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Pattern of sumatriptan use and overuse in general practice

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Abstract *Objective*: To investigate the frequency of use and misuse of sumatriptan, and to explore the characteristics of patients reporting overuse.
Setting: A postmarketing cohort study on adverse reactions to sumatriptan, performed with the assistance of drug-dispensing general practitioners in the Netherlands.
Methods: Questionnaires were sent to patients on sumatriptan of drug-dispensing general practitioners in the Netherlands. Use of sumatriptan was classified into five groups: < 1, 1–10, 11–20 and 21–30 times per month and a group of patients who reported daily use of sumatriptan more than 10 times per week. Patients in the latter group were regarded as "overusers".
Results: The request to the 1720 patients yielded a response rate of 1202 (70%). Of 952 (79%) of these patients, details of their sumatriptan intake were available. Most patients (718, 75%) took sumatriptan 1–10 times each month. However, 36 patients (4%, 95% CI 2.8–5.2%) took sumatriptan daily or more than 10 times each week. The group with the highest intake consisted mainly of males, and many patients who reported a poor efficacy of sumatriptan. Age was not related to use of sumatriptan.
Conclusions: A small group of patients (4%) used sumatriptan too often. A high intake was associated with both male gender and a reported poor efficacy of sumatriptan, but not with age, reported adverse reactions, or headache attributed to sumatriptan. It is important to explain to patients that sumatriptan is only for the treatment of acute attacks, and not for prophylactic use. Drug consumption patterns have to be evaluated, in particular in patients who report low efficacy of sumatriptan.

Key words Sumatriptan, Postmarketing surveillance, Migraine; overuse, pharmacoepidemiology

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The serotonin-1 agonist sumatriptan is a relatively new drug used in the treatment of acute attacks of migraine and cluster headache [1]. Adverse drug reactions attributed to sumatriptan in the postmarketing period include acute myocardial infarction [2, 3], depression [4] and skin reactions [5]. A characteristic feature is the recurrence of headache within 24 h after administration of sumatriptan [6]. Since marketing of the drug, several patients have been observed who developed an increase in the frequency of migraine attacks with consequent dependence and misuse, after use of sumatriptan [7–9]. Preliminary results of a postmarketing study based on pharmacy records have also shown misuse of sumatriptan by approximately 1% of consumers [10]. We investigated the frequency of use and misuse of sumatriptan in a postmarketing cohort study, and explored the characteristics of patients reporting overuse.

Methods and data analysis

In May 1991, sumatriptan was registered in the Netherlands for the treatment of acute attacks of migraine and cluster headache. In July 1992, we conducted an enquiry and all 687 drug-dispensing general practitioners (GPs) in the Netherlands were contacted, to obtain the date of birth and gender of every person to whom they had dispensed sumatriptan since marketing. Subsequently, they were asked to send a questionnaire to the patients who had used sumatriptan, to be completed at home. The questionnaires were sent via the GP in prestamped envelopes with a standard letter from our centre. In the questionnaire, the patients were asked

whether they had indeed used sumatriptan and, if so, how often sumatriptan was used, what the efficacy of sumatriptan was and whether they had observed any adverse reaction after use of sumatriptan. No adverse reactions were mentioned by name in the questionnaire. Some details of the study have been published previously [11, 12].

Use of sumatriptan was classified into five groups: < 1, 1–10, 11–20 and 21–30 times per month, and a fifth group of patients who reported daily sumatriptan use or use more than 10 times each week. Patients in the latter group were regarded as "overusers".

Differences between group means were tested by Student's *t*-test. A chi-square test was used to assess differences between proportions, with use of Fisher's exact test if there was an expected cell value of less than 5. All calculated *P* values are two-tailed. Statistical significance was defined as a two-sided *P*-value of less than 0.05. Relative risks (RR) were calculated with 95% confidence intervals (95% CI).

Results

Of the 589 Dutch GPs (86%) who participated in this study, 474 had dispensed sumatriptan on at least one occasion to a total of 1727 patients (24% males, 76% females). During the study period, seven patients were lost to follow-up, all from change of address. Of the 1720 remaining patients, 1202 (70%) returned the questionnaire. With 952 (79%) of these patients full details of their sumatriptan intake were available.

