Inappropriate use of sumatriptan: population based register and interview study

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BMJ 1998;316:1352–3

Sumatriptan ranked second in expenditure on drugs for outpatients in Denmark in 1995. The 5% of patients who were heavy users of sumatriptan accounted for nearly 40% of consumption.[1 2] We conducted a population based interview study to evaluate the appropriateness of sumatriptan use.

Subjects, methods, and results

Subjects were recruited through community pharmacies in Funen county, Denmark (population 465 000). Patients who presented prescriptions during two weeks in February 1996 were invited to participate, and relevant data for 1992-6 were retrieved from the county prescription registry.[3] Sumatriptan consumption was described as the defined daily dose unit (100 mg for oral sumatriptan and 6 mg for subcutaneous sumatriptan). For each subject, peak dispensing of sumatriptan in any 30 day period was determined from register data. Patients were then classified into three groups: high peak users (≥60 units/30 days), intermediate peak users (30-59 units), and low peak users (<30 units).

After anonymising non-respondents' data, we used register data to evaluate the representativeness of the study population. Participants underwent structured interview by a doctor and were examined by neurologists. Recall was assisted by photographs of drugs and a graph of the patient's monthly sumatriptan use based on register data. Participants completed headache diaries for 30 days.[4] Patients' sumatriptan use was evaluated according to criteria defined in the table. The study was approved by the regional ethics committee and the Danish Board of Registers, and patients gave written informed consent.

Of 435 patients eligible for inclusion (83% women, median age 47), 233 (54%) responded. Response rates were 33% (7/21) in the high use group, 47% (30/64) in the intermediate group, and 56% (196/350) in the low use group. Respondents and non-respondents in the low and intermediate groups had comparable age, sex, and drug use. Non-respondents (14 women) in the high use group had consumed more sumatriptan than respondents (4 women, 3 men) (median 1333 *v* 832 units; P = 0.04). All 37 respondents with high or intermediate peak use completed the interview and medical examination; 30 returned completed headache diaries. Of 30 randomly selected patients in the low use group, 29 completed all study phases.

Patients with peak use ≥30 units/30 days reported previous dependence (need to take the drug every day to function normally) on drugs other than sumatriptan more frequently (table); three reported dependence on sumatriptan. Diagnosis of headaches that occurred before chronic use of strong medication for relief of headache was according to the criteria of the International Headache Society.[5] We were unable to establish a diagnosis of migraine or cluster headache in nine patients (two high use, three intermediate use, four low use). Headache recurred in 12 (18%) patients with migraine (none from the high use group) within 24 hours in 50% or more of treated episodes; they usually repeated the sumatriptan. Six of seven high use subjects and 22/30 with intermediate use fulfilled one or several of the criteria for inappropriate use of sumatriptan. Chronic use (daily or near daily use for ≥3 consecutive months) of analgesics to relieve headache was common in these patients. They also had drug induced headache frequently (headache for ≥180 days/year and concurrent chronic use of any headache medication other than sumatriptan). Inappropriate use was related to frequent use (≥24 times in past 12 months) in 4/29 low peak users for tension headaches and in another four for drug induced headache.

Characteristics of study subjects and their use of sumatriptan in relation to peak sumatriptan consumption. Values are numbers (percentages) unless indicated otherwise

	Peak sumatriptan use*		
	<30 (n=29)	**30-59 (n=30)**	**≥60 (n=7)**
Median (interquartile range) age	47 (41-50)	46 (40-51)	50 (47-64)
Women	26 (90)	23 (77)	4 (57)
Schooling ≥11 years	10 (35)	7 (23)	0
Current smoker	4 (14)	9 (30)	5 (71)
Median (interquartile range) alcoholic beverages consumed per week	3 (2-4)	3 (0-4)	2 (1-3)
Headache type†:			
Migraine	25 (86)	26 (87)	4 (57)
Tension	26 (93)	30 (100)	4 (67)
Cluster	0	1 (3)	1 (14)
Drug induced	4 (14)	14 (47)	6 (86)
Use of drugs			
Sumatriptan‡:			
Median (interquartile range) individual consumption	108 (46-204)	522 (296-651)	832 (248-1048)
Median (interquartile range) duration of sumatriptan use (days)	938 (753-1267)	1349 (1159-1413)	1064 (645-1426)
Previous dependence on medicine (headache drugs, hypnotics, or opioids)‡	2 (7)	14 (47)	4 (57)
Chronic use of drugs for acute relief of headache‡:			
Current	6 (21)	13 (43)	5 (71)
Previous	4 (14)	6 (20)	1 (14)
Criteria for inappropriate sumatriptan use†			
Chronic use and no diagnosis of cluster headache	1 (3)	10 (33)	6 (86)
Frequent use for headaches other than migraine or cluster headache	8 (28)	20 (67)	6 (86)
Frequent use for repetition of ineffective treatment	0	2 (7)	1 (14)
Frequent use for headache prophylaxis	0	1 (3)	0
Fulfilling at least one of the above	8 (28)	22 (73)	6 (86)

*Defined daily dose units per 30 days, where one defined daily dose unit=100 mg oral sumatriptan or 6 mg subcutaneous sumatriptan.
†Not mutually exclusive.
‡Information on use of medication was derived through presciption register data for sumatriptan; information on previous dependence on medicine and chronic use of drugs was obtained from self reports.

