Experimental Heart Preservation for 24 Hours: Benefits of PGE_1 in a Nonpulsatile Coronary Perfusion Solution

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The increase in activity of centers with cardiac transplant programs has been limited because of the unavailability of high quality donor organs. Nonpulsatile coronary perfusion (NPCP) with hypothermia has allowed long-term cardiac preservation in various experimental models.[1-4] This experiment was designed to study the effects of PGE_1 in an experimental NPCP.

MATERIALS AND METHODS

Adult mongrel dogs weighing between 19 and 28 kg were anesthesized with phentobarbital (30 mg/kg IV). A right thoracotomy incision was made. The aorta was clamped and 250 mL of standard cardioplegic solution was administered. The heart was extracted, sectioning the aorta, pulmonary artery, vena cavas, and pulmonary veins at the level of its pericardial reflection. Once the heart was removed, it was connected to the NPCP.

This system consists of a reservoir that contains the selected solution in which is added a mixture of O_2 and CO_2 in a 95:5 ratio through an 8-µm micropore filter. The heart was suspended from the aortic root to a cannula that connects to the reservoir and has an interphase chamber of air. The heart is introduced to another reservoir that allows the experiment to be performed under sterile conditions and also has the same solution at 4°C. A roller pump permits us to recover the solution from the lower reservoir. Two groups were formed according to the preservation solution employed: group 1 (n = 11): The composition of the solution is Na 140 mEq/L; Ca 3 mEq/L; Cl 129 mEq/L; K 20 mEq/L; HCO_3 12 mEq/L; glucose 4 g/L; lidocaine 0.5 g/L; chorpromazine 16 mg/L; dextran 1.8%; osmolarity 380 mosm/L; PO_2 600 to 800 mmHg; PCO_2 25 to 30 mmHg, perfusion pressure 25 to 35 cm H_2O.

The hearts were preserved in this system for 21 to 26 hours after which orthotopic heart transplants were performed in seven dogs. Before unclamping the aorta, a

reperfusion solution composed of lactated Ringer's + 6 mEq/L HCO_3 + 16 mg/L chorpromazine + mannitol was infused. The experiment was concluded three hours after stopping extracorporeal circulation (ECC). In group 2, n = 10. PGE_1 (100 μg/L) was added to the same solution used in group 1, preserving the heart for 21 to 26 hours, and performing orthotopic heart transplants in six cases. The studies performed during the preservation period were: (1) increase in heart weight; (2) serial acid-base equilibriums of the solution; (3) coronary resistance evolution, obtained by the quotient between pressure and flow of the solution; (4) glucose, CPK, K, from the coronary sinus and perfusion solution; (5) myocardial temperature; and (6) light and electron microscope studies. Cardiac function after the transplant was evaluated for: (1) possibility of suspending ECC; (2) cardiac rhythm; (3) need of inotropic agents; and (4) arterial pressure, right atrial and left atrial pressure, cardiac output, and pulmonary artery PO_2.

RESULTS

The increase in weight of the hearts was between 28% to 39% in group 1 and between 28% to 41% in group 2. In spite of this increase, the hearts were flaccid at palpation; the edema disappearing rapidly after stopping ECC. The average increase in coronary resistance at the end of the preservation period was 22 ± 9% in group 1, and 15 ± 6% in group 2 ($P < .05$). These results were correlated with the final coronary flow which was 850 ± 250 mL/h in group 1 and 1,120 ± 270 mL/h in group 2. The evolution of the coronary flow and of CPK seems to us valid parameters to study the quality of preservation. Previously, 20 dogs were operated on to perfect the NPCP technique. In this preliminary series with perfusion defects, the increase in coronary resistance was 82 ± 21% and the average CPK was 276 ± 72 μ/L at the end of the preservation period. The postorthotopic heart transplant results are shown in Tables 1 and 2. The period of preservation was between 21 and 26 hours. In four cases of group 1, the heart started to beat spontaneously and electrical defibrillation was necessary in the three remaining cases. In all cases of group 1 it was possible to end ECC, although in three cases it was necessary to give high doses of isoproterenol and dobutamine. In five of the six cases of group 2, the hearts beat spontaneously. In only one case was it necessary to administer dobutamine at a dose of 5 μg/kg/min. In the rest of the cases, isoproterenol was administered to obtain a mild chronotropic effect.

DISCUSSION

These results show that this system of NPCP along with other systems,[1-4] can provide adequate long-term cardiac preservation. The simplification of this system is based on the concept that the heart at 4°C does not need high flow rates. It is the quality of perfusion and not only the hypothermia that is responsible for these results. As mentioned, in the preliminary series of 20 experiments, in which existed various

irregularities in the perfusion techniques, the median increase in the coronary resistance was 82%.

PGE_1 has demonstrated to be a potent vasodilator in the systemic and coronary circulation.[5,6] PGE_1 was also reported to have cytoprotective effects due to lysosomal membrane stabilization.[7,8] In our study, addition of PGE_1 to the perfusion system reduced coronary resistance and CPK levels at the end of the preservation period. These results were well correlated with those after transplant, achieving better hemodynamic function and less need of inotropic agents in group 2.

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Table 1. Results After Orthotopic Heart Transplant (Group 1)

No.	Preservation (hours)	Weight %	Defibrillation	Cardiac Rhythm	Inotropic	PA PO_2 mm Hg	CO
1	24	30	—	SR	ISO 0.2	>35	
2	21	28	—	SR	DOB 7	>33	1'5 to 2
3	25	39	+	SR	ISO 0.2	>35	>2
4	24	32	—	NR	ISO 0.3	30 to 35	—
					DOB 5		
5	26	25	—	SR	ISO 1	25 to 28	1'4
					DOB 15		
6	23	28	+	NR	ISO 0.4	28 to 32	—
7	22	31	+	NR	ISO 0.4	>35	>2

Abbreviations: PA PO_2, pulmonary artery $P0_2$; CO, cardiac output L/min; ISO, isoproterenol (μg/min); DOB, dobutamine (ug/kg/min); SR, sinus rhythm; NR, nodal rhythm.

Table 2. Results After Orthotopic Heart Transplant (Group 2)

No.	Preservation (hours)	Weight %	Defibrillation	Cardiac Rhythm	Inotropic	PA PO_2 mm Hg	CO
1	25	35	—	SR	ISO 0.1	>35	>2
2	23	27	—	SR	ISO 0.3	>35	>2
3	26	41	—	NR	ISO 0.3	30 to 35	—
					DOB 5		
4	24	30	+	SR	ISO 0.4	30 to 33	1'5 to 2
5	25	35	—	SR	ISO 0.2	>33	>2
6	21	28	—	SR	—	>35	—

Abbreviations: PA PO_2, pulmonary artery $P0_2$; CO, cardiac output L/min; ISO, isoproterenol (μg/min); DOB, dobutamine (ug/kg/min); SR, sinus rhythm; NR, nodal rhythm.