Title : *EFFECTS OF INOSITOL HEXAPHOSPHATE INDUCED HIGH P50 ON AN ISOLATED RABBIT HEART WITH FREE AND LIMITED CORONARY BLOOD FLOW.*

Authors : *J.F. BARON, M.D., E. VICAUT, M.D., O. STUCKER, M.D., M.C. VILLEREAL, Pharm. D., C. ROPARS, Pharm. D., B. TEISSEIRE, Pharm. D., P. VIARS, M.D., M. DUVELLEROY, M.D.*

Affiliation : *Département d'Anesthésie Réanimation Groupe Hospitalier Pitié Salpêtrière - PARIS - Laboratoire de Biophysique - Hôpital Fernand Widal - PARIS - FRANCE.*

INTRODUCTION. In patients with coronary artery disease, several clinical studies have suggested that increased oxyhemoglobin affinity due to blood bank storage is an important aspect to be considered in myocardial oxygen delivery (1). To counterbalance this adverse effect, several biochemical treatments of stored blood have been proposed. However, results from these studies on myocardial oxygen (O2) delivery, consumption and performance remain controversial, probably because in most of these studies the increase in the partial O2 pressure at 50 % of oxyhemoglobin saturation (P50) was too modest. Cardiac effects of a new technique inducing large increases in P50 were investigated on an isolated heart prepartion during both free and limited flow conditions.

METHODS. By a new technique to lyse and reseal erythrocytes, Inositol Hexaphosphate (IHP) was encapsulated in human red blood cells (2). IHP-treated blood (P50 : 42.5±9,3 mmHg) and standard bank stored blood (Control blood) (P50 : 21.2±0.9 mmhg) were washed, centrifuged and resuspended in Krebs-Henseleit Buffer, to achieve a hemoglobin concentration of 10.5 g/dl. Control and IHP-treated bloods were equilibrated and oxygenated to achieve the same acid-base balance, PO2 and O2 content. Seven New Zealand albino male rabbits were anesthetized with ether. The heart was quickly excised by thoracotomy and prepared for cannulation under immersion in a cold isotonic saline solution. The aorta was mounted on a cannula and retrograde perfusion was performed with control blood. The speed of the coronary pump, which reflects coronary blood flow (CBF), may vary to maintain a constant perfusion pressure of 90 mmHg (FREE CBF). The coronary sinus drainage was collected via a cannulated pulmonary artery. A cannulated fluid-filled balloon was placed through a left atrial incision, in the left ventricle (LV) and attached to a pressure transducer, in order to monitor LV pressure. The balloon was inflated to maintain constant LV volume and to produce a LV end diastolic pressure (LVEDP) of 7 mmHg. The right ventricle was paced at a constant rate of 250 b/min. After a recovery period of 30 min, the first set of measurements was performed under control blood with FREE CBF. The second set of measurements was performed under IHP-treated blood with FREE CBF. After switching back to control blood, CBF was restricted and held constant at a value corresponding to 55 % of CBF with control blood. In this condition (RESTRICTED CBF), the perfusion pressure may vary. The same changes in perfusates were carried out in these restricted flow conditions as those performed in free flow conditions. Measurements included : CBF, perfusion pressure (PP), LV developed pressure (LV systolic pressure minus LVEDP) (LVDevP) and its first positive and negative derivatives (dP/dt max and dP/dt min), arterial and coronary sinus PO2 (PaO2, PcsO2) and O2 contents (CaO2, CcsO2). Myocardial O2 consumption (MVO2) was calculated. Data were analysed using the paired Student's t-test and expressed as mean ± SD.

RESULTS are expressed in the table. During free flow conditions, switching from control blood to IHP-treated blood induced a decrease in CBF, an increase in PcsO2 and a decrease in CcsO2. Despite the increase in MVO2, LV performances were poorer. In restricted flow conditions, the increased PP was associated with the same changes in PcsO2, CcsO2 and MVO2 as those observed during free flow conditions. However, in this situation, LVDevP was improved.

DISCUSSION. During both flow conditions, IHP-treated blood induced coronary vasoconstriction which cannot be explained by a rheological phenomenon (2). This vasoconstriction may result from involved metabolic regulation since O2 unloading to the tissue is increased with a high P50. The concommittant increases in PcsO2 and in MVO2 are in line with previously-published studies (2). During free flow conditions, the decrease in LVDevP may be due to a cardiodepressive effect of the preparation. This side-effect might be due to the presence in buffer of IHP (a calcium binder) secondary to a certain hemolysis. During restricted flow conditions, the expected beneficial effect on LV performance of increased O2 unloading, due to a high P50, was lessened by this cardiodepressive effect. It is concluded that a high P50 may be beneficial in the setting of limited myocardial blood flow. Further investigations are required in the whole animal to confirm or weaken this side-effect, before using such an attractive treatment of stored blood in humans.

REFERENCES

1. WEISEL RD, et al. Adverse effects of transfusion therapy during abdominal aortic aneuryssectomy. Surgery 83 : 682-690, 1978

2. STUCKER O, et al. Coronary responses to large decreases of hemoglobin-O2 affinity in isolated rat heart. Am. J. Physiol. 249 : H1224-H1227, 1985

TABLE.

	FREE CBF		RESTRICTED CBF	
	CONTROL	IHP	CONTROL	IHP
PP mmHg	89±6	89±9	36±16	50±21**
CBF ml.min.g	2.7±0.5	1.9±0.5***	1.5±0.4	1.5±0.4
PcsO2 mmHg	34±2	55±10***	28±4	52±6***
CcsO2 ml/100 ml	9.45±1.05	7.37±2.43***	7.91±1.372	5.89±1.43***
MVO2 ml O2/min/g	0.12±0.04	0.14±0.07**	0.09±0.03	0.11±0.03***
LVDevP mmHg	100±25	85±25***	69±15	74±15***
dP/dt max mmHg/s	1925±348	1680±382**	1351±339	1405±339
dP/dt min mmHg/s	-1402±386	-1247±479*	-1173±189	-1254±232

Significant differences between bloods : * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$