Single Use of Sumatriptan: A Patient Interview Study

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Objective.—To investigate the possible reasons associated with the use of a single prescription of sumatriptan.

Background.—A few population-based studies concerning the usage patterns of sumatriptan have revealed a relatively high incidence (approximately 40%) of sumatriptan users who utilize only a single prescription of the drug.

Design and Methods.—Using automated prescription data from 11 community pharmacies, we identified single and multiple sumatriptan prescription recipients. The data were collected from May 1, 1998, to April 30, 2000. Several patient- and medication-related variables possibly associated with single recipiency of sumatriptan were analyzed. In addition, single recipients of sumatriptan were invited for an interview and asked a number of questions related to their clinical status and their experience with the medication.

Results.—Four hundred ninety-five, first-time users of sumatriptan were identified during the patient selection period, of whom 38% were single recipients of sumatriptan. Of the latter, 102 patients were considered eligible for interview. Reasons for terminating treatment after only 1 prescription included: inefficacy and/or occurrence of side effects, 78% (n = 79); uncertain diagnosis of migraine, 39.2% (n = 40); and reduction in headache frequency, 33.3% (n = 34). Almost half of the population had terminated treatment without having consulted their physician. More than half relied upon the use of over-the-counter (OTC) analgesics after having tried sumatriptan. Compared to multiple users of sumatriptan, single recipients were far less likely to have used another form of migraine treatment prior to (odds ratio, 0.35; [95% confidence interval, 019 to 0.67]) and after (odds ratio, 0.34 [95% confidence interval, 0.19 to 0.63]) initiating sumatriptan. Furthermore, single recipients had demonstrated an increased tendency towards benzodiazepine use prior to receiving sumatriptan (odds ratio, 1.80 [95% confidence interval, 1.00 to 3.28]).

Conclusions.—Single use of a sumatriptan prescription reveals some issues that may impact negatively the provision of effective migraine management. These include: rapidly developing dissatisfaction with the treatment provided and a lower tendency to seek out medical care. Our results also suggest that the drug may be used (inappropriately) as a diagnostic tool.

Key words: migraine, sumatriptan, single recipient, inefficacy, diagnosis, consultation

Abbreviations: OTC over the counter, DDDs defined daily doses, NSAIDs nonsteroidal antiinflammatory drugs

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Due to increasing therapeutic options available for acute migraine management, physicians are currently able to achieve better clinical outcomes based on the individual needs of the migraineur.[1,2] In order to realize these goals, it is essential to acquire knowledge concerning patients' perceptions of and experiences with therapy and to obtain an accurate history of the headache after having established a diagnosis of migraine.[3] However, due to the relatively poor medical consultation rates observed within the migraine population in particular, the attempt to individualize and optimize migraine treatment is often weakened.[4,5]

Furthermore, although the guidelines established by the International Headache Society (IHS) have clearly improved the diagnostic quality of migraine and other headaches, challenges still do exist for the practitioner.[6-8] Current information indicates that migraine is underdiagnosed and undertreated. It has been estimated that only 50% of patients with migraine are accurately diagnosed by the physician at the initial visit which will hinder the provision of appropriate and effective treatment for some misdiagnosed patients.[9] In addition, other headaches presenting with similar clinical manifestations as migraine, such as tension-type, cluster, or chronic daily headache can occasionally lead to a misclassification of migraine diagnosis. Lipton et al demonstrated that approximately 17% of physician diagnosis of migraine did not meet IHS criteria for migraine.[10] Although the numbers are small, it is plausible that this could lead to overtreatment and/or inappropriate treatment for the actual headache.[7,8]

Population-based studies concerning the patterns of sumatriptan use have estimated that approximately 40% of patients who try sumatriptan are single recipients of the drug.[11,12] Even though the underlying reasons associated with this particular pattern of use were not addressed, it is possible that diagnostic uncertainty or treatment complications (or both) were involved. Other reasons may include the poor consultation behavior of migraineurs, lack of patient education concerning the appropriate use of sumatriptan, or simply patients suffering from mild forms of migraine.[4,5]

In view of the relatively high incidence of the single recipiency of sumatriptan, we were, therefore, interested in determining whether this pattern of use could be associated with the various documented problems in achieving effective migraine management.[4,5,8] The main outcome of interest was to determine whether this pattern of use is either purely an indication of treatment failure or partially related to diagnostic misclassification or a reduction in the frequency or severity of the migraine attacks.

