natives was more or less identical.

DISCUSSION

The decrease in coronary blood flow occurring in high altitude hypoxia may seem paradoxical because acute hypoxia has been shown to increase coronary blood flow[2-5]. However, whereas hypoxia of a short duration has been shown to increase coronary blood flow, the response of prolonged hypoxia is controversial. Chronic hypoxia due to chronic obstructive lung disease has been shown to cause either no alteration[8,9] or a slight increase[10] in coronary blood flow inspite of hypercapnia, which increases coronary blood flow[11]. Other factors present during high altitude exposure viz. polycythemia, hypocapnia due to hyperventilation and alkalosis may also modify coronary blood flow. Whereas alkalosis has been shown to increase coronary blood flow[12], polycythemia and hypocapnia have been shown to reduce it[13,14]. It is probable that during high altitude hypoxia, the factors which reduce coronary blood flow have a more dominant influence. Grover *et al*[15] in three plainsmen, Vogel *et al*[16] in experimental animals and Moret *et al*[17] in natives of Bolivean Andes have also reported a decrease in coronary blood flow at high altitude. The observations of reduced myocardial oxygen consumption and increased calculated external mechanical efficiency of the left ventricle at high altitude in the present study are in agreement to those of Moret *et al* in high altitude natives. However, Grover *et al* observed that, in contrast to the present study, myocardial oxygen consumption does not decrease significantly at high altitude inspite of decreased coronary blood flow because of the increased myocardial oxygen extraction. Although the arterial lactate content increased at high altitude, the myocardial lactate extraction decreased. This, in association with the observation of increased external mechanical efficiency of left ventricle, may indicate the presence of anaerobic cardiac metabolism at high altitude. It is not clear whether presence of anaerobic cardiac metabolism at high altitude reflects depressed left ventricular function or not because no sophisticated parameters to evaluate the left ventricular function were studied. However, the stroke volume was reduced at high altitude. This may indicate that the left ventricular function was depressed at high altitude. Why the response of the myocardium to high altitude hypoxia should be decreased coronary flow and appearance of anaerobic myocardial metabolism and not increament in the coronary flow and oxygen extraction is not clear. Moret *et al* and Grover *et al* did not find evidence of anaerobic cardiac metabolism due to high altitude hypoxia. The differences in their findings and the present observations need further investigations.

SUMMARY

Coronary haemodynamic and myocardial metabolic parameters were studied in 19 plainsmen at sea level and within 24-96 hours of arrival at high altitude (3658 m above sea level) and 8 high altitude natives at high altitude. The coronary blood flow and myocardial oxygen consumption decreased at high altitude both in plainsmen and high altitude natives. The calculated external mechanical efficiency of the left ventricle increased and the myocardial lactate extraction was reduced suggesting the presence of anaerobic myocardial metabolism at high altitude.

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TABLE I

MYOCARDIAL METABOLISM AND CIRCULATION AT HIGH ALTITUDE

	No.			CBF	MVO2	MO2EC	LVWi	MEILV	AL	CSL	MECL
1.	SL	19	M	83·6	9·08	0·59	4·56	26·0	8·00	5·01	0·37
			SD	7·6	1·93	0·09	1·14	8·3	1·70	1·84	0·18
2.	HA	19	M	75·6	6·77	0·58	5·19	39·0	13·97	11·34	0·21
			SD	7·5	2·08	0·15	1·11	16·7	3·57	3·57	0·16
	p	(1,2)		∠·01	∠·01	NS	NS	∠·01	∠·001	∠·001	∠·05
	HIGH ALTITUDE NATIVES										
3.	HA	8	M	71·9	6·13	0·57	4·44	41·0	11·56	9·10	0·24
			SD	7·5	2·43	0·10	0·57	18·8	2·10	2·79	0·23
	p	(3,1)		∠·05	∠·05	NS	NS	∠·05	∠·05	∠·05	∠·05
	p	(3,2)		NS	NS	NS	NS	NS	NS	NS	NS

SL = Sea Level; HA = High altitude; No. = Number of subjects; CBF = Coronary blood flow ml/100 g LV/min; MVO2 = myocardial oxygen consumption ml/100 gLV/min; MO2EC = myocardial oxygen extraction coefficient, LVWi = External left ventricular work index KgM/min/m2, MEILV = Calculated mechanical efficiency index of left ventricle%, AL = arterial lactate content mg.%, CSL = Coronary sinus lactate content mg.% MECL = myocardial extraction coefficient of lactate%.

