

Migraine and multiple sclerosis

SYLVIA M. WATKINS¹ AND MICHAEL ESPIR²

Department of Neurology, Leicester Royal Infirmary

Migraine is a common condition thought to result from vasomotor changes usually in the distribution of the carotid and vertebro-basilar arteries. According to Kunkle and Wolff (1951) the disorder has been estimated to occur in approximately 8% of patients examined in general practice, but the true incidence is unknown. In the *British Medical Journal* (1963) it is stated that if 'classical' cases only are considered, about 5 to 10% of the population have migraine. In most reports the incidence is higher among females than males. In view of the clinical impression gained by one of us (M.E.) that there is a high incidence of migraine in patients with multiple sclerosis (M.S.), the study reported here was undertaken to try and ascertain whether or not this was so.

CASE MATERIAL

The case material consisted of 100 consecutive patients who were seen personally by one of us (M.E.) in Leicester and diagnosed as having 'definite' or 'probable' M.S. (McAlpine, 1961). 'Possible' and 'suspect' cases were excluded from the series, and only patients who were under the age of 50 when first seen were included, as it was thought that in older patients the histories might be less accurate. A control series was taken from a random selection of hospital visitors matched for age and sex with the M.S. patients. Both groups were asked the same questions by one of us (S.M.W.) regarding headaches and family history of migraine.

¹Present address and address for reprints: Royal Free Hospital, London.

²Present address and address for reprints: Derbyshire Royal Infirmary, Derby.

The diagnosis of migraine (Critchley, 1967) was accepted in patients with recurring headaches, particularly if unilateral or throbbing in nature. Although accompanying symptoms were not regarded as essential for this diagnosis, we were careful to exclude other physical or psychological causes for the headache, and in fact all but two of the migrainous patients (in both M.S. and control groups) also had other well-recognized migrainous symptoms (nausea, vomiting, photophobia, teichopsia or other visual disturbances, vertigo, or paraesthesiae).

RESULTS

There were 64 female and 36 male patients in both groups. Their ages ranged from 15 to 50 at the time of inquiry. Table I shows that the incidence of migraine in the patients with M.S. was 27% compared with 12% of the control group. This difference is statistically significant ($P < 0.00001$). The incidence of migraine was considerably higher in females than males in both groups.

There was also a notable difference in the incidence of a family history of migraine in the two groups (20% of the M.S. patients compared with 10% of the controls). In the group of patients with M.S. there were six patients (from five families) who had another member of the family also affected with M.S.

DISCUSSION

Estimates of the incidence of migraine are likely to vary according to the diagnostic criteria used; restriction of the diagnosis to those with so-called

TABLE I

OVERALL AND SEX INCIDENCE OF MIGRAINE, AND FAMILY HISTORY (F.H.) OF MIGRAINE, IN THE PATIENTS WITH M.S. AND THE CONTROL SERIES

	Total	Migraine				No migraine		Total with F.H. of migraine
		No.	%	-F.H.	+F.H.	+F.H.	-F.H.	
M.S.								
Males	36	5	14	3	2	4	27	6
Females	64	22	34	16	6	8	34	14
Total	100	27	27	19	8	12	61	20
Controls								
Males	36	1	3	0	1	3	32	4
Females	64	11	17	9	2	4	49	6
Total	100	12	12	9	3	7	81	10

'classical' migraine would tend to give lower figures. In this study, however, the same diagnostic criteria were used for both the M.S. group and the controls, and care was also taken to ask the same questions in the same way of each patient and control. Admittedly the questioner (S.M.W.) inevitably knew whether she was dealing with an M.S. patient or a control subject, but the presence or absence of migraine was assessed without bias.

McAlpine and Compston (1952) mentioned that five of their 250 patients with M.S. were suffering from migraine at some time during the three months before the onset of their disease, but do not comment on the overall incidence of migraine in their series. We have not been able to find any other reference to the association of M.S. with migraine. In spite of the possible criticism that our study was not done 'blind', the difference in the incidence of migraine in the M.S. patients compared with the controls (27 to 12%) is very striking. It is, however, difficult to draw any further conclusions at present about the significance of this finding, in view of our ignorance regarding the cause of M.S. Whatever this turns out to be, any association between M.S. and other conditions is clearly of interest.

The incidence of migraine may also be influenced by factors governing the selection of population groups—for example, the figure of 12% for our controls might be slightly higher than in the general population due to the matching with the M.S. group, which contained a higher proportion of females and also excluded subjects under the age of 15 and over 50. This incidence of 12% in our controls is almost the same as that found by Leigh and Marley (1967) who compared the prevalence of migraine (and other conditions) in asthmatics with a control population belonging to practices in South London, using the Weinberg genealogical proband technique. They found no significant difference in the prevalence

of migraine in the two populations, and their findings are compared with ours in Table II.

