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Collection of Medical Drug Information in Pharmacies: Drug Event Monitoring (DEM) in Japan

Sei-ichiro HAYASHI,*,[a] Akira NANAUMI,[b] Yasuji AKIBA,[b] Takako KOMIYAMA,[c] and Koichi TAKEUCHI[d]

Central Pharmaceutical Information Center,[a] The Japan Pharmaceutical Association,[b] Nagai Building 4F, 2–12–15 Shibuya, Shibuya-ku, Tokyo 150–8389, Japan, Division of Clinical Pharmacy, Center for Clinical Pharmacy and Clinical Sciences, School of Pharmaceutical Sciences, Kitasato University,[c] 5–9–1 Shirokane, Minato-ku, Tokyo 108–8641, Japan, and Department of Clinical Pharmacology, Meiji Pharmaceutical University,[d] 2–522–1 Noshio, Kiyose, Tokyo 204–8588, Japan

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To establish a system for collecting and reporting information from community pharmacists such as that on adverse effects, the Japan Pharmaceutical Association (JPA) conducts Drug Event Monitoring (DEM). In the fiscal year 2002, a survey was carried out to clarify the incidence of sleepiness due to antiallergic drugs. The investigated active ingredients were ebastine, fexofenadine hydrochloride, cetirizine hydrochloride, and loratadine. Community pharmacists asked the following question to patients who visited their pharmacies: ''Have you ever become sleepy after taking this drug?'' During a 4-week survey period, reports of 94256 cases were collected. To evaluate the incidence of sleepiness, we analyzed cases in which reports showed alleged absence of concomitant oral drugs, and drug use in conformity with the dose and method described in package inserts. The incidence of sleepiness was significantly different among the drugs (χ^2-test, $p<0.001$). The observed incidences of sleepiness due to the drugs (8.8—20.5%) were higher than those described in each package insert (1.8—6.35%). This may be because an active question was used (''Have you ever become sleepy after taking this drug?''). Active intervention by pharmacists may be useful for collecting more information on improvement in the QOL of patients and safety. In addition, the pharmacists were asked to report events other than ''sleepiness'' in the free description column of the report. Some symptoms not described in the package inserts were reported, suggesting that DEM may lead to the discovery of new adverse effects. These results suggest that community pharmacists have a good opportunity to collect information in DEM, and safety information such as that on adverse effects can be obtained from pharmacies.

Key words——community pharmacy; pharmacist; drug event monitoring; antiallergic drug

INTRODUCTION

In Japan, due to the advanced separation of drug prescribing and dispensing, dispensing has become more regularly performed in community pharmacies. In this situation, community pharmacists are required to perform various roles, including that of drug specialists who express their opinions to physicians and patients, and that of counselors who give patients advice on their worries and anxieties.[1] Among the various roles of community pharmacists, their contribution to the safety of drugs is also socially important.

In pharmacies, pharmacists collect and record information on patients' use of medicines through their interviews and medication counseling and make use this information for patient safety by; for example, preventing adverse effects and drug interactions. Therefore, we considered that analysis of information collected in individual pharmacies may contribute to improvement in the safety of medicines. Although such studies have already been conducted,[2—7] not many pharmacies participate in these studies, We considered it necessary to establish a system in which community pharmacists throughout the nation report information such as adverse effects to the government or pharmaceutical association.

The Japan Pharmaceutical Association (JPA) has conducted projects for the collection of information concerning patients' use of medicines from community pharmacists. In 1999—2001, as a pilot study of Drug Event Monitoring (DEM), data on events in patients taking antihyperlipidemic drugs (HMG-CoA reductase inhibitors) were collected in several model

e-mail: s.hayashi@dream.com

districts.[8] The results suggested that information can be collected from community pharmacists. Therefore, in this study, the JPA expanded DEM to the nationwide level to establish a system for collecting and reporting information such as that on adverse effects from community pharmacists.

In this study, DEM was performed for antiallergic drugs (6 products, 4 active ingredients). Patients taking these drugs were asked whether they developed sleepiness. All pharmacies where JPA members are working (member pharmacies) were asked to participate in this study.

In this study, analysis was performed to determine whether community pharmacists can contribute to improvement in the safety of medicines through DEM, and future problems were evaluated.

