Retinal Bloodvessel Diameter During Migraine*

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SUMMARY

The diameters of retinal arterioles were measured from fundal photographs during the interphase, prodrome and headache phase of migraine and on administration of ergotamine preparations. The 5 patients selected experienced visual phenomena with their migraine. During the total investigative period no variation in diameter of retinal vessels or any other changes were noted in their retinae.

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Accumulated evidence over the years has led to the classical vascular theory as being the cause of migraine. The prodrome or first phase is due to vasoconstriction of the internal carotid artery system resulting in ischaemia. The second phase of migraine, consisting of a throbbing headache, is associated with vasodilation predominantly of the extracranial vessels. This vasodilation and increase in arterial pulse pressure on the side of the headache have been demonstrated experimentally, and the use of vasoconstrictors such as ergotamine and its derivatives usually leads to a relief of symptoms.[1]

Blau and Davis[2] examined the conjunctival vascular responses by slit-lamp microscopy in migraine subjects and found that the headache could be associated with either conjunctival vasoconstriction or vasodilation. They are of the opinion that the anatomical double supply of the conjunctival vessels supports the view that the intracranial vessels contribute to the pain of a migraine headache.

It has been estimated that 10 - 15% of persons subjected to migraine headache have at one stage or another experienced visual phenomena preceding, or in association with, one or more headache attacks.[1] The visual manifestations must be due to either a circulatory disturbance in the cerebral cortex, probably the occipital portion, or in the ophthalmic or retinal vessels of the eye. Certain observers have reported seeing temporary changes in the retinal arterioles during the various phases of migraine.[3,4]

This study was undertaken to measure the diameter of the retinal arterioles from fundal photographs during the various phases of migraine and on treatment with ergotamine preparations.

MATERIAL AND METHODS

The Patients

Five patients who suffered from migraine with visual symptoms were selected.

Patient No. 1 was a male student aged 18 years with a 2-year history of classical migraine. The prodrome consisted of a scotoma of dots and zig-zag lines associated with paraesthesia of both hands and occasional weakness of the left hand. The throbbing headache was always right-sided and associated with the progression of the scotoma into a hemianopia and even total blindness of the right eye. Vomiting partially relieved the headache. The headaches were precipitated by tension and fasting. There was a strong family history of migraine.

Examination both generally and of the central nervous system revealed no abnormality.

Patient No. 2 was a male clerk aged 18 years with a 3-year history of classical migraine with a prodrome of anorexia, nausea and lethargy. The throbbing headache was usually right-sided with unilateral blurring of vision, scotoma and lacrimation on the same side as the headache. Vomiting relieved the headache and an acute attack could be precipitated by fasting. There was a family history of migraine. Salicylates were the only drugs taken for the headache.

Examination both generally and of the central nervous system revealed no abnormality.

Patient No. 3 was a male mechanic aged 34 years with a 25-year history of classical migraine which would begin as a prodrome of flashing lights and blurring of vision in both eyes. This occasionally progressed to a temporary total blindness of the left eye during the acute headache phase. The headache itself was usually bilateral. There was a family history of migraine and known precipitants of an acute attack were cream products in the diet.

Examination both generally and of the central nervous system revealed no abnormality.

Patient No. 4 was a nursing sister aged 25 years with a 6-year history of classical migraine which was always premenstrual. Her prodrome consisted of yellow dots in front of both eyes 2 days before the headache, which progressed to blurring of vision, with occasional ptosis and lacrimation on the side of the headache. There was a family history of migraine. Vomiting relieved her of the headache for about an hour.

Examination both generally and of the central nervous system revealed no abnormality.

Patient No. 5 was a civil servant aged 45 years with a 5-year history of attacks of throbbing headache which had been diagnosed as migraine and successfully treated for 3 years with ergotamine tartrate. The headaches began to increase in frequency and severity over the previous 2 years and were associated with severe left facial pain, nasal congestion, lacrimation, ptosis and visual scotoma always on the left side. The attacks occurred bidaily, lasted for 1 - 2 hours and were totally incapacitating. Associated nausea and vomiting were present. There were no known precipitating

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factors and ergotamine preparations and analgesics no longer afforded relief. There was a family history of migraine.

