PAPERS AND ORIGINALS

Smoking and subarachnoid haemorrhage

B A BELL, LINDSAY SYMON

British Medical Journal, 1979, 1, 577-578

Summary and conclusions

A retrospective study of 208 patients with ruptured cerebral aneurysms showed a highly significant excess of cigarette smokers among both men and women compared with the expected incidence. Results suggested that continued smoking increases the risk of suffering a subarachnoid haemorrhage (SAH) by a factor of 3.9 for men and 3.7 for women.

Other factors besides smoking must affect the genesis of aneurysmal SAH since it is found in non-smokers, but continued cigarette smoking appears to increase substantially the risk of aneurysmal SAH occurring.

Introduction

Since 1765, when Biumi^{1,2} gave the first clear description of an intracavernous carotid aneurysm, cerebral aneurysms have been known to rupture and produce subarachnoid haemorrhage (SAH). The precise aetiology of aneurysms has, however, remained elusive. Bruce *et al*³ described a carefully documented case of an anterior cerebral artery aneurysm and concluded that the aneurysm had formed at a congenital defect in the medial muscle layer of the artery, and this explanation received later support.^{4,5} These congenital "defects," however, were subsequently shown⁶ to be present in the axillae of most arterial branches throughout the body, and du Boulay⁷ described how the existence of such a physiological defect in the medial muscle was essential to avoid a buttonhole stenosis of the branch during vasoconstriction of the main trunk. In a large co-operative study of SAH⁸ the peak age incidence of rupture of an aneurysm was found to be between 40 and 60. This finding and the rare occurrence of aneurysms in a postmortem study of children's brains⁹ would indicate that they usually arise after birth.

The cerebral arteries are unique in lacking an external elastic lamina, the vessel structure at the major divisions being maintained solely by the internal elastic lamina supported by the cerebrospinal fluid. Carmichael^{10,11} attributed the formation of aneurysms to the weakening effect of atheroma on the internal elastic lamina, and du Boulay⁷ found a clinical association between aneurysms and angiographically visible atheroma. Coronary atheroma was also associated with cerebral aneurysms in a postmortem study of men aged 45-70.¹² The relation between smoking and coronary atheroma and between smoking and aortic aneurysms are well known,¹³ and thus a study of smoking in relation to cerebral aneurysms seemed justified.

Patients and methods

The notes of all the patients admitted with SAH under one of us (LS) during 1965-78 were examined to ascertain smoking habits. A total of 106 men and 162 women were studied. Of the men 74 had aneurysms, six arteriovenous malformations, and 26 no angiographic abnormality to account for their SAH. Of the women, 134 had aneurysms, nine arteriovenous malformations, and 19 no angiographic abnormality. The accuracy of the information in the notes was

TABLE 1—Number of smokers, ex-smokers, and non-smokers in patients with aneurysms, arteriovenous malformations, or no angiographic abnormality, and number expected in similar-sized sample of general population

	Men		Women	
	Patients	General population	Patients	General population
<i>Aneurysms</i>				
Smokers	63	51.3	96	61.1
Ex-smokers	8	13.2	12	11.3
Non-smokers	3	9.5	26	61.6
χ^2	4.4		17.7	
P	<0.04		<0.0005	
Relative risk	3.9		3.7	
90% confidence limits	1.3-12.0		2.3-5.9	
<i>Arteriovenous malformations</i>				
Smokers	4	4.1	5	3.8
Ex-smokers	..	0.9	..	0.7
Non-smokers	2	1.0	4	4.5
<i>No angiographic abnormality</i>				
Smokers	19	17.6	6	8.1
Ex-smokers	4	4.0	2	1.5
Non-smokers	3	4.4	11	9.4
χ^2	0.01		0.14	
P	>0.9		>0.7	

Gough-Cooper Department of Neurological Surgery, The National Hospital, Queen Square, London WC1

B A BELL, FRCS, MRC fellow in neurosurgery
LINDSAY SYMON, TD, FRCS, professor of neurosurgery

TABLE II—Age distribution and numbers of cigarettes smoked daily by patients with aneurysms

Age group (years)	No of cigarettes smoked daily												
	Nil	<5	5	6-9	10	11-14	15	16-19	20	21-24	25	26-29	30
<i>Men</i>													
16-19					1								1
20-24									1				
25-29													
30-34									1				1
35-49	1		1	1					9		1	1	5
50-59	1	1	2		1		2		4		2		4
≥60	1		1		2		2		5		1		1
<i>Women</i>													
16-19	1												
20-24		1	1				1		1				2
25-29	2						1		2				5
30-34					1								
35-49	9	1	4		3	1	5		13		1		3
50-59	8	2			2	1	7		14		3		1
≥60	6	3			4	1	1		4				1

checked with a postal questionnaire sent to all traceable patients, and a response was obtained from 73 men and 104 women. No information on smoking habits was available from the notes or the questionnaire for six men and 24 women, who were excluded from further study.

