Effect of nicergoline on cerebral blood flow

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SUMMARY Cerebral blood flow (CBF) was measured before and after intravenous injection of the cerebral vasodilator nicergoline in 13 patients with cerebrovascular disease. CBF increased in seven. The possibility that the effect of the drug in the remainder may have been masked by a fall of CBF which occurs during sequential measurement of patients at rest is discussed.

Nicergoline (1, 6-dimethyl-8 beta- (5-bromonico-
tinoyl-oxymethyl) -10 alpha-methoxy-ergoline) is
an alpha-adrenergic receptor blocking agent
(Arcari *et al.*, 1968) which affects cerebral blood
flow by reducing cerebrovascular resistance (Benzi
et al., 1971). The present study was undertaken to
assess the acute effect of the drug on cerebral
blood flow and blood pressure in patients with
cerebrovascular disease.

Methods

Thirteen patients (10 with multi-infarct dementia
of moderate degree and three with transient
ischaemic attacks) gave informed consent to
measurement of cerebral blood flow before and
after intravenous injection of 2 mg nicergoline,
using the intracarotid ¹³³Xenon technique de-
veloped by Wilkinson *et al.* (1969). The studies
were performed under general anaesthesia before
cerebral angiography carried out for diagnostic
purposes. Anaesthesia was induced by methohexi-
tone and acoline, and maintained by nitrous oxide
and oxygen supplemented by phenoperidine.
Cerebral blood flow was estimated from the slope
of the first two minutes of the semilogarithmic
display of the clearance curve described by
Olesen *et al.* (1971). PaCO₂ and blood pressure
were monitored throughout. A first estimation of
cerebral blood flow was made not less than 30
minutes after induction of anaesthesia. A second
estimation was made 30 minutes after the first at
varying times after intravenous injection of
nicergoline.

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Results

Cerebral blood flow was measured at times
ranging from two to 20 min after intravenous in-
jection of 2 mg nicergoline; the results are given in
the Table. In no case did the PaCO₂ vary by more
than 2.0 mmHg between the pre- and post-
injection measurements of cerebral blood flow.
Blood pressure fell by not more than 10 mmHg
in all but one case in which it rose by 10 mmHg.
The cerebral blood flow showed an increase in
seven cases, a decrease in four, and was unchanged
in two.

Discussion

The finding in seven out of 13 cases of an increase
in cerebral blood flow, without significant change

Table Cerebral blood flow before and after 2 mg
nicergoline intravenously

Patient	Time after nicergoline of second CBF measurement (min)	Cerebral blood flow		
		Before nicergoline	After nicergoline	% change
1	2	35.3	43.7	+23
2	2	24.6	20.3	-20
3	2	23.0	20.5	-9
4	10	31.7	47.8	+50
5	10	43.9	44.5	+2
6	10	23.4	20.3	-13
7	10	27.0	34.9	+30
8	10	19.6	19.6	0
9	12	37.3	51.3	+38
10	15	16.0	19.4	+19
11	20	30.8	21.0	-32
12	20	35.1	41.0	+17
13	20	25.9	25.4	0

Cases 3, 4, and 9 had transient ischaemic attacks; the remainder had
dementia.

in blood pressure or PaCO_2 , clearly indicates a cerebral vasodilator action of nicergoline in those cases. This action was obtained despite the presence of cerebrovascular disease in these patients.

Previous work in our laboratory indicates that the effect of nicergoline may have been greater than is demonstrated in these results (Palmer *et al.*, 1977). In sequential measurements of cerebral blood flow at an interval of about 30 minutes under the general anaesthetic regime used in the present study, there was a fall in flow at the second measurement ranging from 0 to 46% (mean 24%) in a series of 11 patients. Even under local anaesthesia an average reduction of 10% (range 0 to 27) at the second measurement of cerebral blood flow was evident in a series of 20 patients unless psychological activation continued throughout the period of study. This sequential fall may obscure part, or all, of any rise in cerebral blood flow caused by an administered pharmacological agent. The concept of the 'steady state' which has hitherto been restricted to physiological parameters such as PaCO_2 and blood pressure must be extended to include the degree of activation of the brain. Studies of the effect of pharmacological agents must take into account the fall in cerebral blood flow during sequential measurements unless the brain is activated. Without attention to this point the effect of drugs on cerebral blood flow may well be underestimated.

The findings of the present study, therefore,

indicate that nicergoline can produce an appreciable short-term increase of cerebral blood flow in patients with established cerebrovascular disease.

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