Title: EFFECTS OF FENOLDOPAM ON RENAL BLOOD FLOW AND SYSTEMIC HEMODYNAMICS DURING ISOFLURANE ANESTHESIA IN DOGS

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INTRODUCTION

The dopamine 1(DA1) receptor agonist, fenoldopam (FDP), is an effective antihypertensive agent in man (1). FDP acts as a vasodilator while increasing renal plasma flow, glomerular filtration rate (GFR), and sodium excretion (1,2). The natriuresis induced by FDP suggests that it might have a unique role as an agent to induce hypotension during general anesthesia. We investigated the hemodynamic and renal vascular effects of FDP and sodium nitroprusside (SNP) induced hypotension in dogs receiving isoflurane general anesthesia.

METHODS

Ten healthy adult unpremedicated male dogs weighing 10-20 kg were studied. Anesthesia was induced using intravenous surital 15-25 mg/kg. Endotracheal intubation was performed and anesthesia was maintained with 1-1.5 MAC end tidal isoflurane, 60% N2O and 40% O2. Ventilation was controlled to maintain an end tidal CO2 between 30-35 mmHg as measured by an Engstrom-Emma End Tidal CO2 Analyzer. End tidal isoflurane concentration was measured with a Puritan-Bennett End Tidal Anesthetic Agent Analyzer. A catheter was inserted into the left carotid artery for arterial blood pressure measurement and blood gas sampling. A pulmonary artery catheter was placed via the external jugular vein. Pulmonary capillary wedge pressure was maintained between 8-11 mmHg with infusion of 0.9% normal saline through a large bore peripheral intravenous catheter. The electrocardiogram and pulmonary artery blood temperature were recorded continuously; the latter was maintained between 36-37• C using humidified gases and a heating blanket. Through a flank incision, an electromagnetic pulse doppler flow probe (Narco) was secured around the left renal artery with care to avoid vessel constriction. Thirty minutes after completion of the surgical preparation, control measurements (renal blood flow [RBF], heart rate [HR], systolic and diastolic arterial blood pressure [SBP and DBP], cardiac output [CO], central venous pressure[CVP] and pulmonary capillary wedge pressure [PCWP]) were recorded. Dogs were then randomly assigned to groups receiving either FDP or SNP as the initial drug. Either drug was infused intravenously to produce a 25-30% decrease in mean arterial pressure [MAP], and 15 minutes later hemodynamic variables were recorded as before. Thirty minutes later, after discontinuation of the drug, new control values were obtained before infusion of the second drug. MAP was calculated as 1/3(SBP-DBP)+DBP and renal vascular resistance [RVR] as RBF/MAP. Systemic and pulmonary vascular resistance[SVR and PVR] were calculated using standard formulae. For each variable, the percent change from baseline was calculated for infusion of both SNP and FDP. Values for SNP vs FDP were compared using a paired t test with p<.05 as the cutoff for statistical significance.

RESULTS

Baseline MAP was 91±5 mmHg prior to FDP and 92±6 mmHg prior to SNP. Hypotension was easily obtained in all ten dogs using either SNP or FDP. The absolute values for MAP with hypotension: 67±8 (FDP) and 64±6 (SNP) mmHg were not significantly different. These values represent a percent decrease from baseline of 26±9% and 30±6% respectively (NS). Significant decreases in systemic vascular resistance but no significant changes in cardiac output occurred with either drug(Table). Renal blood flow (RBF) decreased 23±15% compared to baseline for SNP and decreased 7±14% for FDP. This difference was statistically significant (p<.001). The percent change in renal vascular resistance was -19±13% for FDP and -7±21% for SNP (p<.02). Percent changes from baseline were not significantly different for any of the other measured variables. The average dose administered during intravenous infusion was 6±2 µg/kg/min for both FDP and NTP.

DISCUSSION

Fenoldopam causes selective vasodilatation in renal, cerebral, coronary, and mesenteric vessels. Our data show that FDP is more likely to preserve RBF during deliberate hypotension while SNP fails to do so at similar levels of MAP. Preserving RBF during induced hypotension is a unique advantage of FDP and suggests that it may be clinically useful.

Fenoldopam N=10

	Control	FDP	%Δ vs control
HR(bpm)	113±12	113±16	.4±8
SBP(mmHg)	116±8	96±9†	-17±8
DBP(mmHg)	78±5	53±11†	-32±12
MAP(mmHg)	91±5	67±8†	-26±9
CO(l/min)	3.64±.65	3.79±.50	6±15
RBF(ml/min)	214±50	197±50	-7±14¶
RVR	.44±.12	.35±.07‡	-19±13§
PCW(mmHg)	12±3	11±2	-7±10
SVR	1814±400	1214±220†	-31±16

Sodium nitroprusside N=10

	Control	SNP	%Δ vs control
HR(bpm)	117±11	118±11	.8±6
SBP(mmHg)	119±8	95±13†	-20±9
DBP(mmHg)	79±7	49±6†	-38±7
MAP(mmHg)	92±6	64±6†	-30±6
CO(l/min)	4.02±.79	4.04±.86	3±29
RBF(ml/min)	223±55	167±37††	-23±15
RVR	.45±.15	.40±.11	-7±21
PCW(mmHg)	11±2	11±2	-2±17
SVR	1652±237	1127±325‡	-30±24

*p<.001 vs control ¶ p<.001 vs % Δ from baseline for SNP
†p<.001 vs control § p<.02 vs % Δ from baseline for SNP
‡p<.005 vs control ††p<.002 vs control

REFERENCES
1. Goldberg LI: Dopamine receptors and hypertension: Physiologic and pharmacologic implications. Am J Med 77:37-44, 1984
2. Goldberg LI, Rajfer SI: Dopamine receptors: Applications in clinical cardiology. Circ 72:245-248, 1985