The control figures for the incidence of smoking in the general population were taken from figures published by the Tobacco Research Council,¹⁴ which were corrected so that the age distribution of the control data matched that of the patients. The figures apply to the population of Great Britain in 1965, the beginning of this study. Since 1965 the incidence of smoking has fallen for men and remained stable for women.¹⁵

Results

Table I shows the number of smokers, ex-smokers, and non-smokers in each group of patients, and the numbers expected in a sample of the general population of similar size. The ex-smokers had stopped smoking on average 8.8 years before their SAH (range 2-30 years), and were added to the non-smokers for statistical comparison with the smokers. The χ^2 value was calculated, using Yates's correction for continuity, for each group of patients except those with arteriovenous malformations, for whom the numbers were too small for analysis.

A greater proportion of smokers was found among the patients with aneurysms than was expected from the general population. This was not the case for patients with arteriovenous malformations or no angiographic abnormality, in whom the proportion of smokers was closely similar to that expected. The relative risk in continuing smokers of sustaining an aneurysmal SAH was increased by a factor of 3.9 for men and 3.7 for women when compared with lifelong non-smokers.

On average the women smoked fewer cigarettes than the men (table II) and had smoked for a shorter period before their SAH. Oral contraceptives had been used by 27% of the women who answered the questionnaire, a high proportion given the predominance of postmenopausal women. The proportion of women with previous pregnancies was 71%, and many had had more than one child. Three of the patients with aneurysms had diabetes mellitus, as did the relatives of a further 17.

Discussion

Although SAH accounts for up to 14% of deaths from vascular disease of the brain,¹⁶ any prospective study of environmental factors that may contribute to aneurysm formation or rupture is hampered by the relatively few cases in a studied population. Petitti and Wingerd¹⁷ followed up 16 759 women for six and a half years in a study of contraceptive drugs in California, and SAH occurred in only 11 cases. A significant correlation between smoking, oral contraceptive use, and SAH was shown in all of them, with a synergistic effect when both factors were combined. This resembles the effects of smoking and oral contraceptive use on myocardial infarction.¹⁸

Results of the present retrospective study showed a highly significant excess of male and female smokers compared with the general population. These excesses were not found when SAH had occurred without the presence of an aneurysm, and the implication is that smoking is one of the environmental factors that may influence aneurysm formation or possibly rupture. Women were less exposed to cigarette smoking than men, as they smoked fewer cigarettes for a shorter period before their SAH. Their exposure to oestrogens, however, both in oral contraceptives and during multiple pregnancies, may have acted synergistically with their smoking.

Clearly other factors besides smoking are implicated in the genesis of aneurysmal SAH, as it occurred in 26 women and three men who had never smoked. Other factors must also explain the change in the incidence of SAH by sex above and below the age of 40. The incidence is greater in women aged over 40 but in men below the age of 40.⁸ Cigarette smoking, however, contributes to the formation of atheroma,¹⁹ and atheroma is associated with cerebral aneurysms.⁷ The present retrospective findings suggest that continued cigarette smoking increases the risk of suffering a SAH from a cerebral aneurysm by a factor of 3.9 for men and 3.7 for women.

We are grateful to Miss E A Paul, statistician, The National Hospital, for her help with analysing the data. BAB is funded by the Medical Research Council.

Reprint requests should be addressed to Professor Lindsay Symon.

References

- 1 Biuni, F, *Observationes Anatomicae: Observatio V*. Milan, 1765. Cited by Sandifort.²
- 2 Sandifort, E, *Thesaurus Dissertationum*, vol 3. Leyden, Luchtmans, 1778.
- 3 Bruce, A, Pirie, J H H, and MacDonald, W K, *Review of Neurology and Psychiatry*, 1908, **6**, 449.
- 4 Turnbull, H M, *Quarterly Journal of Medicine*, 1915, **8**, 201.
- 5 Turnbull, H M, *Brain*, 1918, **41**, 50.
- 6 Forbus, W D, *Bulletin of the Johns Hopkins Hospital*, 1930, **47**, 239.
- 7 Du Boulay, G H, *British Journal of Radiology*, 1965, **38**, 721.
- 8 Locksley, H B, *Journal of Neurosurgery*, 1966, **25**, 219.
- 9 Uttley, D, *British Journal of Hospital Medicine*, 1978, **19**, 138.
- 10 Carmichael, R, *Journal of Pathology and Bacteriology*, 1945, **57**, 345.
- 11 Carmichael, R, *Journal of Pathology and Bacteriology*, 1950, **62**, 1.
- 12 Crawford, T, *Journal of Neurology, Neurosurgery and Psychiatry*, 1959, **22**, 259.
- 13 Doll, R, and Peto, R, *British Medical Journal*, 1976, **4**, 1525.
- 14 Lee, P N, *Statistics of Smoking in the UK*, table 9, research paper 1, 7th edn, p 30. London, Tobacco Research Council, 1976.
- 15 Royal College of Physicians of London, *Smoking or Health*, Third Report, p 17. London, Pitman Medical, 1977.
- 16 Kannell, W B, *Stroke*, 1971, **2**, 295.
- 17 Petitti, D B, and Wingerd, J, *Lancet*, 1978, **2**, 234.
- 18 Mann, J I, et al, *British Journal of Preventive and Social Medicine*, 1976, **30**, 94.
- 19 Wald, N, et al, *British Medical Journal*, 1973, **1**, 761.

(Accepted 15 December 1978)