TITLE: THE SPINAL BLOOD FLOW EFFECT OF SUBARACHNOID CLONIDINE

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INTRODUCTION: Subarachnoid clonidine, an alpha-2 adrenergic agonist, appears to be more effective than epinephrine in prolonging the duration of sensory blockade which follows tetracaine spinal anesthesia.[1] Although spinal vasoconstriction could explain this observation (delayed vascular absorption of tetracaine) and intravenous clonidine reduces cerebral blood flow substantially,[2] it is not known whether intrathecal clonidine produces spinal vasoconstriction. Accordingly, we speculated that subarachnoid clonidine reduces spinal cord blood flow (SCBF) and studied its effect in conscious animals.

METHODS: Male Sprague-Dawley rats were prepared 24-48 h in advance with polyethylene (PE 10) lumbar subarachnoid catheters. These were inserted through the cisternal membrane and advanced caudad until the tip lay near the lumbar enlargement. On the day of the experiments, the animals were reanesthetized briefly with halothane-N_2O for femoral artery and vein catheterization and were immobilized partially with a pelvic plaster cast. Animals were then allowed at least 2 h to recover before experiments were begun.

The animals were divided into four groups: Group 1 (n = 5) rats received only saline intrathecally (i.t.), while Groups 2 (n = 5) and 3 (n = 7) received clonidine, 100 nM and 400 nM i.t., respectively. All i.t. drugs were administered in 10 ul of saline followed by an additional 10 ul to flush the catheter. To control for a possible effect of systemic absorption, four additional animals (Group 4) with subarachnoid catheters received clonidine 400 nM intravenously (i.v.). Standard physiologic variables, including rectal temperature, mean arterial blood pressure (MAP), and blood gases and pH were monitored. Analgesia was evaluated with the tail-flick test.

Local SCBF was measured autoradiographically with the iodo-[^{14}C]antipyrine method[3] in the lumbar spinal cord 15-20 min after drug administration. Optical density measurements of the autoradiographs were made with the aid of a computerized image-processing system and local SCBF calculated according to the operational equation of the method.[3] Statistical analysis of the data was performed with Dunnett's test for multiple comparisons.

RESULTS: MAP was higher than control in Group 3 animals (136 ± 6 vs. 118 ± 4 mmHg, $P < 0.05$). Intravenous administration of clonidine also increased MAP (140 ± 6 mmHg, $P < 0.05$). As anticipated, the latency of the tail-flick response was prolonged approximately 30% and 50%, respectively, in Groups 2 and 3.

Clonidine reduced SCBF in all spinal regions examined (Table). Profound spinal vasoconstriction occurred in Group 2 animals; flow in gray matter was only 51-62% of control. Higher dose clonidine (Group 3) also reduced SCBF, but the effect was less marked (16-29% decrease in gray matter flow) and not statistically significant in all regions. In addition, the SCBF effect of this dose given i.v. was not significantly different from its i.t. effect (Group 4, data not shown). While MAP was higher in Groups 3 and 4, no correlation between MAP and SCBF was evident.

Table

BLOOD FLOW ($ml.100g^{-1}.min^{-1}$)

	Group 1 (5)	Group 2 (5)	Group 3 (7)
Gray Matter			
Lamina(e) I-III	68 ± 6	42 ± 6 †	45 ± 3 †
IV-VI	110 ± 9	65 ± 8 †	87 ± 5
VII	136 ± 12	73 ± 10 †	113 ± 7
VIII	127 ± 11	69 ± 9 †	102 ± 7
IX	117 ± 11	60 ± 7 †	83 ± 6 *
White Matter			
Dorsal	23 ± 2	19 ± 1 *	19 ± 2 *
Lateral	40 ± 2	26 ± 4 *	22 ± 2 †
Ventral	33 ± 3	21 ± 2 †	20 ± 2 †

Data are mean ± SEM; * $P < 0.05$, † $P < 0.01$

DISCUSSION: We conclude that intrathecal clonidine causes spinal vasoconstriction and speculate that this accounts for its ability to prolong tetracaine spinal anesthesia. In fact, clonidine may be more effective in this regard than epinephrine because the latter does not decrease SCBF but rather prevents local anesthetic-induced vasodilation. Our studies do not support a dose-response relationship for clonidine, however, and suggest either that the high dose altered SCBF partially by systemic absorption or that i.v. and i.t. administration produce similar SCBF effects. In addition, it seems unlikely that the higher perfusion pressure in Groups 3 and 4 affected the results because i.v. clonidine does not impair cerebral autoreguation[2] and there was no correlation between SCBF and MAP. Finally, since there is no evidence that clonidine produces spinal neurotoxicity,[4] decreases in SCBF of this magnitude are evidently well tolerated.

References

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