Title: REGIONAL CEREBRAL BLOOD FLOWS DURING DELIBERATE HYPOTENSION COMPLICATED BY HEMORRHAGE

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Introduction: Controlled hypotension is employed intraoperatively to reduce blood loss and improve operating conditions. However, in procedures with major blood loss, hypovolemia may complicate induced hypotension and increase the risk for organ ischemia. Sodium nitroprusside (SNP), deep isoflurane (dISO) or adenosine have been used to produce deliberate hypotension. This study was designed to evaluate the effect of hemorrhage on regional cerebral blood flow (rCBF) during hypotension induced with dISO, SNP, or 2-chlorodenosine (2AD).

Methods: 24 male Sprague-Dawley rats (360±6 gm) were divided into four groups: control (ISO) and those receiving SNP, 2AD, or dISO. All animals were anesthetized with isoflurance (inspired concentration 1.4 vol%) and ventilated (FIO_2=0.3). Body temperature was kept constant between 36 and 37°C. Cannulae were placed in a femoral artery and vein and the left cardiac ventricle. After a 30 min stabilization period the mean arterial blood pressure (MAP) was decreased in the treated groups to 50±2 mmHg by infusion of SNP, 2AD, or by increasing the inspired concentration of isoflurane (steady state = 3.8 vol%). After 10 min of hypotension, the treated groups were hemorrhaged by removing 20% of estimated blood volume over 5 min. The hypotensive agents were continued throughout hemorrhage and a subsequent 10 min stabilization period. Radiolabeled microspheres (^{141}Ce) were then injected into the left ventricle; cardiac output (CO) and blood flows to 8 areas of brain were measured using the reference sample technique. Arterial blood gases and hematocrits were measured also. Heart rate (HR) and MAP were measured throughout. Results were analyzed by ANOVA and Duncan's Multiple Range test; $p<0.05$ was considered to be significant.

Results: Hemodynamic results among the treated groups are summarized in the table. $PaCO_2$ (33±2 mmHg), PaO_2 (108±7 mmHg), and hematocrits (34±1%) were similar in all groups. HR was similar during dISO and ISO but greater during SNP and less during 2AD. After hemorrhage, MAP in all treated groups was less than ISO, but MAP was greater in those receiving SNP or 2AD as compared with dISO. CO was less during 2AD or dISO than during SNP or ISO. Hemorrhage during hypotension induced with dISO or 2AD resulted in significantly decreased blood flows to all regions of the brain when compared with hemorrhage during SNP or ISO.

Discussion: Unpublished data from our laboratory show no differences in rCBF during induced hypotension to 50 mmHg with SNP, 2AD, or dISO. The current study demonstrates significant differences in rCBF when hypotension is complicated by hemorrhage. Because the MAP of our animals was below the limit of cerebral blood flow autoregulation[1] it was expected that rCBF would decrease as MAP decreased during hemorrhage. However, our results indicate that hemorrhage alters rCBF variably depending upon the hypotensive technique. Hemorrhage decreased rCBF to all areas of the brain during 2AD when compared with SNP despite similar arterial pressures. Because deep isoflurane decreases cerebral metabolism,[2] brain O_2 supply-demand balance might be better preserved with dISO than with 2AD despite similar rCBF. Indeed, there is evidence that brain O_2 tension and energy charge are greater during deliberate hypotension with dISO as compared with other hypotensive techniques.[3,4] SNP preserves rCBF to all areas of the brain more effectively than dISO or 2AD when deliberate hypotension is complicated by hemorrhage. However, the effects of a decrease in rCBF with dISO may be, at least in part, offset by the depression of brain O_2 demand by dISO.

Table

	SNP (n=6)	2AD (n=6)	dISO (n=6)
HR	442±24	296±16**	357±19¥,**
MAP(mmHg)	58±5	47±6	33±1¥,**
CO ($ml \cdot min^{-1}$)	100±7	76±9	62±4**
BLOOD FLOW ($ml \cdot min^{-1} \cdot 100g^{-1}$)			
Cortex	156±17	93±15*	82±22**
Hippocampus	129±32	64±11*	53±2**
Striatum	135±21	66±14**	63±5**
Thalamus	173±36	95±19*	88±7*
Hypothalamus	112±20	58±13*	51±6**
Cerebellum	238±34	112±23**	96±14**
Colliculi	241±42	117±12**	112±7**
Brain Stem	231±30	104±16**	115±8**
Total Brain	175±24	90±15**	81±7**

All values mean ± SE
*p<0.05; **p<0.01 (dISO or 2AD vs SNP);
¥p<0.05 (dISO vs 2AD)

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