PULMONARY AND SYSTEMIC BLOOD PRESSURE RESPONSES TO LARGE DOSES OF ALBUMIN MICROSPHERES

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Toxicity of intravenously injected particles for lung scanning depends directly upon the degree of pulmonary vascular-bed occlusion (*1*). Although change in diffusing capacity has been used as an indication of such toxicity, pulmonary artery pressure may double without any change in diffusing capacity and hence provides a more sensitive index of toxicity (*2,3*). We assessed the effect of the newly introduced lung scanning agent, albumin microspheres (*4*), on pulmonary artery pressure and systemic blood pressure in dogs.

METHODS

Eight adult mongrel dogs weighing between 18 and 26 kg were anesthetized using 30 mg/kg sodium pentobarbital administered intravenously; the dogs were ventilated with a cuffed endotracheal tube using a constant-volume ventilator adjusted to maintain the end tidal CO_2 at 5.0–5.5 volumes % measured by an infrared CO_2 analyzer. Mean pulmonary artery and aortic pressures were measured on an Electronics for Medicine recorder using catheters fluoroscopically placed in the main pulmonary artery and aortic arch and connected to strain gages. An electrocardiogram recorded heart rate. One gram of albumin microspheres (3M albumin microspheres) with a mean diameter of 22 microns (approximately 1.4×10^8 particles) was suspended by sonicating for 5 min in 247.5 ml of saline with 2.5 ml of 5% tween 80 added to make a suspension containing approximately 560,000 particles/ml. Before infusion the particles were suspended by manual shaking. Control pressures were recorded and each of five separate increments was infused over 30 sec. Each increment contained 7.15 mg/kg of microspheres in 32.2–46.5 ml, which was 500 times the usual human dose. Pressures were measured 1 min after infusing each increment.

RESULTS

The data in Table 1 subjected to Dunnett's t-test (*5*) shows that although there was a significant rise in pulmonary artery pressure after the infusion of

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TABLE 1. CORRELATION OF MEAN PULMONARY AND AORTIC PRESSURES WITH AMOUNT OF MICROSPHERES INFUSED

	Control pressure		After increment I*		After increment II		After increment III		After increment IV		After increment V	
Dog weight (kg)	Pulmonary	Aortic	Pulmonary	Aortic	Pulmonary	Aortic	Pulmonary	Aortic	Pulmonary	Aortic	Pulmonary	Aortic
18	15	124	16	134	17	141	19	150	21	128	14	81
19	13	131	13	127	15	122	18	95	18	70	15	54
19	14	110	14	133	14	82	12	42	25	51	31	48
20	13	115	14	119	14	118	18	140	20	105	11	47
26	8	117	2	34	2	29	3	33	6	44	8	49
19	11	111	14	129	15	134	16	122	17	64	15	61
18	10	131	11	136	12	136	13	137	14	126	15	90
25	11	111	12	121	14	137	15	118	14	92	13	60
Mean ± s.d.	12±2	119±9	12±4	117±34	13±5	117±39	14±5	105±45	17±6	85±3	15±7	62±16
Level of significance of change from control			None	None	None	None	None	None	0.05	0.05	None	0.05

* Increment contained 7.15 mg/kg body weight.

28.6 mg/kg or 8.2×10^7 of the microspheres, the pulmonary artery pressure in only a single instance reached twice the control value. In contrast to this, mean aortic pressure decreased significantly after the injection of 28.6 mg/kg of the microspheres, while there was no significant change in heart rate.

CONCLUSION

The dose required to elevate pulmonary artery pressure exceeds the usual clinical dose of 0.0143 mg/kg of body weight by a factor of 2,000, showing that there is a wide margin of safety between the clinically recommended dose and toxicity in dogs. The anomalous fall in aortic pressure without undue rise in pulmonary artery pressure suggests that there may be toxic effects of the particles other than mechanical blockade of pulmonary vessels since the pulmonary artery pressure usually increases by a factor of two or more preceding systemic hypotension when inert particles such as barium or glass beads are injected. These findings deserve further investigation and are reminiscent of histamine infusion into the pulmonary artery which causes pulmonary vasoconstriction and systemic hypotension (*6*).

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