PATIENTS AND METHODS

Study Setting.—This patient interview study was conducted in 11 community pharmacies providing pharmaceutical care to approximately 120 000 registered inhabitants, residing in 3 metropolitan localities in The Netherlands. In view of a high patient pharmacy registration commitment in The Netherlands, as well as the availability of sophisticated pharmacy software in most community pharmacies, the prescription medication history in each pharmacy for each patient is virtually complete and can be electronically linked to other community pharmacies. This allows for an accurate estimation of drug use for patients on an individual and population level.[13] All participating pharmacies were equipped with prescription records that could provide drug use information over a 7-year period (January 1994 until date of the actual patient selection procedure). Relevant information per prescribed medicine includes date of dispensing, drug, dosage regimen, quantity supplied, and type of prescriber. Patient information includes gender and date of birth. Information concerning the indications for use of the medicines, in this case the diagnosis of migraine versus cluster headache, or registration of nonprescription medicines (eg, over-the-counter [OTC] use of salicylates or paracetamol) is often incomplete.

Patient Selection.—Using automated prescription records, the participating pharmacists were asked to initially select all patients who had presented a prescription for sumatriptan for the first time from May 1, 1998, to April 30, 2000. This was termed *start date sumatriptan*. First-time use was defined as a drug-free interval of at least 2 years prior to the start date sumatriptan. Sumatriptan was approved for use in The Netherlands in 1991, for which the tablet form became fully reimbursable by 1997. The patient selection procedure was performed during May 2001. Hereafter, a review of the full medication history was required in order to identify "single recipient patients" (presentation of only 1 prescription for sumatriptan) and "continuing patients" (presentation of more than 1 prescription for sumatriptan). Follow-up lasted from the start date of sumatriptan until the medication review date by the pharmacist. In order to be included in the study, all patients were required to possess a medication history covering a period of more than 6 months before and after the start date of sumatriptan. In order to reveal a potential association with the single recipiency of sumatriptan, several

determinants were analyzed by analyzing prescription history data of all single-recipient patients (index group) and compared with continuing users of sumatriptan (reference group). For each interviewed patient, 1 continuing user was chosen by matching the date of their first sumatriptan prescription ("reference index date") with the corresponding start date sumatriptan determined for single recipients. Characteristics of interest included age, gender, prescriber of sumatriptan at start date, and the use of specific abortive migraine drugs (ergotamine or other triptans) or migraine prophylactic drugs prior to and after the start date.

Patient Interview.—In addition, single-recipient patients were interviewed by the pharmacist. A minimum of 5 single recipients of sumatriptan per participating pharmacy, in whom the start date of sumatriptan was the most recent during the period of May 1998 to April 2000, were contacted and asked to complete a structured questionnaire via telephone. Interviewed patients were further eliminated from the study and considered continuers of sumatriptan if, upon questioning, they had presented more than 1 sumatriptan prescription at another pharmacy or were certainly intending to use sumatriptan again in the future. In these cases, the interview was discontinued and a new study patient was chosen to complete the questionnaire. A completed questionnaire corresponded to discontinuation of sumatriptan as well as the patient's (adamant or uncertain) intent not to use the drug in the future following the use of the single presented prescription.

Patients provided informed consent for all interviews and for the review of the medication histories. Several questions were asked concerning confirmation of single recipiency: prescriber of the sumatriptan prescription, whether sumatriptan had actually been discontinued and the reasons thereof, whether the physician had been contacted, the number of defined daily doses (DDDs) used, and the number of attacks treated with sumatriptan. One DDD of sumatriptan corresponded to one 100-mg tablet, a 6-mg subcutaneous injection, or 20 mg of nasal spray. Additional information included the use of specific (ergotamine or other triptan) or nonspecific (nonsteroidal anti-inflammatory drugs [NSAIDs], paracetamol) migraine analgesia (nonprescription and prescription) and prophylactic use, prior to and after sumatriptan use, and satisfaction concerning overall treatment. Clinical information such as headache diagnosis, number of headache attacks per month, number of physician contacts during the last year, and comorbidity was also asked.

