

3. Chiang J, Kowada MD, Ames A III et al: Cerebral ischemia. III Vascular changes. *Am J Pathol* 52: 455-476, 1968
4. Olsson Y, Hossmann K-A: The effect of intravascular saline perfusion on the sequelae of transient cerebral ischemia. *Acta Neuropathol* 17: 68-79, 1971
5. Salzman EW: Prostaglandins, cyclic AMP, and platelet function. *Thromb Diath Haemorrh Suppl* 60: 311-319, 1974
6. McGiff JC: Prostaglandins as regulators of blood pressure. *Hosp Pract* 10(4): 101-112, 1975
7. Flower RJ: Drugs which inhibit prostaglandin biosynthesis. *Pharmacol Rev* 26: 33-67, 1974
8. Reivich M, Jehle J, Sokoloff L et al: Measurement of regional cerebral blood flow with ¹⁴C-antipyrine in awake cats. *J Appl Physiol* 27: 296-300, 1969
9. Eklöf B, Lassen NA, Nilsson L et al: Regional cerebral blood flow in the rat measured by the tissue sampling technique; a critical evaluation using four indicators ¹⁴C-antipyrine, ¹⁴C-ethanol, H³-water and ¹³³Xenon. *Acta Physiol Scand* 91: 1-10, 1974
10. Vlahov V, Betz E: Effects of indomethacin and D600 on the smooth muscles of pial vessels. In Cervós-Navarro J (ed) *Pathology of Cerebral Microcirculation*. Berlin, de Gruyter, pp 130-136, 1974
11. Pickard JD, Vinall PE, Simone FA: Prostaglandins and cerebral vasospasm: a problem of interpretation. *Surg Forum* 26: 496-498, 1975
12. Pickard JD, MacDonell LA, Mackenzie ET et al: Response of the cerebral circulation in baboons to changing perfusion pressure after indomethacin. *Circ Res* 40: 198-203, 1977
13. Vlahov V: The role of prostaglandins in regulation of cerebral vessel wall reactivity. In Cervós-Navarro J, Betz E, Matakas F et al (eds) *The Cerebral Vessel Wall*. New York, Raven Press, pp 143-147, 1976
14. Pickard JD, Mackenzie ET: Inhibition of prostaglandin synthesis and the response of baboon cerebral circulation to carbon dioxide. *Nature (New Biol)* 245: 187-188, 1973
15. Olesen J: Cerebral blood flow methods for measurement regulation, effects of drugs and changes in disease. *Acta Neurol Scand* 50 (Supp 57): 67, 1974
16. Jonsson HT Jr, Daniell HB: Altered levels of PGF in cat spinal cord tissue following traumatic injury. *Prostaglandins* 11: 51-61, 1976
17. Yamamoto YL, Feindel W, Wolfe LS et al: Experimental vasoconstriction of cerebral arteries by prostaglandins. *J Neurosurg* 37: 385-397, 1972
18. Hamberg M, Svensson J, Samuelsson B: Thromboxanes: a new group of biologically active compounds derived from prostaglandin endoperoxides. *Proc Nat Acad Sci USA* 72: 2994-2998, 1975
19. Moncada S, Gryglewski R, Bunting S et al: An enzyme isolated from arteries transforms platelet endoperoxides to an unstable substance that inhibits platelet aggregation. *Nature (London)* 263: 663-665, 1976
20. Furlow TW Jr, Bass NH: Stroke in rats produced by carotid injection of sodium arachidonate. *Science* 187: 658-660, 1975
21. Heuser D, Fieschi C, Volante F: Platelet emboli and focal cerebral ischemia: an experimental study on the circulatory and metabolic effects of intracarotid infusion of ADP and arachidonic acid in rabbits. In Cervós-Navarro J, Betz E, Matakas F et al (eds) *The Cerebral Vessel Wall*. New York, Raven Press, pp 149-156, 1976
22. Saeed SA, McDonald-Gibson WJ, Cuthbert J et al: Endogenous inhibitor of prostaglandin synthetase. *Nature (London)* 270: 32-36, 1977
23. Osburne RC, Halsey JH: Cerebral blood flow: a predictor of recovery from ischemia in the gerbil. *Arch Neurol* 32: 457-461, 1975
24. Heiss WD, Hayakawa T, Waltz AG: Patterns of changes of blood flow and relationships to infarction in experimental cerebral ischemia. *Stroke* 7: 454-459, 1976

Ergotamine and Cerebral Blood Flow

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SUMMARY We measured the cerebral blood flow (CBF) of 16 patients by the xenon-133 intracarotid method before and after the intramuscular injection of ergotamine tartrate. The regional and hemispheric CBF was unaltered, even in 3 migraineurs in whom ergotamine relieved the headache. Ergotamine tartrate in therapeutic doses has no effect on the cerebral circulation.

EVIDENCE for an ergotamine effect on the cerebral circulation is indirect and contradictory; therefore, we measured cerebral blood flow (CBF) directly, before and after the administration of therapeutic doses of ergotamine tartrate.