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REFERENCES

1. Berne, R. M.: "Regulation of coronary blood flow." Physiologic Reviews, 44, 1, 1964.
2. Berne, R. M., Blackmon, J. R. and Gardner, T. H.: "Hypoxemia and coronary blood flow." J. Clin. Invest., 36, 1101, 1957.
3. Hellems, H. K., Ord, J. W., Talmers, F. N. and Christensen, R. C.: "Effect of hypoxia on coronary blood flow and myocardial metabolism in normal human subjects." Circ. Research, 16, 893, 1957.
4. Guz, A., Kurland, G. S. and Freedberg, A. S.: "Relation of coronary flow to oxygen supply." Am. J. Physiol., 199, 179, 1960.
5. Haddy, F. J.: "Physiology and pharmacology of coronary circulation and myocardium particularly in relation to coronary artery diseases." Am. J. Med., 47, 274, 1969.
6. Fick, A.: "Veber die Messung des Blutgnantums in den Hezventrikeln." Sitzungshr der phys. med. Gessellsch zu Wurzburg, 1870.
7. Goodale, W. T. and Hackel, D. B.: "Measurement of coronary blood flow in dogs and man from rate of myocardial nitrous oxide desaturation." Circulation Res., 1, 502, 1953.
8. Moret, P. R.: "Circulation coronaire et hypoxemic chronique angiologica." Basel, 4, 184, 1967.
9. Moret, D. R., Bopp, P., Grosgurin, J., Hatam, R., Ahmadi, N. and Odier, J.: "Comparative study of electrocardiogram, vectorcardiogram, coronary circulation and myocardial metabolism in chronic cor pulmonale." Cardiologia, 48, 182, 1966.
10. Fukuda, M.: "Coronary circulation in chronic pulmonary disease." Jap. Circ. J., 30, 6, 93, 1966.
11. Feinberg, M., Gerola, A. and Katz, L. N.: "Coronary flow and myocardial oxygen consumption in hypercapnia." Fed. Proc., 17, 45, 1958.
12. Goodyear, A. V. N., Eckbarldt, W. F., Hostberg, R. and Goodkind, M. J.: "The effect of acidosis and alkalosis in lactate and pyruvate of dog heart in situ." Am. J. Physiol., 200, 628, 1961.
13. Regan, T. J., Frank, M. J., Lehan, P. H. and Hellems, H. K.: "Influence of red cell mass on myocardial blood flow and oxygen uptake." Clin. Res., 8, 367, 1960.
14. Rowe, G. G., Castello, C. A. and Crumpton, C. W.: "Effects of hyperventilation on systemic and coronary haemodynamics." Am. Heart J., 63, 67, 1962.
15. Grover, R. F., Lufschanowski, R. and Alexander, J. K.: "Decreased coronary blood flow in man following ascent to high altitude." In Hypoxia, High Altitude and Heart pp. 77-79, S. Karger, Basel, New York, 1970.
16. Vogel, J. H. F., Jamieson, G., Papadopoulos, H. D., Lenker, R. D., Brammell, H. L. and Brake, D.: "Coronary blood flow during short term exposure to high altitude." Ibid. pp. 80-85.
17. Moret, P. R., Coverrubias, E., Coudert, J. and Ducholas, F.: "Coronary circulation and myocardial metabolism in subjects living at high altitude." VI World Congress of Cardiology, London, Sept. 1970.