METHODS

1) Items of Survey The following 4 active ingredients and 6 products (trade name: company name) were surveyed: ebastine 5 mg/10 mg tablets (EBASTEL® Tablets 5 mg/10 mg: Dainippon Pharmaceutical Co., Ltd., Meiji Seika Kaisha, Ltd.); fexofenadine hydrochloride 60 mg tablet (allegra® 60 mg Tablets: Aventis Pharma Ltd.); cetirizine hydrochloride 5 mg/10 mg tablets (Zyrtec® Tablet 5/10: Sumitomo Pharmaceuticals Co., Ltd., Daiichi Pharmaceutical Co., Ltd.); and loratadine 10 mg tablet (Claritin®: Shionogi & Co., Ltd., Schering-Plough K.K.).

As shown in the report form (Fig. 1), the reported items were the age and gender of the patient, the trade name used by the patient, its daily dose, method of use, the presence or absence of concomitant oral drugs, the presence or absence of the development of sleepiness, and events other than sleepiness. The items ''age'' and ''events other than sleepiness'' were described. ''Events other than sleepiness'' were described only when pharmacists noticed them during their consult with the patient. For the other items, more than 1 choice was presented, and the most applicable one was checked. Pharmacists described or checked all items.

2) Systems of Survey Prior to the survey, the JPA produced report forms and posters (Fig. 2) asking for the cooperation of patients in the survey. In November 2002, 1 report form and 1 poster were distributed to each member pharmacy (a total of about 45000 pharmacies) via the prefectural pharmaceutical associations.

The member pharmacies were requested to participate in the survey via the prefectural pharmaceutical associations. Participation was also requested in the Journal of the Japan Pharmaceutical Association and the JPA Website.

In pharmacies that participated in the survey, the report form was copied to obtain the necessary number, and the results of the survey were entered in the report papers. In Kumamoto Prefecture, in addition to the report paper method, a Website for reporting was constructed, and members who could access the page reported the results of the survey there. During the survey period, a poster requesting cooperation was posted in pharmacies, and adequate consideration was given to the privacy of patients.

After the termination of the survey, completed report papers were collected from the pharmacies by the prefectural pharmaceutical associations, which sent them to the JPA before the end of March 2003.

3) Methods of Survey In the survey, the ''Patient pick-up period (Period A)'' (2003. 2. 1—2. 14) and ''Event collection period (Period B)'' (2003. 2. 15—2. 28) were established.

During ''Period A'', patients as ''candidates'' for the survey were preliminarily selected. In pharmacies, pharmacists identified patients who brought a prescription containing one of the survey drugs as ''candidates'' for the survey.

During ''Period B'', whether sleepiness had developed was determined ''in the selected candidates''. Only when patients who became ''candidates'' during ''Period A'' visited the pharmacies again during ''Period B'' did pharmacists ask them whether sleepiness had developed using the following standardized question: ''Have you ever become sleepy after taking this drug?'' When the patient voluntarily reported sleepiness before the pharmacist ask this question, the item ''The patient voluntarily reported sleepiness.'' in the report form (Fig. 1: 8–2) was checked off.

The JPA were concerned that the rules of the survey might not be adequately observed due to high frequency of dispensing of the survey drugs in some pharmacies. Therefore, the JPA permitted pharmacies to shorten ''Period A'' and ''Period B'' when necessary at their discretion while requesting them not to intentionally select particular patients.

4) Statistical Methods Register numbers were assigned to all entered report papers sent to the JPA.

