THE TREATMENT OF VASCULAR HEADACHES OF THE MIGRAINE TYPE

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The *Ad Hoc* Committee on the Classification of Headache has recently (1962) attempted to draw up a classification of headache, and in this review of treatment of vascular headache this classification will be used.

It is not proposed to comment on the classification, which is accepted, but headaches falling into the first category only will be discussed. This primary class has been labelled 'Vascular headache of migraine type', and it has been subdivided into 5 sub-categories: (*A*) 'Classic' migraine, (*B*) 'common' migraine, (*C*) 'cluster' headache, (*D*) 'hemiplegic' and 'ophthalmoplegic' migraine, and (*E*) 'lower-half' headache.

This categorization has been briefly explained by the American *ad hoc* committee and it is pertinent to discuss the syndromes falling under the 5 divisions of vascular headaches.

(*A*) 'Classic' migraine is frequently, but not always, hemicranial in distribution. What makes it classical is its sharply defined prodromal symptoms, which may be visual, sensory or motor, but which are most commonly visual teichopsia consisting of bright lights, dark spots or zig-zag fortification spectra, or at times hemianopic phenomena. The headache lasts some hours or even 2 or 3 days.

(*B*) 'Common' migraine lacks the prodromata of (*A*) and is less often strictly hemicranial. It is often related to environmental factors such as the weekend or the premenstrual week.

(*C*) 'Cluster' headache. This is predominantly unilateral, and unlike (*A*) it nearly always confines itself to one particular side. It is usually associated with cranial autonomic phenomena such as flushing, sweating, rhinorrhoea and lacrimation, and it is named 'cluster' because the attacks, which last only about 30 minutes, occur in closely packed groups, almost daily for several weeks. Identical or closely allied to this group are Bing's erythroprosopalgia, Harris's ciliary neuralgia, Horton's histamine cephalalgia and Gardner's petrosal neuralgia.

(*D*) 'Hemiplegic' migraine and 'ophthalmoplegic' migraine are characterized by the features implied in their name.

(*E*) 'Lower-half' headache is confined to the lower half of the face and has been named sphenopalatine neuralgia, Vidian neuralgia and atypical facial neuralgia.

Of these 5 sub-categories only those in (*A*), (*B*), (*C*) and (*E*) will be discussed since no one falling into (*D*) was seen in this series.

Case Material

A total number of 31 patients with vascular headache were treated, all adult, comprising 18 males and 13 females. They were subdivided as follows:

	Total	*Male*	*Female*
Classic migraine	10	4	6
Common migraine	8	3	5
Cluster headache	10	10	0
Lower-half headache	3	1	2

In a small series such as this no conclusions can be drawn about the relative frequencies or sex-distribution of the different headaches, but it is noted that, as usual, the cluster headache is predominantly found in males.

Methodology

All these headaches were accepted as being vascular in origin, so that a uniform type of treatment could be tried out. It seemed doubtful whether 2 of the 3 lower-half headaches really were due to a vascular disturbance, but they certainly did not fall under the heading of typical

cranial neuralgias since the pain was not confined to within the limits of any one nerve; so for therapeutic purposes they were treated as the others.

All patients were subjected to full physical examination, and none were found to be suffering from any general disease or from hypertension.

All subjects had tried common analgesics without satisfactory relief.

X-rays of the skull were done on all patients and found to be normal.

Several subjects had histories of various types of allergy, but in no one was the headache obviously due to allergy.

Because the headaches were thought to be due to vasodilation they were treated with vasoconstrictors — ergotamine tartrate and caffeine in the form of 'cafergot' (Sandoz), or 'ancofen' (B.D.H.), and if not satisfactorily controlled by these preparations they were given an antiserotonin substance, 'deseril' (Sandoz). The rationale of this is discussed below.

There is no control series for comparison with these 31 cases which are simply the last 31 consecutive subjects seen since the introduction of deseril.

Cases

Of the 10 subjects with classic migraine, 8 found satisfactory relief with cafergot for the actual headache. Of these 8 there were 2 who found that the cafergot, although relieving the headache, produced nausea. Both these found that ancofen was a satisfactory substitute for the pure ergotamine and caffeine product.