On general examination there was nil of note, but central nervous system examination revealed mild ptosis, lacrimation and hyperaesthesia over the area served by the upper and middle branches of the trigeminal nerve on the left. Skull X-ray, electro-encephalogram and the cerebrospinal fluid were all normal. A diagnosis of cluster headache was now made which responded dramatically to methysergide with no further acute attacks of pain.

Technique

Retinal photographs were taken using a Zeiss Fundus camera with a built-in electronic flash and Kodachrome II colour film (ASA 25). The pupils were dilated with a mydriatic containing a solution of cyclopentolate hydrochloride 0·02% and phenylephrine hydrochloride 1·0% (Cyclomydril). A series of photographs were taken during the interphase, the prodrome, and headache phase (in patients 1 - 4) and with the administration of ergotamine tartrate (orally in case 1 and intravenously in cases 2 - 4). All symptoms and signs were recorded in the sequence of their occurrence during the investigations and correlated with the photographs being taken.

The retinal vessels were measured, using the technique described by Kagan *et al.*[5] The coloured retinal slides are projected onto a screen with two concentric circles of 10 cm and 20 cm radius respectively. The smaller circle is drawn with a thick broken line and the larger with small dots. The magnification and projection were so arranged that the disc always filled the smaller circle. The width of the retinal vessels was measured at right angles to the vessel wall, irrespective of the angle at which the vessel crossed the outer circle. A pair of sharp-pointed dividers and a ruler marked in millimetres were used to measure the vessel diameter. The most distinct portion of the vessel outline on either side was confirmed as the two points of measurement. A second observer (the projectionist) confirmed these points while measurements were being taken. Since the size of the disc was kept constant by a suitable choice of magnification, the measurements were consistent as far as size and position of the disc for one particular patient were concerned.

RESULTS

The diameter of the retinal arterioles and clinical details of the attack are presented in Tables I - V.

The grading of headache is given as

0 = No headache.
1+ = Awareness or unpleasant sensation in the head without pain.
2+ = Ache, whether localized or generalized.
3+ = Throbbing headache.
4+ = Throbbing headache with either nausea or photophobia.[6]

TABLE I. RETINAL ARTERIOLAR DIAMETER OF PATIENT NO. 1

		Arteriole (right retina)			
		Sup. temp.	Sup. nasal	Inf. temp.	Inf. nasal
Interphase	**Mean**	**12**	**9·2**	**11·3**	**9·0**
	SD	**0**	**0·3**	**0·3**	**0·3**
Migraine					
Fasting 10 a.m. Headache +++, (right sided)	**Mean**	**12**	**9·2**	**11·5**	**9·1**
	SD	**0**	**0·25**	**0.25**	**0·1**
Fasting 12.30 a.m. Headache +++	**Mean**	**12**	**9·2**	**11·4**	**9**
	SD	**0·1**	**0·2**	**0·3**	**0**
Non-fasting 1.30 p.m. Headache +++		**12**	**9**	**11·5**	**9**
Non-fasting 2 p.m. Headache +++	**Mean**	**11·9**	**9·2**	**11·5**	**9·1**
	SD	**0·1**	**0·2**	**0·3**	**0.1**
Ergot solution orally (3 mg dihydroergotamine)					
0 min					
3 min Headache ++++		**12**	**9**	**11·5**	**9**
5 min Headache +++		**12**	**9**	**11·8**	**9**
8 min Headache +++		**12**	**9**	**11·5**	**9**
10 min Headache ++		**12**	**9·5**	**11·5**	**9**
13 min Headache ++++		**12**	**9**	**11·5**	**9**
20 min Scotoma — right inf. quadrant on temporal side (not shown on perimetry).		**12**	**9·2**	**11·8**	**9**
25 min No headache, scotoma smaller.		**12**	**9**	**11·5**	**9·2**
30 min Headache ++ (1·5 mg dihydroergotamine)		**12**	**9·0**	**11·0**	**9**
35 min Headache ++		**11·8**	**9·0**	**11·2**	**9·2**
40 min Headache ++		**12**	**9·2**	**11·5**	**9**
45 min Headache +		**12**	**9·5**	**11·5**	**9**
48 min Headache 0		**12**	**9**	**11·5**	**9**
53 min Headache 0		**12**	**9·2**	**11·0**	**—**
60 min Headache 0		**11·8**	**9**	**11·5**	**9**
65 min Headache ++++ of sudden onset with total blindness of right eye.	**Mean**	**12**	**9·1**	**11·5**	**9**
	SD	**0**	**0·1**	**0**	**0**
70 min Headache 0 of sudden onset with return to normal vision. No other symptoms nor signs.	**Mean**	**12**	**9**	**11·4**	**9·0**
	SD	**0**	**0**	**0·2**	**0·1**