Comment

The relatively low response rate, particularly in high peak users, raises concern about the representativeness of this study. When the higher total consumption of sumatriptan among non-respondents in this group is taken into consideration, this bias could lead to underestimation of sumatriptan overuse. Appropriate heavy use of sumatriptan for cluster headache was rare. We conclude that heavy consumption of sumatriptan generally represents inappropriate use, mainly for tension and drug induced headaches. Inappropriate use may be related to the patient rather than the drug. Patients at greatest risk have generally been excluded from clinical trials conducted before the drug was marketed. Greater awareness of the problem among doctors could lead to more rational use of sumatriptan.

We thank Bente Overgaard Larsen, Lars Clemmensen, and all staff at participating pharmacies for excellent teamwork, and Anne Rosenkrantz for secretarial assistance.

Contributors: DG had the original idea for the study, was principal investigator and study coordinator, interviewed all patients, did statistical analyses, and had main responsibility for writing the article; he is guarantor of this paper. IT and SHS advised on design of the structured interview and criteria for inappropriate use, examined patients, and participated in evaluation of drug use. JH and JK advised on the recruitment part of the study. JH was also responsible for retrieval of prescription data. BKR commented on the part of the structured interview on headaches and the criteria for inappropriate use and was consulted regarding difficult cases. LFG was responsible for funding and advised on the overall design and intrepretation of data. All authors contributed to the writing of the paper.

Funding: Danish Health Science Research Council (grant Nos 12-1970-1 and 9501767).

Conflict of interest: None.

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(Accepted 31 October 1997)

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Is cardiothoracic ratio in healthy middle aged men an independent predictor of coronary heart disease mortality? Whitehall study 25 year follow up

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Aetiological studies of myocardial ischaemia have tended to concentrate on factors which influence atherothrombotic processes in the coronary arteries rather than myocardial pathophysiology.[1] The commonest clinical measure of heart size—cardiothoracic ratio—was included in the original Whitehall study of healthy middle aged civil servants. Cardiothoracic ratio is associated with left ventricular mass[2] and left ventricular systolic function; since left ventricular mass determined by echocardiography has been shown to predict coronary heart disease in elderly people,[1] we hypothesised that increased cardiothoracic ratio would independently predict mortality from coronary heart disease. Unlike previous studies[3] we did not include mortality from stroke since it may be related to heart size through different pathophysiological mechanisms.

Subjects, methods, and results

We studied the 1203 male British civil servants aged 40-69 years who participated in the original Whitehall study and were randomly selected (by random number tables) for measurement of cardiothoracic ratio from 100 mm chest radiographs. The rate ratio for all cause mortality among those in the random sample compared with those not in the sample was 1.01 (95% confidence interval 0.93 to 1.11) making a serious selection bias unlikely. Details of the standardised methods of risk factor, electrocardiographic and radiographic measurements and their quality control have been reported.[4 5] Cardiothoracic ratio was calculated as the ratio of the maximal transverse diameter of the cardiac silhouette to the distance between the internal

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BMJ 1998;316:1353–4

Adjusted hazard ratios (95% confidence intervals) for the effect of cardiothoracic ratio on all cause and coronary heart disease mortality

	All causes (534 deaths)			Coronary heart disease (196 deaths)		
Cardiothoracic ratio (fifths)	Adjusted for age	Adjusted for age and blood pressure*	Fully adjusted†	Adjusted for age	Adjusted for age and blood pressure*	Fully adjusted†
<0.4	1.0	1.0	1.0	1.0	1.0	1.0
0.4-0.439	1.07 (0.80 to 1.42)	1.08 (0.80 to 1.45)	1.08 (0.80 to 1.46)	1.15 (0.69 to 1.92)	1.04 (0.62 to 1.75)	1.02 (0.61 to 1.73)
0.44-0.449	0.96 (0.72 to 1.28)	0.94 (0.69 to 1.27)	0.98 (0.72 to 1.34)	1.11 (0.67 to 1.87)	1.03 (0.61 to 1.74)	1.02 (0.60 to 1.74)
0.45-0.469	0.96 (0.72 to 1.28)	0.93 (0.69 to 1.26)	1.02 (0.75 to 1.38)	1.45 (0.89 to 2.37)	1.32 (0.81 to 2.16)	1.33 (0.81 to 2.20)
≥0.47	1.38 (1.05 to 1.82)	1.27 (0.95 to 1.70)	1.28 (0.95 to 1.73)	2.15 (1.35 to 3.44)	1.84 (1.14 to 2.97)	1.65 (1.01 to 2.70)

*Adjusted for systolic pressure and diastolic pressure.
† Adjusted for age, systolic blood pressure, diastolic blood pressure, heart rate, total cholesterol concentration, smoking habit, Rose angina, and electrocardiographic evidence of ischaemia (Minnesota codes: 1-1 to 1-3, 4-1 to 4-4, 5-1 to 5-3, and 7-1).