Methods

Regional cerebral blood flow (rCBF) studies¹ were carried out prior to clinically indicated carotid arteriography in 16 patients. Their age, sex and diagnosis are listed in the table. Although cases 5, 6, 8, 10 and 11 were investigated because of suspected brain disease, no brain lesions were demonstrated; hence these patients were, in effect, non-migrainous controls. Informed consent was obtained in all cases. Three millicuries of xenon-133 were injected through an indwelling catheter into the internal carotid artery. The intracarotid catheter was also used for mean arterial blood pressure (MABP) measurements and arterial blood gases analysis. The clearance rate of the isotope, and hence the rCBF, was measured by 16 extra-

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TABLE 1 Cerebral Blood Flow Before and After Ergotamine Tartrate

Patient	Age	Sex	Diagnosis	Paco ₂ (mm Hg)		MABP (mm Hg)		CBF (ml/100g/min)		CBF corrected to Paco ₂ of 40 (mm Hg)	
				B	E	B	E	B	E	B	E
1	52	M	Normal pressure hydrocephalus	46	47	75	85	38	38	29	28
2	49	F	Dementia	40	41	80	100	40	40	40	39
3	53	M	Parasagittal meningioma	42	41	90	90	58	61	53	59
4	62	M	L. temporal glioma	36	29	55	75	35	27	42	43
5	28	M	Temporal lobe epilepsy	43	44	85	100	54	55	47	46
6	46	M	Temporal lobe epilepsy	43	44	85	85	58	61	51	52
7	57	M	L. cerebral infarct	40	41	110	115	57	60	57	58
8	61	M	TIA (R. hemiparesis)	43	47	130	140	41	46	36	34
9	55	M	R. hemisphere infarct (minimal)	43	47	135	135	47	51	42	38
10	68	F	R. arm weakness	54	50	75	75	47	45	26	29
11	43	M	Suspected brain tumor	42	43	115	115	84	89	77	78
12	59	F	L. parietal angioma	34	33	140	140	41	47	53	63
13	65	F	Progressive supranuclear palsy	40	39	125	130	42	37	42	39
14	18	F	Migraine	34	31	115	120	63	64	81	91
15	38	M	Migraine	37	35	110	110	48	46	54	56
16	24	M	Migraine	38	36	80	80	48	43	52	51
Mean				41	41	100	106	50	51	49	50
Standard Deviation				5	6	25	23	12	15	15	17

Paco₂ = partial arterial pressure of carbon dioxide; MABP = mean arterial blood pressure; CBF = mean hemispheric cerebral blood flow; CBF corrected = equivalent mean hemispheric cerebral blood flow at a Paco₂ of 40 mmHF according to the formula of Olesen, et al.³; B = baseline; E = post-ergotamine.

There was no statistically significant difference between any of the baseline and post-ergotamine variables (*t*-test for paired observations).

cranial probes, and expressed as CBF_{initial}² (milliliters of blood per 100 grams of brain per minute). rCBF studies were carried out before and 15–20 minutes after an intramuscular injection of 0.2–1.0 mg of ergotamine tartrate. Thus each patient served as his own control.

Results

Ergotamine tartrate did not change the focal cerebral blood flow in any of the patients. Three migraineurs received the drug during the headache phase with relief of pain, but no change in rCBF.³ The mean hemispheric CBF value showed a slight rise after ergotamine tartrate injection, but this rise was not statistically significant (table).

Discussion

Observations of the effect of ergotamine on cerebrospinal fluid pulsatility,⁴ retinal vessels,^{5, 6} and carotid angiograms,⁷ as reflections of CBF, have been equivocal. Lennox et al.⁸ reported that ergotamine increased CBF; however, their data were obtained from thermoelectric flowmeter studies of the internal

jugular vein, an indirect and unreliable way of estimating CBF. Shenkin,⁹ by using the nitrous oxide method, found reduced CBF after ergotamine; but his high control values for CBF and his failure to note Paco₂ suggest that these data, too, may be unreliable. Using the more reliable intracarotid xenon-133 method, Simard and Paulson¹⁰ demonstrated that 1 mg of ergotamine, given intravenously, had no effect on rCBF during a prolonged migranous aura, nor 3 months later, when the patient was asymptomatic. The present study suggests, further, that ergotamine tartrate in therapeutic doses has no effect on CBF during the symptomatic headache phase of migraineurs, nor on the cerebral circulation of non-migraneurs.

Since we did not measure rCBF in the vertebrobasilar circuit, we cannot rule out an effect of ergotamine on this area of blood flow.

References

1. Lassen NA, Ingvar DH: Radioisotopic assessment of regional cerebral blood flow, pp 376–409. *In* Potchen EV, McCready VP (eds) Progress in Nuclear Medicine. Baltimore, University Park Press, 1972

2. Olesen J, Paulson OB, Lassen NA: Regional cerebral blood flow in man determined by the initial slope of the clearance of the intraarterially injected ^{133}Xe . *Stroke* **2**: 519-540, 1971
3. Hachinski VC, Norris JW, Cooper PW et al: Migraine and the cerebral circulation, pp 11-15. *In* Green R (ed) *Current Concepts in Migraine Research*. New York, Raven Press, 1978
4. Graham JR, Wolff HG: Mechanisms of migraine headache and action of ergotamine tartrate. *Res Publ Assoc Res Nerv Ment Dis* **18**: 638-669, 1938
5. Dalessio DJ: *Wolff's Headache and Other Head Pain*. Third Edition. New York, Oxford University Press, 1972
6. Joffe SN: Retinal blood-vessel diameter during migraine. *Eye Ear Nose Throat Monthly* **52**: 58-66, 1973
7. Friedman AP, Feiring E, Davidoff LM et al: Arteriographic study of drugs on intracranial vessel in patients with chronic headache. *Arch Neurol Psychiat* **62**: 818-822, 1949
8. Lennox WG, Gibbs EL, Gibbs FA: Effect of ergotamine on the cerebral circulation of man. *J Pharmacol* **53**: 113-119, 1935
9. Shenkin HA: Effects of various drugs upon cerebral circulation and metabolism in man. *J Appl Physiol* **3**: 465-471, 1951
10. Simard D, Paulson OB: Cerebral vasomotor paralysis during migraine attack. *Arch Neurol* **29**: 207-209, 1973

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