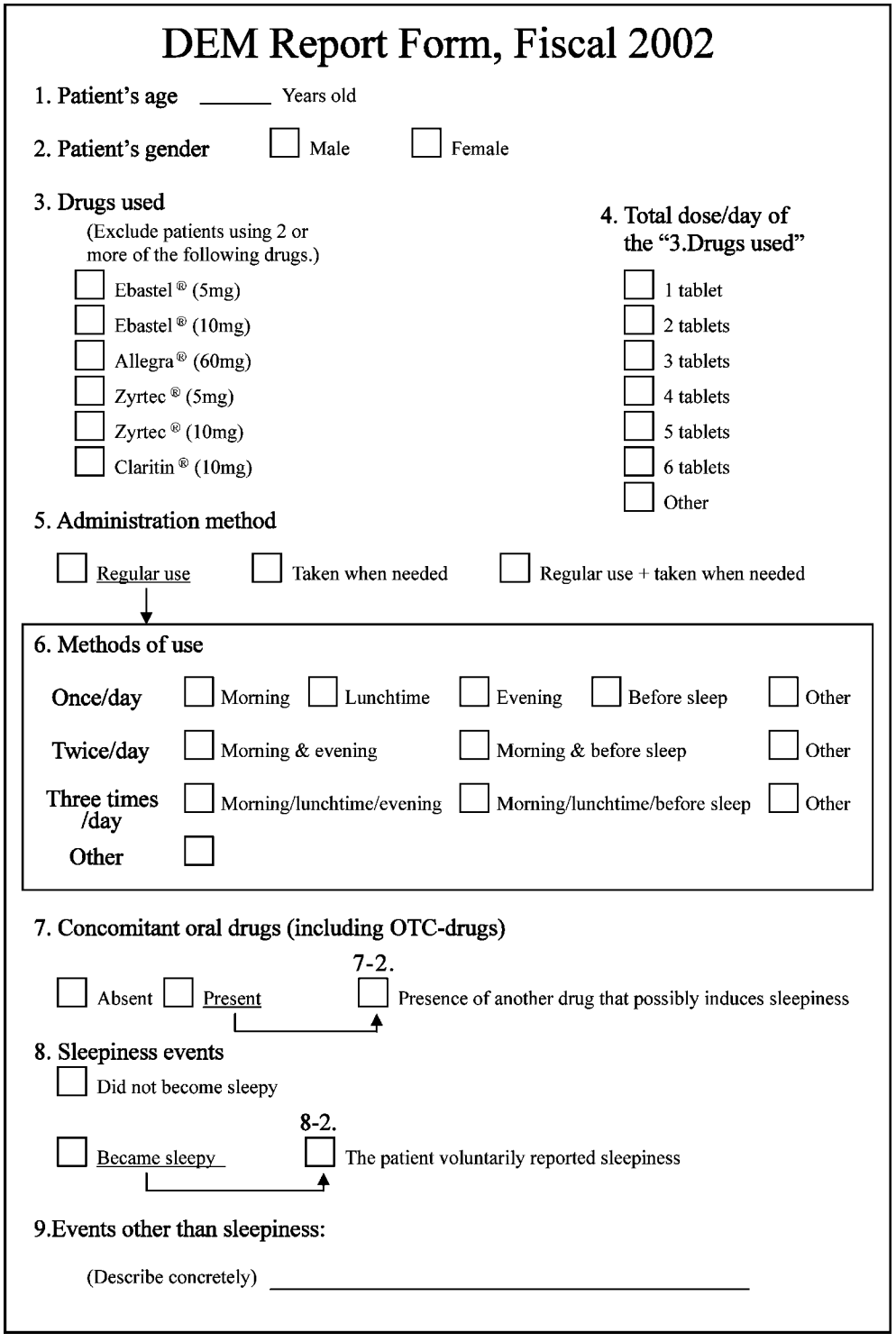

Fig. 1. Report Form

Items other than ''events other than sleepiness'' were read by a scanner and converted into electronic data. Subsequently, all electronic data were confirmed by comparing them with the original report papers. Data on ''events other than sleepiness'' were classified and organized based on the package inserts by one investigator.

First, simple statistical calculations were performed for each survey item.

Subsequently, statistical analysis was performed in cases in which reports showed alleged absence of concomitant oral drugs, and drug use in conformity with

Fig. 2. Poster for Hanging in Pharmacies

the following method and dose described in each package insert: 1 tablet once daily for ebastine (5 mg/10 mg tablets) and loratadine (10 mg tablet), 1 tablet twice daily for fexofenadine hydrochloride (60 mg tablet), and 1 tablet once daily before sleep for cetirizine hydrochloride (5 mg/10 mg tablets). Based on information on fexofenadine hydrochloride from the reports (total daily dose, 2 tablets; 2 divided doses), cases, for example, taking ''0.5 tablet in the morning and 1.5 tablet in the evening'' could also be considered. However, since these cases were considered to be very few, all cases were considered to use ''1 tablet twice a day''.

In addition, to determine whether the incidence of sleepiness in the population can be estimated based on obtained results, reports on fexofenadine hydrochloride (60 mg tablet) were analyzed. In cases in which reports showed no alleged use of concomitant oral drugs, and drug use in conformity with the method and dose described in package inserts, random sampling was performed with 500 samples as a unit up to 5000 samples, and the incidence of sleepiness in each sampling number was obtained. Similar work was performed for the sampling numbers of 50, 100, and 300. For sampling, pseudorandom numbers for each number were generated using a computer, and reported cases with the same register numbers as the obtained figures were selected. For each sampling number, 10 trials were performed, and the mean value and standard deviation were calculated.