Blood pressure taken every 10 minutes remained constant.

TABLE II. RETINAL ARTERIOLAR DIAMETERS OF PATIENT NO. 2

		Arteriole (right retina*)		
		Sup. temp.	Sup. nasal	Inf. nasal
Interphase	Mean	9·2	11·3	10·2
	SD	0·3	0·3	0·4
Prodrome 12.30 p.m.	Mean	9·8	11·1	10·0
Nausea for 3 hours. Blurring of vision with scotomata. Headache + unilateral on right side.	SD	0·3	0·5	0·7
Migraine 3.00 p.m.	Mean	9·4	11·5	9·8
Headache ++++	SD	0·2	0·7	0·4
Ergot intravenously				
(Ergotamine tartrate 0·5 mg)				
0 min				
½ min Headache +++ with paraesthesia of tongue.		9·2	12	—
4 min Headache ++ with generalized feeling of warmth and facial sweating.		9·5	12	10
6 min Headache +		9·2	11·5	10·5
10 min Headache + with nausea.		9·0	11	9·5
15 min Headache + with nausea increasing.		9·0	12	9·5
18 min Headache + vomiting.		9·0	12	10
30 min Headache 0. No symptoms nor signs.		9·0	12	10

* The inf. temp. arteriole could not be measured for anatomical reasons. Blood pressure taken every 10 minutes remained constant.

TABLE III. RETINAL ARTERIOLAR DIAMETERS OF PATIENT NO. 3

		Arteriole (left retina)			
		Sup. temp.	Sup. nasal	Inf. temp.	Inf. nasal
Interphase	Mean	11·3	10·8	10·0	10·1
	SD	0·3	0·3	0·6	0·2
Prodrome 12.15 p.m.	Mean	11·5	10·8	10·5	10·2
Scotomata initially left eye, after 20 minutes bilaterally. Slight nausea.	SD	0·1	0·6	0·1	0.3
Migraine 1.40 p.m.		11·5	10·5	10·7	9·7
Headache ++++, unilateral on left.					
Ergot intravenously					
(Ergotamine tartrate 0·5 mg)					
0 min					
1½ min Headache ++++		11	11	10·7	9·7
2 min Headache ++++ with nausea more intense and generalized cold sweat.		11	10·5	10·5	9·5
7 min Headache +		11·7	11·0	10·5	9·7
15 min Headache + vomiting.		11·5	10·5	10·5	9·5
22 min Headache 0, minimal nausea.		11	10·5	10·7	9·5

TABLE IV. RETINAL ARTERIOLAR DIAMETERS OF PATIENT NO. 4

	Arteriole (left retina)			
	Sup. temp.	Sup. nasal	Inf. temp.	Inf. nasal
Interphase	9·0	8·0	7·5	7·0
Prodrome				
Fleeting scotomata for 2 days predominantly on left side.				
Migraine				
Headache +++ on left.	8·6	8·0	8	7
Ergot intravenously				
(Ergotamine tartrate 0·25mg)				
Headache ++++	—	8	8·2	6·8
Headache ++++	9.5	8·2	7·5	7·0
Nausea increasing				
Headache ++++	8·0	7	—	6·2
Headache ++++	9·2	7·5	7·5	6·2
Headache ++++	9·2	8·2	7·5	6·5
Headache ++++	9	7·2	6·8	6·0
Headache ++				
Vomiting	9	7·0	7·0	7·0
Headache +	10	—	—	7·0
Headache 0	9·5	8·2	7·2	6·2
Headache 0	8·8	7·5	7·0	6·5