With regard to the aetiology of migraine, attention has recently been given to the possibility that vasomotor changes in migraine may be related to the metabolism of amines (*British Medical Journal*, 1966; Hanington, 1967), and it is generally recognized that stress of various types may aggravate attacks in migrainous subjects. In 15 of our patients with migraine and M.S., the age of onset of the first symptoms of both conditions was clear; only four of these already had symptoms of M.S. when they first experienced migraine, but it is possible that the disease, or stress resulting from the neurological disability, was responsible for the development of their migraine. Alternatively, other common factors may have aggravated both conditions. On the other hand 11 of the patients had migraine first, so that in these the migraine could not be regarded as a stress reaction to M.S. We were not able to establish whether these patients had more severe migraine after the development of their symptoms of M.S., nor whether the relapses of M.S. were directly related to bouts of migraine. The average age of onset of M.S. was the same in patients who already had migraine, as in those who did not or who developed it after the onset of M.S. Furthermore the incidence of migraine in our patients with M.S. could not be correlated with the severity of their neurological disability. In fact we found a slightly higher proportion of M.S. patients who had severe persistent neurological disability without migraine, than with migraine.

We found no evidence that focal neurological accompaniments to the headache were more common in patients with M.S. and migraine, nor that the prodromata of their attacks of migraine were more liable to involve the brain stem rather than the cerebral hemispheres. The high incidence of other

TABLE II
COMPARISON OF INCIDENCE OF MIGRAINE IN BRONCHIAL ASTHMA AND MULTIPLE SCLEROSIS, WITH CONTROLS

	Leigh and Marley (1967) <i>Bronchial asthma</i> ¹			Watkins and Espir (1968) <i>Multiple sclerosis</i>		
	<i>Males</i>	<i>Females</i>	<i>Total</i>	<i>Males</i>	<i>Females</i>	<i>Total</i>
Total	260	334	594	36	64	100
No. and % with migraine	20 (8%)	63 (19%)	83 (14%)	5 (14%)	22 (34%)	27 (27%)
	<i>Controls</i> ¹			<i>Controls</i>		
Total	256	283	539	36	64	100
No. and % with migraine	23 (9%)	47 (17%)	70 (13%)	1 (3%)	11 (17%)	12 (12%)

¹The figures under these headings have been taken from Table 67 in the book *Bronchial Asthma* with permission from the authors and the publishers, Pergamon Press, Ltd.

types of transient neurological disturbances (T.N.D.) in M.S. has been commented on before (McAlpine, Lumsden, and Acheson 1965; Espir, Watkins, and Smith, 1966). Our series of M.S. patients and controls were also questioned specifically about T.N.D. of all types; they occurred in 46% of the M.S. patients, and only 7% of the controls. However, the incidence of T.N.D. unassociated with headache in M.S. patients with migraine was not statistically different from those without migraine. Fourteen of the M.S. patients with migraine also had T.N.D. unassociated with headache, but in only one were the T.N.D. identical with the prodromata of her migraine. Thus there was no clear cut correlation between the incidence of migraine and other T.N.D. in this series of M.S. patients, and no evidence therefore that transient neurological disturbances in M.S. are generally due to vasomotor changes analogous to the ischaemic phenomena of migraine without headache (Whitty, 1967).

It is well recognized that migraine shows a strong hereditary tendency, and that M.S. also has a small but definite familial incidence. In our series the findings of six patients (from five families) with a family history of M.S. is in keeping with previous reports (Pratt, Compston, and McAlpine 1951; McAlpine *et al.*, 1965); however, the considerably higher incidence of a family history of migraine in M.S. patients compared with the controls was surprising to us and worthy of note.

SUMMARY

A significantly higher incidence of migraine has been found in a series of 100 consecutive patients with multiple sclerosis, compared with a similar series of controls matched for age and sex. The figures were 27% in the multiple sclerosis group

compared with 12% in the control group. As expected, the incidence of migraine was considerably higher in females than males in both groups. There was also a notable difference in the family history of migraine in the two groups, 20% in the multiple sclerosis patients compared with 10% in the controls. Although in the patients with multiple sclerosis there was a higher incidence of other transient neurological disturbances, these had no obvious correlation with migraine. Some of the possible reasons for the higher incidence of migraine in the patients with multiple sclerosis are also discussed.

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