Report papers were read using a Win Reader Hand S (Media Drive Corp.), and statistical work was performed primarily using Access 2000 and Excel 2000 (Microsoft Corp.).

RESULTS

1) Number of Collected Report Papers A total of 94256 report papers were sent to the JPA. For each of the 47 prefectures, the number of report papers ranged from 121 to 7490. The number of pharmacies that presented "at least 1 report paper" in each prefecture was reported by 25 of the 47 prefectures, but a total national number could not be clarified. Based on reports by the 25 prefectures, a total of 5234 pharmacies presented at least 1 report paper, and the number of papers presented by these pharmacies was 42073. Therefore, each pharmacy presented about 8 report papers. Since the total number of health insurance pharmacies in the 25 prefectures during the survey period was 20770, the percentage of "the number of pharmacies that presented at least 1 report paper" to this total number was about 25%.

In the statistical analysis, report papers with an inadequate entry in even 1 item were excluded. As a result, 82531 reported cases (87.6%) were statistically analyzed.

2) Results of Statistics

Patient's Age The mean age of the patients was 48.2 years. The percentages of patients according to age groups were: 1.4%, <10 years of age; 8.2%, 10—19 years; 9.9%, 20—29 years; 16.4%, 30—39 years; 16.6%, 40—49 years; 15.7%, 50—59 years; 13.5%, 60—69 years; and 18.3%, ≥70 years.

Patient's Gender Females accounted for 58.7% and males for 41.3%.

Number of Reported Cases According to Drugs The numbers (%) of reported cases according to the survey drugs were: 2560 (3.1%) for ebastine (5 mg tablet), 14052 (17.0%) for ebastine (10 mg tablet), 24304 (29.5%) for fexofenadine hydrochloride (60 mg tablet), 2142 (2.6%) for cetirizine hydrochloride (5 mg tablet), 19801 (24.0%) for cetirizine hydrochloride (10 mg tablet), and 19672 (23.8%) for loratadine (10 mg tablet).

Total Administration Dose/Day The total administration dose/day is shown in Table 1.

Methods of Use "Regular drug use" was reported in 81130 (98.3%) of the 82531 cases analyzed, "drugs taken when needed" in 1052 cases (1.3%), and both in 349 cases (0.4%). In the 81130 cases showing "regular drug use", the frequency of drug use/day is shown in Table 2, and the times of day for drug use are shown in Tables 3 and 4.

Table 1. Total Dose/Day

	1 tablet /day	2 tablets /day	Other	Total
Ebastine 5 mg tab	1923	610	27	2560
Ebastine 10 mg tab	13788	167	97	14052
Fexofenadine 60 mg tab	1355	22875	74	24304
Cetirizine 5 mg tab	1696	430	16	2142
Cetirizine 10 mg tab	19259	512	30	19801
Loratadine 10 mg tab	19488	139	45	19672
Total	57509	24733	289	82531

Note: Each value is the number of reported cases. "Fexofenadine" indicates fexofenadine hydrochloride preparations, and "Cetirizine" indicates cetirizine hydrochloride preparations (in this and other tables).

Table 2. Frequency of Drug Use/Day in Cases Showing "Regular Use of the Drug"

	Once /day	Twice /day	Other	Total
Ebastine 5 mg tab	2069	443	17	2529
Ebastine 10 mg tab	13669	156	14	13839
Fexofenadine 60 mg tab	1225	22634	28	23887
Cetirizine 5 mg tab	1762	325	3	2090
Cetirizine 10 mg tab	19006	422	14	19442
Loratadine 10 mg tab	19209	119	15	19343
Total	56940	24099	91	81130

Note: Each value is the number of reported cases.

Presence or Absence of Concomitant Oral Drugs "Presence of concomitant oral drugs" was reported in 45048 (54.6%) of the 82531 cases for statistics; the percentage according to the drugs was 51.2%—57.0%. "Presence of another drug that possibly induces sleepiness" was reported in 17016 (20.6% of the 82531 cases) of the 45048 cases showing presence of concomitant oral drugs; the percentage according to the drugs was 17.4%—22.8%.