Data Analysis.—By applying logistic regression analysis, the strength of the association between the investigated determinants and the single recipiency of sumatriptan was expressed as odds ratios (OR) with 95% confidence intervals (CI) with adjustments made for age and gender.

Completed anonymized questionnaires for the interviewed patients and prescription history data for all patients were analyzed. The prescription history data corresponded to 1 year prior to and after the start date of sumatriptan until the patient selection period and was required to evaluate the representativeness of the patient information. Interviewers were also asked to report data corresponding to the number of first-time sumatriptan users identified during the patient selection period (n = 495), number of single recipients identified (n = 188) and number of single-recipient patients interviewed (n = 143).

Microsoft Access®, a relational database software package, was used for database management and internal quality and validation procedures. The statistical package, SPSS version for Windows, was used for data analysis.

RESULTS

Four hundred ninety-five patients were identified by the computerized prescription records who had presented a prescription for sumatriptan for the first time between May 1, 1998 and April 30, 2000. Review of the medication histories of each of these patients identified 188 single recipients (38%) and 307 continued users (62%) of sumatriptan.

A random sample of 141 single recipients were contacted to complete the questionnaire, of which the response rate was 89% (n = 125). All interviewed patients confirmed their date of first-time use of sumatriptan determined by the prescription records. In 23 patients, the first few questions of the interview revealed that there was a positive intent to use

Table 1.—Determinants of Single Use Compared to Continuous Use of Sumatriptan According to Prescription Data*

Determinant	Single Use Group (n = 102)	Continuous Use Group (n = 102)	Odds Ratio (95% Confidence Interval)
Sex			
Male	17.6	23.5	1.0 (reference)
Female	82.4	76.5	1.44 (0.72-2.87)
Age, y			
<25	9.8	9.8	1.03 (0.40-2.68)
25-44	58.8	61.8	1.0 (reference)
45-64	26.5	25.5	1.13 (0.59-2.18)
>64	4.9	2.9	1.81 (0.41-7.93)
Prescriber			
General practitioner	87.3	83.3	1.0 (reference)
Neurologist	12.7	16.7	0.73 (0.34-1.61)
Abortive migraine analgesic use†			
Prior	12.8	22.5	0.49 (0.23-1.04)
Post	18.6	27.5	0.60 (0.31-1.16)
Prophylactic migraine use‡			
Prior	7.8	18.6	0.39 (0.16-0.95)
Post	10.8	23.5	0.39 (0.18-0.87)
Prior co-medication			
Antidepressant	9.8	16.7	0.56 (0.24-1.28)
Benzodiazepine	39.2	26.5	1.80 (1.00-3.28)
Cardiovascular	7.8	4.9	1.83 (0.56-6.08)
Oral contraceptive	47.1	41.2	1.20 (0.67-2.15)
Gastrointestinal	21.6	17.6	1.28 (0.64-2.58)

* Values for single use and continuous use groups are given as percentages.
† Ergotamine or other triptans.
‡ Propranolol, metoprolol, pizotifen, flunarizine, methysergide, clonidine, or valproic acid.

sumatriptan again in the future and they were excluded from the study. For the 102 interviewed single-recipient patients an equivalent number of continuing users was sampled.

Baseline characteristics of the single recipients and the continuing users are provided in Table 1. Fewer single recipients of sumatriptan had been using ergotamine or another triptan prior to (OR, 0.49 [95% CI, 0.23 to 1.04]) or after (OR, 0.60 [95% CI, 0.31 to 1.16]) the start date of sumatriptan as compared to continuing users. Likewise, single recipients were least likely to have initiated migraine prophylactic drugs prior to (OR, 0.39 [95% CI, 0.16 to 0.95]) or after (OR, 0.39 [95% CI, 0.18 to 0.87]) the start date. The use of benzodiazepines prior to the start date of sumatriptan seemed to be indicative of single recipiency (OR, 1.80 [95% CI, 1.00 to 3.28]).

