Discussion

We suggest that this man's acute rise in blood pressure was the result of his stopping methyldopa, which probably resulted in infarction of the medial longitudinal bundle. Supporting this supposition was his description of symptoms during times when he had previously stopped his treatment which were similar to those reported on clonidine withdrawal. We believe this case to be important because previously rebound hypertension has been reported only with clonidine. Possibly rebound hypertension is a more general property of hypotensive agents.

[1] Hokfelt, B, Hedeland, H S, and Dymling, F, *European Journal of Pharmacology*, 1970, **10**, 389.

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History of regular aspirin use among patients with acute myocardial infarction (AMI) and controls according to geographical region, sex, and age. Evaluation of AMI rate ratio (RR) for aspirin users relative to non-users is also shown

Sex	Age (years)	Patients with AMI: Regular aspirin use: Yes	Patients with AMI: Regular aspirin use: No	Patients with AMI: Regular aspirin use: Total	Controls: Regular aspirin use: Yes	Controls: Regular aspirin use: No	Controls: Regular aspirin use: Total
North America							
Men	40-49	1	48	49	42	891	933
	50-59	0	77	77	65	1079	1144
	60-69	1	95	96	66	980	1046
Women	40-49	0	10	10	39	549	588
	50-59	0	21	21	51	687	738
	60-69	1	44	45	55	697	752
Other areas							
Men	40-49	2	50	52	6	269	275
	50-59	0	78	78	6	362	368
	60-69	0	127	127	7	501	508
Women	40-49	1	13	14	13	271	284
	50-59	0	35	35	13	385	398
	60-69	0	54	54	11	451	462
Total		6 (·9%)	652	658	374 (5%)	7122	7496

Crude RR: point estimate[2] 0·18; 95% confidence limits[3] 0·09, 0·36; test statistic $\chi = -4{\cdot}76$; $P < <0{\cdot}00005$.
Residual RR: point estimate[1] 0·23; 95% confidence limits[3] 0·11, 0·48; test statistic $\chi = -3{\cdot}89$; $P = 0{\cdot}0001$, 2-sided.

Regular aspirin use and myocardial infarction

We have reported a negative association between regular aspirin intake and the risk of acute myocardial infarction (AMI)[1] based on a case-control study as part of a continuing programme of intensive drug monitoring. In that study three out of 325 patients with AMI (0·9%) had a history of regular aspirin use before admission compared with 188 out of 3807 controls (4·9%). Since that report data on additional patients have been accumulated, and we now re-examine the relationship of AMI to regular aspirin use in the light of all the data now available.

Patients, methods, and results

Information on "regular" drug intake for the month before admission was obtained from all patients enrolled in the programme, and final diagnoses were abstracted at the time of discharge. Further details of the programme can be found in our previous report.[1]

As in our previous study,[1] we have excluded from the final analyses patients below 40 or above 69 years of age and those whose first listed diagnosis was a condition likely to be associated with aspirin use. The final analyses were based on a total of 658 patients with a discharge diagnosis of AMI and 7496 controls admitted to selected medical services of the hospitals monitored.

The combined data for the previously reported and the new series, covering 325 and 333 cases of AMI respectively, are given in the table. Six out of 658 (0·9%) of the patients and 374 out of 7496 (5·0%) controls took aspirin regularly. The estimated AMI rate ratio at this level was therefore 0·18 for regular aspirin users compared with controls. Taking into account region (North America *v* Israel, New Zealand, or Scotland), sex, and age, the rate ratio estimate[2] then became 0·23, with a 95% confidence interval ranging from 0·11 to 0·48.

The incidence of aspirin use among AMI patients and controls with diabetes was 2·1% (2/96) and 4·1% (48/1171) respectively; among people with hypertension 1·6% (1/64) and 3·9% (45/1103) respectively; and among those with a *secondary* diagnosis of arthritis 0% (0/16) and 18·6% (36/194) respectively.

Discussion

The present updating of the findings of the Boston Collaborative Drug Surveillance Program confirms the previous indication of a negative association between regular aspirin use and the risk of AMI, as the new data conform very closely with those previously reported.[1]

We are unaware of any special problems with the data or the analysis. Regular use of aspirin in itself is unlikely to influence the possibility of admission to hospital in people with AMI or in those with illnesses diagnosed in the comparison series. Our data on aspirin use does not appear to be biased and we can think of no other factors that might influence the association sufficiently to explain them. Some support for causal interpretation is provided by the experimental data of Elwood *et al.*[3] On the other hand, an acute experiment on the elderly[4] gave no evidence of a preventive effect of aspirin in thrombosis-related illnesses, and a large non-experimental study indicated no association between using aspirin "often" and the risk of AMI.[5]

Our data continue to be provocative, and it would be premature to conclude that regular aspirin use prevents non-fatal AMI or other cardiovascular disease. Nevertheless, this evidence, together with the documented effect of aspirin in reducing platelet adhesiveness, calls for further evaluation of aspirin as a potential preventive agent for thrombotic disease.

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