Of the 8 patients with common migraine, 7 found satisfactory relief from headache with cafergot or ancofen.

Of the 10 patients with cluster headache, 4 found relief with cafergot and 5 with ancofen, but these represented 7 subjects only since some used both preparations.

Of the 3 with lower-half headaches none found satisfactory relief with either cafergot or ancofen, but 2 were relieved with deseril.

So much for a brief résumé of the drug treatment of these patients. As to prophylaxis of the headache in both the classic and common migraine groups, ergotamine preparations gave a satisfactory response (distinct lessening in frequency and lessening of severity and duration of headache) in 11 out of 18 cases. It was found generally that 1 ancofen tablet each evening gave the most satisfactory ergotamine prophylaxis. However, when it came to prophylaxis, it was found that deseril gave a better response and, when given instead of ergotamine, it was satisfactory in 12 out of 16 cases. It also proved satisfactory in 1 out of 2 cases where deseril and ergotamine were both given.

In the cluster type of headache it is difficult to distinguish between prophylaxis and treatment since these patients are subject to long remissions, and patients are liable to take whatever tablets they can at the slightest suggestion of an impending attack. No attempt will be made to separate prophylaxis from treatment. Seven of the 10 found relief with ergotamine and 9 of the 10 relief with deseril — a highly satisfactory figure.

Deseril was not used in the treatment of the migraine type of headache once the pain had commenced since there have been reports of it making the headache worse.

Of the 3 lower-half headaches, again there was no separation of prophylaxis from treatment, but the pains are sufficiently dramatic and unusual to warrant brief descriptions.

Case 1

A.M., male, 40 years. This patient was an Indian traveller who complained of bouts of intense pain, lasting hours to days, in the upper gum, posterior pharynx, ear and side of neck, all on the right side. Ergotamine preparations gave only very slight amelioration of symptoms and deseril did not help.

Case 2

M.P., female, 44 years. Severe burning pain in posterior fauces, side of tongue, lower jaw, ear and side of neck, all on the right side. No relief from ergotamine preparations, but excellent relief from deseril, 2 mg. *t.d.s.*

Case 3

B.A., female, 24 years. Severe lancinating pain in lower jaw and ear, occasionally going up over malar region in dull ache, all on right side. The pain was so severe that various dental procedures were carried out as emergencies without relief. Another attack some weeks later did not respond so completely to deseril, but when it was given in 2 mg. doses *q.d.s.* she obtained reasonable amelioration of her pain.

The results in these cases may be briefly tabulated:

Response of headache to ergotamine preparation:

Classic migraine	8 out of 10 satisfactory
Common migraine	7 out of 8 satisfactory
Cluster headache	7 out of 10 satisfactory
Lower-half headache	No satisfactory response.

Response of headache to deseril, given prophylactically in the case of migraine:

Both types of migraine	13 out of 16 satisfactory
Cluster headache	9 out of 10 satisfactory
Lower-half headache	2 out of 3 satisfactory.

By 'satisfactory' is meant satisfactory to the patient in that he no longer complained of being unable to carry on and was satisfied with the results and did not seek further medical aid. It should be noted in particular how remarkable were the results with cluster headache in response to the antiserotonin substance.

Dosage

Cafergot was given in the following dosage: 1 or 2 tablets at first sign of impending headache in any of the 4 sub-groups, followed by 1 or 2 tablets in half an hour if necessary. If nausea or gastro-intestinal symptoms were disturbing, chlorpromazine was added, 25 mg. with the first tablet.

At times it was found that an ergotamine preparation containing an antihistamine, medozine hydrochloride, was more satisfactory — in which case ancofen tablets were used in the same scheme. In general as a prophylactic dosage, ancofen tablets, used one each night or morning, were most satisfactory.

Deseril tablets* were used only prophylactically except in the patients with lower-half headache. They were given 2 - 3 tablets daily, and in case B.A., with lower-half headache, the dose had to be raised to 4 each day.

Side-effects from deseril were not frequent, but 3 subjects complained of markedly unpleasant alterations in their sensorium varying from confusion to difficulty in concentration. Two patients complained of dyspeptic upsets. There were no patients who complained of peripheral vascular disturbances.