Table 2 provides some characteristics of the single recipients of sumatriptan. The mean age of the patients interviewed was 39 years (range, 10 to 72), of whom the majority were women (82%). The preferred dosage form of sumatriptan to be prescribed was tablets (73%) of which 66% consisted of the 50-mg strength. Prior to starting sumatriptan, 99 patients (97.0%) had been using some form of medication to treat their headache attacks, of whom 48 (51.6%) had been using prescription analgesics (NSAIDs, ergotamine or another triptan), 8 (8.8%) had been using prophylactic medication, and 73 (71.5%) had been using OTC analgesics. After the discontinuation of sumatriptan, the majority of the interviewed patients (85.3%) had retained some form of migraine treatment (either OTC or prescription only [or both]). However, the reported use of OTC medication had

Table 2.—Characteristics of Single Users of Sumatriptan by Interview

Characteristic	No. (%) of Single Recipients (n = 102)
Sex	
Female	84 (82.4)
Male	18 (17.6)
Age, mean ± SD, y	39.3 ± 13.0
<25	10 (9.8)
25-44	60 (58.8)
45-64	27 (26.5)
>64	5 (4.9)
Sumatriptan dosage form	
Oral	74 (72.5)
Subcutaneous injection	5 (4.9)
Nasal spray	23 (22.5)
Defined daily doses per prescription, mean ± SD	3.9 ± 3.1
Defined daily doses consumed, mean ± SD	2.1 ± 1.7
Physician	
General practitioner	89 (87.3)
Neurologist	13 (12.7)
Headache diagnosis	
Migraine without aura	34 (33.3)
Migraine with aura	26 (25.5)
Cluster	2 (2.0)
Tension-type	6 (5.9)
Unknown	34 (33.3)
No. of headache years, mean ± SD	10.9 ± 8.5
Comorbidity	
Cardiovascular	7 (6.9)
Endocrine	6 (5.9)
Gastrointestinal	1 (1.0)
Respiratory	8 (7.8)
Psychiatric	18 (17.6)
Prior migraine drug use	
Over the counter*	73 (71.5)
Prescription nonsteroidal anti-inflammatory	19 (18.6)
Opioid (codeine or tramadol)	16 (15.7)
Ergotamine	12 (11.8)
Another triptan	1 (1.0)
Migraine prophylaxis	8 (7.8)

* Includes paracetamol ± caffeine, ibuprofen, naproxen, aspirin, and/or homeopathy.

dropped substantially to 56.9%. On average, 2 DDDs (range, 0 to 10) of sumatriptan were consumed to treat two attacks (range, 0 to 10).

During interview, 60 patients (58.5%) stated that they were suffering from migraine of whom 26 (43.3%) were suffering from the aura form.

Table 3 shows that overall dissatisfaction with and discontinuation of treatment due to inefficacy or occurrence of side effects (or both) had occurred in 79 patients (78%): insufficient headache relief in 36 patients (35.3%), occurrence of side effects in 16 patients (15.7%), and occurrence of both insufficient headache relief and side effects in 27 patients (26.5%). Approximately half of the interviewed patients discontinued sumatriptan on their own initiative. More than two thirds of the patients (n = 27) in whom side effects had occurred had described side effects commonly associated with sumatriptan use (tingling, paresthesias, flushing, dizziness, and malaise). In addition, 15 patients (32.6%) reported side effects such as palpitations and pressure in the chest. Forty-nine (62%) of the 79 patients were using some other type of prescription-only migraine medication (acute or preventive) after sumatriptan use.

