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Title : CARDIOPULMONARY EFFECTS OF PROTAMINE IN MAN

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Intravenous administration of protamine following cardiopulmonary bypass (CPB) is widely believed to cause a moderate fall in blood pressure and in PaO₂. Recently, a delayed anaphylactic response to protamine was reported.¹ The literature on protamine is often conflicting.^{2,3} Reports claim that protamine is a negative (positive) inotrope; it decreases (increases) cardiac output, etc.

In this study, we have examined the hemodynamic effects of protamine injection following CPB, compared the effects of rapid vs slow injection, and have recorded the effects of protamine in patients who had received protamine previously.

Methods 20 patients having heart surgery were divided into two groups. The anesthetic (high dose fentanyl) and CPB management, and the use of cardioplegia during aortic cross-clamping were similar for both groups. We followed the Bull⁴ protocol for heparinization and its reversal with protamine. Group 1 (n=10) received intravenous protamine slowly over 5 minutes; while Group 2 (n=10) received intravenous protamine rapidly in less than 0.5 minute. We measured heart rate, mean arterial pressure, mean pulmonary artery pressure, pulmonary artery occluded pressure, thermodilution cardiac output, and arterial and mixed-venous blood gases. We made the first set of measurements when steady-state anesthesia was achieved prior to surgical incision; the second set following successful weaning from CPB prior to the administration of protamine and when cardiovascular stability had been achieved; the third and fourth measurements, 5 minutes and 15 minutes after protamine injection, respectively. From this data we derived several hemodynamic indices.⁵ Changes in cardiopulmonary parameters were considered significant at $p < 0.05$.

Results With slow protamine injection, we noted no significant changes in MAP. CI increased by 24% at 5 minutes but had returned to pre-protamine levels at 15 minutes. LVSWI increased by 39% and 30% at 5 minutes and 15 minutes respectively. We detected no significant changes in HR, right heart performance, PVRI, SVRI, SI and Qs/Qt.

We noted a transient (2 minute) decrease of 10-15% in MAP with fast protamine injection. HR, CI, SI, right heart indices, PVRI, SVRI, and Qs/Qt were not significantly different at 5 minutes and at 15 minutes. LVSWI increased by 33% at 5 minutes, but had returned to baseline by 15 minutes.

Two patients with prior exposure to protamine showed no difference in response.

Discussion The increase in CI and LVSWI and the lack of change in Qs/Qt, SVRI and PVRI following protamine injection is contrary to most published data. There may have been a transient decline in indices 1 minute after protamine but, if so, they were not evident at 5 minutes.

Our data show that protamine has a positive ino-

tropic effect on the myocardium 5 minutes after intravenous injection. It is not a drug to be feared because of its negative hemodynamic or pulmonary effects. There is little to be gained in most instances by slow vs rapid injection. In our limited sample we could detect no increased sensitivity to protamine in patients with prior exposure.

	SLOW INJECTION									
	BEFORE PROTAMINE		5 MIN. AFTER PROTAMINE				15 MIN. AFTER PROTAMINE			
	X	S.E.	X	S.E.	P	%	X	S.E.	P	%
CI	2.54	0.23	3.15	0.25	<0.05	24.02	2.942	0.18	N.S.	
SI	27.32	3.43	35.26	3.30	N.S.		33.84	2.44	N.S.	
RVSWI	4.77	0.92	6.29	1.24	N.S.		5.59	1.22	N.S.	
RVSW/CVPI	0.245	0.06	0.520	0.27	N.S.		0.3210	0.12	N.S.	
LVSWI	22.75	3.07	31.76	3.58	<0.04	39.60	29.53	2.27	<0.05	29.8
LVSW/PAOI	0.700	0.09	0.972	0.13	N.S.		0.8990	0.10	N.S.	
SVRI	572.2	57.4	485.6	43.78	N.S.		506.7	44.51	N.S.	
PVRI	66.15	15.28	53.9	11.74	N.S.		46.20	9.28	N.S.	
Qs/Qt	0.268	0.02	0.2550	0.05	N.S.		0.2210	0.03	N.S.	
HR	97.1	5.32	91.8	5.00	N.S.		89.6	5.37	N.S.	
MAP	78.9	4.51	83.5	4.88	N.S.		83.4	3.06	N.S.	

	FAST INJECTION									
	BEFORE PROTAMINE		5 MIN. AFTER PROTAMINE				15 MIN. AFTER PROTAMINE			
	X	S.E.	X	S.E.	P	%	X	S.E.	P	%
CI	2.56	0.14	2.7050	0.14	N.S.		2.623	0.13	N.S.	
SI	30.48	3.91	34.23	2.47	N.S.		32.19	2.40	N.S.	
RVSWI	3.84	0.98	2.625	0.48	N.S.		3.92	0.80	N.S.	
RVSW/CVPI	0.215	0.06	0.1270	0.02	N.S.		0.203	0.08	N.S.	
LVSWI	22.75	2.60	30.39	3.46	<0.05	33.58	30.65	4.37	N.S.	
LVSW/PAOI	0.988	0.19	1.334	0.19	N.S.		1.134	0.13	N.S.	
SVRI	560.3	56.8	488.5	55.67	N.S.		593.5	46.95	N.S.	
PVRI	51.73	6.71	43.7	7.70	N.S.		46.17	7.14	N.S.	
Qs/Qt	0.2160	0.03	0.31	0.08	N.S.		0.1920	0.03	N.S.	
HR	90.8	8.20	83.0	7.53	N.S.		84.7	6.5	N.S.	
MAP	71.5	5.05	78.9	4.58	N.S.		77.4	2.96	N.S.	

CI = Cardiac Index SI = Stroke Index
 RVSW = Right Ventricular Stroke Work
 Qs/Qt = Intrapulmonary Shunt
 LVSW = Left Ventricular Stroke Work
 PAO = Pulmonary Artery Occluded Pressure
 SVRI = Systemic Vascular Resistance Index
 PVRI = Pulmonary Vascular Resistance Index

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