

FRANZ, D.N., HARE, B.D. & NEUMAYR, R.J. (1978). Depression of sympathetic preganglionic neurones by clonidine. Evidence for stimulation of 5-HT receptors. *Clin. Exp. Hypertens.*, **1**, 115-140.

YAKSH, T. L. & RUDY, T.A. (1976). Chronic catheterization of the spinal subarachnoid space. *Physiol. Behav.*, **17**, 1031-1034.

Effect of dihydroergotamine on the arteriovenous oxygen content difference and shunting of 15 μ m microspheres over the cranial circulation of the cat

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Dihydroergotamine (DHE) is a potent antimigraine drug used for treatment of the acute attack as well as in migraine prophylaxis. The beneficial effect of DHE in migraine is generally attributed to its vasoconstrictor action. Vascular changes, dilatation of the cranial arteries in particular, have been strongly implicated in the pathogenesis of the migraine headache (Dalessio, 1972). Opening up of arteriovenous anastomoses or shunts, which are normally occurring pre-capillary communications between the arteriolar and venular side of the circulation, has been proposed by Heyck (1969) as the basic derangement underlying the migraine attack. In order to support this hypothesis, Heyck measured in 7 migraine patients the arteriovenous oxygen content difference (CavO_2) over the

lowed by subsidence of headache resulted in a significant increase in CavO_2 (from 0.64 ± 0.58 to 2.26 ± 0.74 mmol/l).

We studied the effect of DHE on the CavO_2 over the cranial circulation of the cat and were able to confirm Heyck's observation (Table 1). Although DHE also decreased the shunting of 15 μ m microspheres (Table 1), the changes in the above two parameters were not correlated which suggested that the CavO_2 is not an index of the proportion of carotid blood flow shunted through the arteriovenous anastomoses (PSFr). This notion was further supported by the observation that no correlation existed between the base-line values of the two parameters ($r_s = -0.14$, $n = 8$).

The mode of action of DHE as demonstrated by the use of 15 μ m microspheres, which by their size become trapped in the tissue capillaries but pass through most arteriovenous anastomoses to enter the venous circulation, supports the concept of a primary involvement of arteriovenous anastomoses in the hemodynamic changes underlying the migraine headache. However, the lack of correlation between the shunting of microspheres and the CavO_2 sheds doubt on the validity of Heyck's assumption that the CavO_2 is an index of PSFr.

Table 1 The effect of dihydroergotamine on the arteriovenous oxygen content difference (CavO_2) and shunting of 15 μ m microspheres (PSFr) over the cranial circulation of the cat

	Base-line Values ($n = 16$)	Saline ($n = 24$)	Dihydroergotamine ($n = 8$)		
			5	10	20 μ g/kg
CavO_2 (mmol/l)	0.81 ± 0.09	0.89 ± 0.07	1.07 ± 0.10	$1.37 \pm 0.12^*$	$1.73 \pm 0.20^*$
PSFr (%)	35.1 ± 4.9	31.8 ± 1.8	27.5 ± 5.3	22.3 ± 4.2	$16.2 \pm 3.1^*$

Mean \pm s.e. mean; * $P \leq 0.05$, two-tailed Wilcoxon rank sum test vs. saline.

cranial circulation by sampling blood from the external jugular vein assuming it to be an index of fractional shunting. The CavO_2 amounted to significantly less on the side of the headache (0.76 ± 0.44 mmol/l) as compared to the non-diseased side (1.78 ± 0.76 mmol/l). Furthermore, administration of DHE fol-

References

- DALESSIO, D.J. (1972). *Wolff's Headache and other Head Pains*. New York: Oxford University Press.
HEYCK, H. (1969). Pathogenesis of migraine. *Res. Clin. Stud. Headache*, **2**, 1-28.