DISCUSSION

This paper is not concerned with discussing the aetiological causes of migraine — that has been done many times previously (Wolff 1948, Selby and Lance, 1960). What has been done is that an attempt has been made to evaluate the efficacy of certain vasoconstrictor preparations and an antiserotonin substance in the treatment of headaches which are generally accepted as arising from vasodilation, at least in part.

The beneficial effect of vasoconstrictors such as caffeine and ergotamine tartrate on migraine has been known for many years. Ergotamine has been used by Symonds in the cluster type of headache with success and also in the type

* Originally we used UML-491 tablets containing 2 mg. of methysergide. Deseril has now become available in tablets containing 1 mg. of methysergide (called 'sansert' in the USA).

now classified as lower-half headache by Brickner and Riley. It is not proposed to discuss the vasodilator aspect *per se* further, except to say that postulating such a mechanism still leaves open the question of how the vasodilation comes about.

A derivative of lysergic acid, methysergide (supplied in this study by courtesy of Sandoz Limited, under the label UML-491, and later as deseril), was known to have an antiserotonin and anti-oedema action (Doepfner *et al.*). This substance was used successfully by Sicuteri in the treatment of vascular headache, and subsequent reports by others have confirmed that this preparation is useful in the prophylaxis of this type of headache. Friedman and Losin reported excellent results in 65% of patients with migraine, and in 71% of those with cluster headaches, using UML-491.

Serotonin has not been shown by bio-assay to be present during the migraine attack, though Chapman *et al.* implicated a polypeptide vasodilator substance which they named neurokinin.

The side-effects of the drug have been noted by Friedman and Losin to be dizziness, nausea, epigastric discomfort, and difficulty in concentration, while Dalessio has reported a patient with severe peripheral vasoconstriction who recovered whenever the drug was withdrawn. Dalessio and his co-workers consider that UML-491 depends for its therapeutic effects upon its capacity to induce an increased sensitivity of the subject to his own vasoconstrictor agents.

In a later paper Dalessio and his colleagues showed that when UML-491 is administered during a period of oliguria it damps down the vasodilator response of vessels to catecholamines. This may be relevant to its action in migraine, since there is evidence that at least some migraine patients retain fluids before the onset of headache (Ostfeld *et al.*).

There is as yet not any evidence to show whether or not lower-half headache and cluster headache are due to the same mechanisms as migraine, but clinically their symptoms could be explained on the basis of vasodilation, and their partial response to vasoconstrictors or to deseril suggests that they share some of the steps prodromal to migraine itself.

SUMMARY

31 patients with vascular headaches were treated with ergotamine caffeine preparations and by an antiserotonin substance, deseril.

In the majority of cases, with the exception of the lower-half type of headache, ergotamine caffeine was satisfactory in treating the headache. Deseril given prophylactically was of use in the majority of all types of headache.

BIBLIOGRAPHY

Brickner, R. M. and Riley, H. A. (1935): Bull. Neurol. Inst. N.Y., **4,** 422.
Chapman, L. F., Ramos, A. O., Goodell, H., Silverman, G. and Wolff, H. G. (1960): Arch. Neurol., **3,** 223.
Dalessio, D. J., Camp, W. A., Goodell, H. and Wolff, H. G. (1961): *Ibid.*, **4,** 235.
Dalessio, D. J., Chapman, L. F., Zideli, T., Cattell, M., Ehrlich, R., Fortuin, F., Goodell, H. and Wolff, H. G. (1961): *Ibid.*, **5,** 590.
Doepfner, W. and Cerletti, A. (1958): Int. Arch. Allergy, **12,** 89.
Friedman, A. P. and Losin, S. (1961): Arch. Neurol., **4,** 241.
Ostfeld, A. M., Reiss, D. J., Goodell, H. and Wolff, H. G. (1955): Trans. Assoc. Amer. Phycns., **68,** 255.
Selby, G. and Lance, J. W. (1960): J. Neurol. Neurosurg. Psychiat., **23,** 23.
Sicuteri, F. (1959): Int. Arch. Allergy, **15,** 300.
Symonds, Sir Charles (1956): Brain, **79,** 217.
Wolff, H. G. (1948): *Headaches and other Head Pains*. London: Oxford Univ. Press