Basic characteristics of the study population are summarized in Table 1. A total of 34 patients (4%) reported (rebound) headache due to use of sumatriptan, 6 males and 28 females (gender distribution not significantly different from the other patients). In Fig. 1 the consumption of sumatriptan is depicted. Most patients (718, 75%) consumed sumatriptan 1–10 times each month. Thirty-six patients (4%, 95% CI 2.8–5.2%) used sumatriptan daily or more than 10 times each week, and were regarded as "overusers", of whom 17 patients used sumatriptan once every day, 14 patients took sumatriptan 2 times each day, 3 patients three times each day, and 2 patients reported that they used sumatriptan more than 10 times each week (not specified per day). Of the 36 patients, 13 (36%) were males, which was more than in the patients who used sumatriptan less than 10 times per month (192 males, relative risk 1.9, 95% CI 1.0–3.7). There were no differences in age, duration of headache complaints or route of administration between the five intake groups. Of the 36 patients who took sumatriptan daily or more than 10 times each week, 6 patients reported the efficacy of sumatriptan as poor, compared to 49 patients of the 916 patients who used sumatriptan less than 30 times each month (RR = 3.3 95% CI 1.4–7.5). One or more adverse reactions were reported by 18 patients (50%) of the overusers, compared to 511 patients (56%) of the others (*P* = 0.5). Headache as an adverse reaction to sumatriptan was reported by 1 "overuser" (2.8%), compared to 33 patients in the other groups (3.6%; not significantly different).

Table 1 Basic characteristics of 952 patients with information on sumatriptan consumption (*SD* standard deviation)

Characteristic	Number or mean
Age (years)	44 (SD: 11)
Males	224 (24%)
Reported efficacy of sumatriptan	
– Good	729 (77%)
– Moderate	77 (8%)
– Poor	55 (6%)
– Not reported	91 (9%)
Route of administration	
– Oral	318 (33%)
– Subcutaneous	458 (48%)
– Both routes	82 (9%)
– Missing	94 (10
Average duration of headache complaints (years)	21 (SD: 13)
Any adverse reaction	529 (56%)
Headache after sumatriptan	34 (4%)

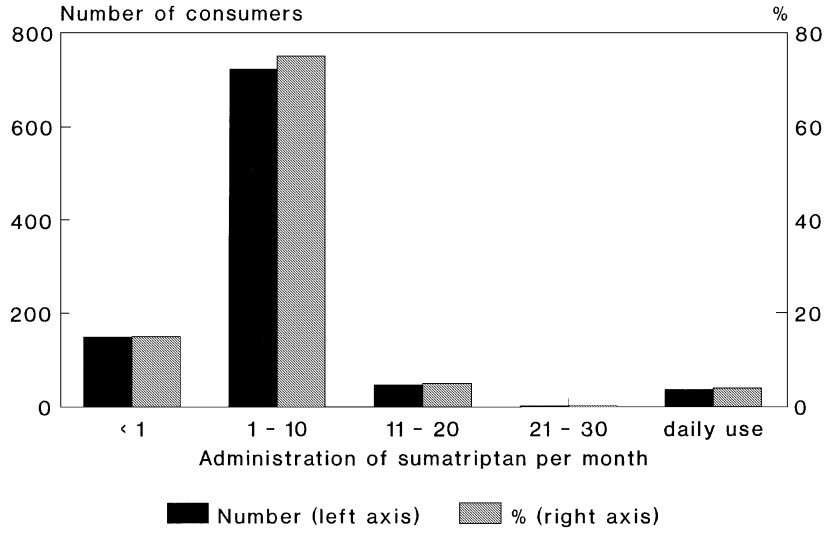

Fig. 1 Consumption of sumatriptan in 952 patients of drug-dispensing general practitioners. Consumption was classified into five groups: < 1, 1–10, 11–20 and 21–30 times per month and a group of patients who reported daily use sumatriptan or use more than 10 times each week

Discussion

We found that a small proportion (4%) of the consumers used sumatriptan daily or more than 10 times each week. Since sumatriptan is a drug for acute attacks of migraine or cluster headache, and not for prophylactic use, we regarded this group as "overusers". It has previously been recommended that patients with headaches should never take analgesics every day, and that ergotamine should not be taken more than 10 times a month [13]. Overuse in our study was significantly more frequently observed in males, and in patients who reported the efficacy of sumatriptan as poor.