Table 3.—Characteristics and Possible Causes of Single Use of Sumatriptan

Feature	No. (%) of Single Recipients (n = 102)
Drug related	
Inefficacy	36 (35.3)
Side effects	16 (15.7)
Inefficacy and side effects	27 (26.5)
Contraindications	2 (2.0)
Fear	7 (6.9)
Headache related	
Diagnosis uncertainty	40 (39.2)
Reduction of migraine frequency	34 (33.3)
Initiator of discontinuation	
Physician	56 (54.9)
Patients	46 (45.1)
No intention of future use	90 (88.2)
Postmigraine drug use	
Over the counter*	58 (56.9)
Prescription nonsteroidal anti-inflammatory	19 (18.6)
Opioid (codeine or tramadol)	11 (10.8)
Ergotamine	5 (4.9)
Another triptan	14 (13.7)
Migraine prophylaxis†	11 (10.8)

* Includes paracetamol ± caffeine, ibuprofen, naproxen, aspirin, and/or homeopathy.
† Includes propranolol, metoprolol, pizotifen, flunarizine, methysergide, clonidine, or valproic acid.

Forty patients (39.2%) stated that they discontinued sumatriptan as the diagnosis for migraine was uncertain, of whom 24 patients (60%) stated that this was confirmed by the treating physician upon further medical evaluation. Of these patients, 5 were diagnosed with tension-type headache and 1 patient with cluster headache. The remainder (n = 34) were uncertain as to the origin of their headache in whom 19 (55.9%) were still suffering from occasional headache attacks during interview which required the use of OTC analgesics after sumatriptan. Nine (22.5%) of the 40 patients were still using another prescription medication as acute medication, such as paracetamol with codeine or NSAIDs, following sumatriptan use.

Another headache-related reason for discontinuing or not even having initiated sumatriptan was attributed to a natural reduction in headache attack frequency or severity (or both) in 34 patients (33.3%).

COMMENTS

During the study period, we found that 38% of sumatriptan first-time users were a single recipient of the drug, the proportion of which being similar to data obtained from other population-based studies concerning sumatriptan use.[11,12] Major reasons explaining this pattern of use included treatment failure with sumatriptan associated with rapid dissatisfaction with treatment, diagnostic uncertainty, and a reduction in the frequency of migraine attacks.

The positive clinical outcomes of sumatriptan and other triptans have clearly been established by a number of patient interview and clinical trial studies.[2,14-16] However, these studies and others have also shown that approximately 25% of sumatriptan users do not achieve the anticipated benefits and discontinue treatment, mainly due to inadequate pain relief or drug-related side effects (or both).[14,15,17] Our study revealed that 18% of all first-time users of sumatriptan discontinue treatment after a single prescription primarily due to insufficient migraine relief and occurrence of side effects. These results are, in fact, strikingly similar to those obtained by Lipton and Stewart who demonstrated that 16% of their study population were dissatisfied with their current treatment, primarily due to inefficacy of the specific drug.[3]

It must be considered that the majority of the patients (53%) who had terminated sumatriptan treatment solely due to inefficacy and who were still suffering from migraine attacks during interview had been prescribed the 50-mg sumatriptan tablet. These patients may have benefited from the higher dosage strength since it has been shown that the 100-mg dosage form can provide beneficial effects in many patients who were previously dissatisfied with the 50-mg tablet form.[18] Instead, those patients who did consult their physician were prescribed another analgesic for migraine, either an NSAID or another triptan.

In addition, it seems that nonresponse to sumatriptan may be heightened by patients suffering from migraine and generalized anxiety.[19] This may very well explain the increased use of benzodiazepines by patients of single use compared to continued users. In addition, patients suffering from anxiety disorders often elicit a hypochondriacal behavior due to a general reduction in well-being which has shown to be associated with a hypersensitivity towards somatic complaints, such as pain or headache, whereby the physician may be manipulated and forced to prescribe an analgesic medication, for instance.[20,21]

As observed in other studies, our study shows that consumption of OTC analgesic medication by the migraine population occurs on a large scale (60%).[5,22,23] A few documented reasons associated with the discontinuation of prescribed treatment and heavy reliance on OTC analgesics include patients suffering from mild headache or treatment failure and/or dissatisfaction with treatment and medical management due to expectations not being optimally realized.[4,5] These reasons can likewise be applied to our study population, and our findings further highlight the need to ensure regular follow-up visits and provide adequate information and patient education concerning treatment and the diagnosis.[4]