DISCUSSION

In the past various techniques of measurements of the retinal vessels have been used. Cusick and Herill[7,8] used a graticule or micrometer in the ophthalmoscope, and later Hickam[9,10] used photographs under a dissecting microscope with a micrometer in the eye piece. We found the easiest, most accurate and practical method of measuring retinal vessels using the technique described by Kagan *et al.*[2] Blau and Cummings[11] have shown that fasting overnight with resultant hypoglycaemia, can precipitate an acute attack in about 50% of patients. This method was used to precipitate an acute attack of migraine in patients No. 1 and 2.

Pathological changes in the internal carotid artery system have rarely been demonstrated in various phases of migraine. Dukes and Vieth[12] reported a patient who had developed an attack of migraine during angiography, in whom there had been progressively poor filling of the

TABLE V. RETINAL ARTERIOLAR DIAMETERS OF PATIENT NO. 5

	Arteriole (left retina)			
	Sup. temp.	Sup. nasal	Inf. temp.	Inf. nasal
Interphase	7·7	8·7	10·8	—
Prodrome	8·2	8·6	11·0	—
Pain on left side of face with unilateral ptosis, lacrimation and nasal stuffiness and blurring of vision on the left.				
Did not proceed onto the next phase of headache.				

vessels of the internal carotid tree during the prodroma, with a subsequent return to normal diameters during the headache phase. O'Brien[13] and Skinhoj[14] have also shown a pronounced decrease in the regional cerebral blood flow during the prodromal phase of migraine using Xenon 133. It was especially marked in the areas related to symptoms. An angiogram showed no arterial spasm, indicating that the cerebral vascular resistance was increased at the arteriolar level, which is the site of normal metabolic regulation of cerebral blood flow. During the headache phase in another patient there was an increase of blood flow suggesting intracranial vasodilation.[14]

The retinal arterioles are branches of the internal carotid artery via the ophthalmic artery. Thus any change occurring in the internal carotid artery system should be reflected in the retinal vessels. Although all our patients presented with visual manifestations either during prodrome or headache phase, we have been unable to demonstrate any change in the retinal arteriolar diameters during either of these phases.

The rationale of using a vasoconstrictor such as ergotamine tartrate in the treatment of an acute attack of migraine is universally accepted.[15-19] Wolff's photographs of the retinal vessels taken before and after the administration of ergotamine tartrate showed no reduction in the calibre of the arteries, although he conceded in retrospect that relevant arteries were minimally narrowed.[1] Thuranszky[20] claims that in man the retinal vessels contract with ergot alkaloids.

Our results show no change in the retinal arteriolar diameters when ergotamine preparations were given both orally or intravenously, although they had a profound effect on clinical presentation. In the patients given ergotamine tartrate intravenously (patients No. 2 - 4) there was a rapid relief of the throbbing component of the headache, followed by nausea and vomiting. The headache then decreased in intensity and disappeared. This occurred more rapidly in the patients given intravenous rather than oral therapy (mean time of 24 minutes as compared with 70 minutes). Although the first patient developed a scotoma and then later total monocular blindness we were unable to show any retinal changes. Retinal veins were also measured in all cases and although the results are not given, they showed no alteration.

Each colour slide was carefully examined, but failed to show any vasoconstriction either locally or generally, nor any evidence of intravascular red cell aggregation.[21] The results presented in our few cases are all negative. The visual defects which arise could be either at a cortical or at a capillary level which we have not been able to detect. Retinal fluorescein angiography may clarify this position.

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