Analyses of medication consumption based on dispensing or reimbursement data have two major limitations: (1) no information is available on non-compliance and (2) no information is available on drugs which are bought "over the counter". Furthermore, these pharmacy record based studies do not provide direct information on efficacy, clinical events or adverse drug reactions observed by consumers. In our post-marketing study we used information of drug use obtained directly from consumers. Because of strict privacy rules in the Netherlands, we were not able to validate these data by evaluating the records of the drug-dispensing general practitioners. We think, however, that these data give good insight into the consumption of sumatriptan in these patients, although negative misclassification may exist.

Several explanations for overuse may be considered. The most important reason for more frequent use of sumatriptan is possibly a higher attack rate of migraine or cluster headache, but information on attack rates was not available in our study. However, it was demonstrated in our study that an observed low efficacy of sumatriptan accompanied more frequent overuse. Previously, headache recurrence after sumatriptan use was reported [14–16]. It has been suggested that the rebound headache may be the underlying mechanism of over-use of sumatriptan [10, 15]. However, the (rebound) headache was not associated with overuse in our study. Another explanation, more compatible with our data, is that some patients use sumatriptan in too low a dose or that in some patients the activity of sumatriptan is too short.

In conclusion, we found that 4% of patients consuming sumatriptan used this drug daily or more than 10 times per week. Overuse was associated with a reported poor efficacy of sumatriptan and with male gender, but not with (rebound) headache after sumatriptan use. Drug consumption patterns of sumatriptan have to be evaluated in all patients, but in particular in patients who report low efficacy of sumatriptan.

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References

1. Plosker GL, McTavish D (1994) Sumatriptan: a reappraisal of its pharmacology and therapeutic efficacy in the acute treatment of migraine and cluster headache. Drugs 47:622–651
2. Ottervanger JP, Paalman HJA, Boxma GL, Stricker BHCh (1993) Transmural myocardial infarction with sumatriptan. Lancet 341:861–862
3. Weidmann B, Jansen W, Bojko P, Hänseler Th, Hinzmann S, Tauchert M (1994) Sumatriptan-induzierter Myokardinfarkt. Intensivmedizin 31:353
4. La Porta LD (1995) Recurrent depression after sumatriptan administration for treatment of migraine. J Clin Psychopharmacol 15:81–82
5. Black P, Caldwell J (1994) Skin sensitivity to sumatriptan [letter]. NZ Med J 107:20–21
6. Brown EG, Endersby CA, Smith RN, Talbot JCC (1991) The safety and tolerability of sumatriptan: an overview. Eur Neurol 31:339–344
7. Osborne MJ, Austin RCT, Dawson KJ, Lance L (1994) Is there a problem with long term use of sumatriptan in acute migraine? BMJ 308:113
8. Kaube H, May A, Diener HC, Pfaffenrath V (1994) Sumatriptan. BMJ 308:1573–1574
9. Pini LA, Trenti T (1994) Does chronic use of sumatriptan induce dependence? Headache 34:600
10. Gaist D, Sindrup S, Hallas J, Gram LF (1994) Misuse of sumatriptan. Lancet 344:1090
11. Ottervanger JP, Witsen van TB, Valkenburg HA, Stricker BHC (1993) Postmarketing study of cardiovascular adverse reactions associated with sumatriptan. BMJ 307:1185
12. Ottervanger JP, Valkenburg HA, Grobbee DE, Stricker BHCh (1994) Adverse reactions attributed to sumatriptan: a post-marketing study in general practice. Eur J Clin Pharm 47:305–309
13. Olesen J (1995) Analgesic headache. A common, treatable condition that deserves more attention. BMJ 310:479–480
14. Dahlof C (1992) Headache recurrence after subcutaneous sumatriptan. Lancet 339:425–426
15. Sucherowsky O (1993) Rebound headaches due to sumatriptan. Neurology 43 (Suppl 2):A326
16. Anonymous (1995) Sumatriptan: rebound headache and migraine exacerbation. Can Adv Drug React Newslett 5:1