TITLE: THE PERIPHERAL EFFECTS OF ISOPROTERENOL IN THE POST-OP LOW-CARDIAC-OUTPUT STATE

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Introduction. Previous studies examining the hemodynamic effects of isoproterenol in a low-cardiac-output state have not isolated the peripheral and pulmonary vascular effects of isoproterenol from the cardiac effects of the drug, because of the presence of the heart in the system. Initial studies by Liu, Stanley, et al, were successful in isolating the peripheral and pulmonary vascular effects of isoproterenol from the cardiac effects with the use of the total artifical heart (TAH).[1] However, these studies were carried out after the animal had completely recovered from the surgical implantation of the TAH and after the cardiovascular dynamics and cardiac output approximated pre-TAH implantation values. The purpose of this study was to examine the acute postoperative peripheral effects of isoproterenol in a low-cardiac-output state.

Methods. Following approval by the institutional animal resources committee, 5 Holstein calves weighing 70-90 kg were studied. Under halothane anesthesia a 7 French introducer was placed in the right external jugular vein along with 18 gauge right femoral artery catheter. The animals were allowed to recover from the anesthesia and were extubated. Six hours post-extubation a pulmonary artery catheter was placed and baseline measurements were obtained. Isoproterenol infusion was then begun through the sheath introducer at the rate of 0.25 ug/min. Measurements were obtained after 30 minutes and the infusion rate was increased to 2 ug/min. After an additional 30 minutes, measurements were again taken and the infusion was turned off. Data was collected 30 minutes after discontinuation of the infusion. Hemodynamic measurements obtained included heart rate, (HR) systemic blood pressure (SBP), mean arterial pressure (MAP), pulmonary artery pressure (PAP), central venous pressure (CVP), pulmonary capillary wedge pressure (PCWP), and cardiac output (CO). Systemic (SVR) and pulmonary vascular resistance (PVR) and stroke volume (SV) were calculated from the above data. The following day the calves underwent placement of the TAH. On postoperative day 2, following a collection of baseline measurements, a protocol identical to the above was implemented with the exception of the left atrial pressure (LAP) was measured rather than the PCWP. CO was determined by the cardiac-output monitoring diagnostic unit (COMDU), which monitors the performance of the TAH.[2] The drive parameters and heart rate of the TAH were held constant throughout this study. Statistical analysis of the data was performed with a two-way ANOVA and Student's t-test for unpaired and paired data. Significance was set at $p < 0.05$.

Results. CVP and PAP were significantly elevated in the low-cardiac-output state as compared to the normal-cardiac-output state, and isoproterenol had no significant effect on these values during the protocol. HR, MAP, PCWP, CO, SVR, and PVR results are tabulated in Tables 1 (pre-TAH, normal-cardiac-output state) and 2 (post-TAH, low cardiac-output state). In the low-cardiac-output state, the SVR significantly increased ($p < 0.05$). With the normally intact heart and the normal-cardiac-output state HR and CO significantly increased ($p < 0.05$). SVR significantly decreased with isoproterenol in the normal-output-cardiac state, but there was no significant effect on PVR. In the artificially induced low-cardiac-output state postoperatively, HR was fixed, and MAP, PCWP, CO, and PVR were not significantly affected by either low-dose or high-dose isoproterenol. SVR, however, was significantly decreased with high-dose isoproterenol (2 ug/min) ($p < 0.05$).

Discussion. Isoproterenol did not demonstrate the decrease in MAP which was demonstrated by dobutamine using the same low-cardiac-output model.[3] Liu and Stanley demonstrated decreased PAP and PVR with the use of isoproterenol in healthy post-TAH calves with a normal cardiac-output.[1] Also, isoproterenol has been demonstrated to decrease PVR in primary pulmonary hypertension.[4] However, it may not have the same effects during the acute postoperative phase with a low cardiac-output state as it does after recovery from operation, when the cardiac output is normal.

References

1. Liu W, , et al. Anesth Analg 55:560-566, 1976.
2. Willshaw P, et al. Artif Organs 8:215, 1984.
3. Cork RC, et al. Presented at the Society of Cardiovascular Anesthesiologists, Palm Desert, CA, May 9-13, 1987.
4. Daoud PS, et al. Am J Cardiol 42:817-822, 1978.

TABLE 1: PRE-TAH

	Baseline	Low-Dose Isoproterenol 0.25 ug/min	High Dose Isoproterenol 2 ug/min	Off
HR (beats/min)	116 ± 23	105 ± 10	158 ± 12*#	102 ± 13
MAP (mm Hg)	114 ± 7	119 ± 9	108 ± 9	125 ± 10
PCWP (mm Hg)	6.6 ± 0.4	7.6 ± 1.7	7.8 ± 1.3#	8.6 ± 2.9
CO (L/min)	10.0 ± 1.1#	11.9 ± 1.1#	15.5 ± 1.0*#	11.3 ± 1.3#
SVR (dynes-sec cm^{-5})	933 ± 88#	803 ± 62#	547 ± 61*#	894 ± 101#
PVR (Wood Units)	1.30 ± 0.17#	0.94 ± 0.14#	0.86 ± 1.2#	1.32 ± 0.26#

TABLE 2: POST-TAH

HR (beats/min)	100 ± 5	100 ± 5	100 ± 5#	100 ± 5
PAP (mm Hg)	120 ± 8	127 ± 4	120 ± 8	128 ± 6
LAP (mm Hg)	9.3 ± 1.5	11.0 ± 1.5	13.8 ± 1.1#	14.0 ± 1.7
CO (L/min)	6.7 ± 0.5#	6.9 ± 0.4#	7.2 ± 0.6#	7.3 ± 0.5#
SVR (dynes-sec cm^{-5})	1321 ± 77#	1363 ± 86#	1181 ± 66*#	1269 ± 64#
PVR (Wood Units)	3.30 ± 0.85#	3.51 ± 0.71#	2.97 ± 0.86#	3.20 ± 0.70#

* Significantly different from baseline at $p < 0.05$.
# Significantly different pre- vs. post-TAH at $p < 0.05$.