Providing an accurate diagnosis of migraine is often complex, primarily due to the frequent presence of additional headaches and/or the inability of the patient to provide the physician with an accurate history of signs and symptoms of the presenting headache.[8,24] Of our patients, 40% stated they were not suffering from migraine as confirmed upon further medical evaluation in almost two thirds of these

patients. Our findings are far higher to those obtained by Lipton et al who found that 17% had been incorrectly diagnosed.[10] However, their study had used the IHS criteria to assess the accuracy of migraine diagnosis. Since our study relied purely on patient information, we cannot claim that these patients had been given an incorrect diagnosis. Nevertheless, it cannot be ruled out that in these patients sumatriptan may have been prescribed as a diagnostic tool in order to differentiate migraine from other primary or secondary headaches such as chronic tension-type headache, idiopathic stabbing headache, or chronic daily headache.[7,8,24] This can further be supported by our findings that single recipients were less likely to have been exposed to other specific abortive migraine drugs or migraine prophylactic medication prior to or after the use of sumatriptan when compared to continued users.

The single use of sumatriptan was also associated with patients having experienced a natural reduction in migraine attack frequency which did not require the need to continue or even initiate treatment with the drug. Some of these patients may have been suffering from a mild intensity of migraine in whom initial management with nonspecific migraine analgesics such as NSAIDs including aspirin would generally suffice.[25] Slightly more than half of these patients had not received this form of treatment prior to being prescribed sumatriptan. This raises the question whether initiating specific abortive migraine treatment with sumatriptan was the most appropriate therapeutic option for these patients. Again, the relative lack of use of specific migraine medication, acute or preventative, by single recipients also suggests that single recipiency of sumatriptin corresponds to patients suffering from a migraine of mild severity.

Of interest, almost 50% of the patients had discontinued sumatriptan without having consulted their physician for which the major contributing factor was a reduction in headache frequency and/or severity. This latter finding is consistent with data obtained from other studies investigating the patterns of patient consultation behavior.[3,5,26] Similarly, 50% (data not shown) of the interviewed patients had not consulted their physician for migraine in the year preceding the date of interview. Edmeads et al found that only 36% of their interviewed patients were undergoing medical supervision at the time of interview, whereas Lipton and Stewart had identified 21% of their interviewed population had discontinued consultation due to mild headache, dissatisfaction with medical management, and availability of OTC medications.[3,5] Though slightly higher, our data further confirm that medical follow-up patterns within the migraine population are often irregular.

Several limitations to this study should not be ignored. As in other patient interview studies of migraine,[3,10,26] patient recall bias will undoubtedly occur, particularly diagnostic recall. Patients from our study who had reported that the initial diagnosis of migraine was incorrect may have actually been correctly diagnosed and were simply experiencing a relative long-term absence of their migraine from the start date of sumatriptan until the interview data. However, the majority of these patients (60%) had stated that the diagnosis was found to be incorrect upon further medical evaluation. Furthermore, some patients who had not reported any use of prescription analgesics prior to and/or after sumatriptan may have in fact used these drugs. It must be noted that review of the pharmacy prescription records for each interviewed patient was highly representative of prescribed migraine medication usage patterns reported by the patient. This high correlation between prescription data information and patient information data has been confirmed elsewhere.[23,27]

In conclusion, our study has identified a few underlying reasons concerning the single recipiency of sumatriptin that can exert a negative impact in the provision of successful medical and therapeutic management for the migraineur. These range from poor consultation habits of the migraine population and rapid dissatisfaction with treatment due to unfulfilled expectations concerning the effectiveness and tolerability of abortive treatment. Furthermore, it seems that the initiation of specific abortive migraine treatment with sumatriptan may occasionally be intended as a diagnostic tool. Similar extended research by also investigating the second-generation triptans as well as ergotamine may provide additional valuable data.

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