Title: THE REGIONAL HEMODYNAMIC EFFECTS OF INDUCED HYPOTENSION WITH ISOFLURANE, SODIUM NITROPRUSSIDE OR 2-CHLOROADENOSINE

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Introduction. General anesthetics alter cardiac output (CO), systemic vascular resistance (SVR) and regional hemodynamics. Deliberate hypotension, when added to a background anesthetic, may further impair regional perfusion, but the effects may be unique for each hypotensive drug. This study reports the regional hemodynamic changes produced by three hypotensive techniques. Results are compared to an anesthetized normotensive control group.

Methods. 25 male Sprague-Dawley rats, (362±9g; Mean ± SEM) were anesthetized with isoflurane. The femoral artery, vein and left ventricle were cannulated and tracheostomy was performed. Anesthesia was maintained with isoflurane, 1.4% (ISO), and ventilation was controlled (FIO_2 0.3 in N_2). Body temperature was maintained at 36±1°C. After a 30 min stabilization period, rats were divided into four groups: control (ISO), 2-chloroadenosine (ISO + 2AD), deep isoflurane (dISO) and sodium nitroprusside (ISO + SNP). Hypotension to a mean arterial pressure (MAP) of 50 mmHg was maintained for 30 min prior to measurement of cardiac output (CO) and organ blood flow using radiolabelled microspheres and the reference sample technique. Arterial blood gases and hematocrits were determined also. Individual organ blood flows were calculated using standard formulae. Statistical analysis was by ANOVA and Duncan's Multiple Range Test; $p<0.05$ was considered to be significant.

Results. The $PaCO_2$ and pH were similar in all groups; PaO_2 was greater with SNP treatment. The results for systemic and regional hemodynamic measurements are summarized below (Table). With each drug, the decrease in MAP was due to a reduction in systemic vascular resistance (SVR) ($p<0.05$) rather than CO. In addition, SVR decreased more with 2AD than with dISO ($p<0.05$). During hypotension heart rate (HR) was decreased with 2AD ($p<0.05$). Organ blood flows, when compared with ISO, were unchanged in the brain and gastrointestinal tract (GIT), increased in the heart and decreased in the kidney and liver. Coronary blood flow increased more with SNP than with dISO. Cerebral vascular resistance was decreased both with dISO and SNP. All three drugs decreased coronary vascular resistance, with 2AD having a greater effect than dISO.

Discussion. The changes measured in HR, CO and SVR are similar to those observed in humans.[1] Results among the hypotensive techniques cannot be explained by differences in MAP, $PaCO_2$ or background anesthetic. The cerebral blood flow was unchanged during hypotension although the MAP was below the lower limit of autoregulation.[2] A 60% reduction in cerebral blood flow was reported with deep isoflurane anesthesia in dogs, but those results were compared with values obtained during minimal anesthesia rather than a background of stable anesthesia as used in the present study.[3] All three drugs were profound coronary vasodilators as evidenced by decreases in vascular resistance and increases in myocardial blood flow. Myocardial O_2 demand, as estimated by HR and MAP, should have decreased suggesting a favourable O_2 supply/demand balance. These results indicate that renal blood flow is significantly impaired by deliberate hypotension and these organs may be at risk for ischemia with any hypotensive technique. Further, total hepatic flow is specifically impaired by 2AD, suggesting that the liver may be at risk for ischemia during deliberate hypotension produced by this drug.

Table

	ISO (n=6)	SNP (n=7)	dISO (n=6)	2AD (n=6)
MAP(mmHg)	81± 7	53± 3*	50±.5*	50± 2*
HR (bpm)	371±17	387±17	367± 3	248±14
CO	104± 9	103± 8	88±11	122± 6
SVR	.78±.02	.53±.03**	.60±.06**	.42±.03**α
Organ blood flows ($ml \cdot min^{-1} \cdot 100g^{-1}$)				
BRAIN	148±15	132±15	140±12	118±10
HEART	279±33	681±122**α	340±36*β	629±82**α
KIDNEY	415±38	267±40**	261±30**	281±12**
GIT	116± 9	111±10	90±11	88± 7
LIVER	112± 6	90± 4	95±12	76± 4**
Organ vascular resistances ($mmHg \cdot ml^{-1} \cdot min \cdot g$)				
BRAIN	56± 6	40± 3*	37± 3**	45± 5
HEART	29± 1	9± 2**	14± 1**β	9± 1**
KIDNEY	20± 1	21± 2	20± 2	18± 1
GIT	61± 4	42± 6	48± 7	49± 67
LIVER	368±47	408±67	459±94	42±42

Means ± SEM. *p<0.05 **p<0.01 from control
α p<0.05 from dISO; β p<0.05 from 2AD

Units: CO, $ml \cdot min^{-1}$; SVR, $mmHg \cdot ml^{-1} \cdot min$

References.

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