Presence or Absence of Sleepiness The results in all 82531 cases are shown in Table 5. "Became sleepy" was reported in 12267 cases, of which 2196 showed "The patient voluntarily reported sleepiness".

"Became sleepy" was reported in 4690 (12.5%) of the 37483 cases showing "absence of concomitant oral drugs", 7577 (16.8%) of the 45048 cases show-

Table 3. Time of Day for Drug Use in Cases Showing ''Drug Use Once/Day''

	Morning	Lunchtime	Evening	Before sleep	Other	Total
Ebastine 5 mg tab	456	12	890	708	3	2069
Ebastine 10 mg tab	4003	49	5681	3911	25	13669
Fexofenadine 60 mg tab	558	13	389	262	3	1225
Cetirizine 5 mg tab	105	2	711	943	1	1762
Cetirizine 10 mg tab	1700	41	6950	10289	26	19006
Loratadine 10 mg tab	7848	195	8034	3037	95	19209
Total	14670	312	22655	19150	153	56940

Note: Each value is the number of reported cases.

Table 4. Time of Day for Drug Use in Cases Showing ''Drug Use Twice/Day''

	Morning and evening	Morning and before sleep	Other	Total
Ebastine 5 mg tab	381	60	2	443
Ebastine 10 mg tab	136	19	1	156
Fexofenadine 60 mg tab	20904	1672	58	22634
Cetirizine 5 mg tab	272	50	3	325
Cetirizine 10 mg tab	355	66	1	422
Loratadine 10 mg tab	103	15	1	119
Total	22151	1882	66	24099

Note: Each value is the number of reported cases.

ing ''presence of concomitant oral drugs'', and 3830 (22.5%) of the 17016 cases showing ''presence of another drug that possibly induces sleepiness'' as a concomitant oral drug.

Reported Events Other than Sleepiness Descriptions regarding the survey drugs were observed in 2764 (3.3%) of the 82531 cases analyzed. The major descriptions are shown in Table 6.

Statistical Analysis of Drugs Used in Conformity with the Method and Dose Described by Package Inserts Of the cases showing ''absence of concomitant oral drugs'', only cases using ''1 tablet once daily'' for ebastine (5 mg/10 mg tablets) or loratadine (10 mg tablet), those using ''1 tablet twice daily'' for fexofenadine hydrochloride (60 mg tablet), and those using ''1 tablet once daily before sleep'' for cetirizine hydrochloride (5 mg/10 mg tablets) were extracted and statistically analyzed, and Table 7 shows the results.

Results of Evaluation for Fexofenadine Hydrochloride (60 mg Tablet) Both alleged absence of concomitant oral drugs and drug use in conformity with the method and dose described by package inserts were reported in 10259 cases (Table 7). Therefore, in the range of 1–10259, pseudorandom numbers for the designated sampling numbers (50, 100, ... 4500, 5000) were generated. The reported cases with the same register numbers as the obtained numbers were collected, and the incidence of sleepiness was calculated. The results of 10 trials for each sampling number are shown in Fig. 3.

DISCUSSION

1) Design of Survey The JPA carried out DEM mainly to establish a ''system for collecting and reporting information from community pharmacists such as that on adverse effects''. In this survey, very simple methods and contents were applied to increase the number of community pharmacists participating in DEM.

Although there is a system of reporting throughout the year,[9] we determined the total survey period to be 4 weeks, considering that a concentrated survey for a short period increases the will to participate in community pharmacists.

The ''Patient pick-up period for the survey (Period A, 2 weeks)'' was used to simplify the survey by limiting the number of subjects. However, since a subsequent ''Event collection period (Period B, 2 weeks)'' was established, patients with a prescription for a long period (for example, prescription for 30 days) were excluded. ''Easiness of participation'' may often be contrary to the usefulness of the results of the survey, which is a problem that should be evaluated in future DEM.

The survey period was February 2003 because the cooperation of the prefectural pharmaceutical associations was easy to obtain. Since drugs for pollinosis are frequently prescribed during this period (February), antiallergic drugs were selected for this survey.

Table 5. Incidence of Sleepiness in All Cases for Statistical Analysis

	Became sleepy	Did not become sleepy	Total	Incidence
Ebastine 5 mg tab	364 (75)	2196	2560	14.2% (2.9%)
Ebastine 10 mg tab	2301 (396)	11751	14052	16.4% (2.8%)
Fexofenadine 60 mg tab	2832 (433)	21472	24304	11.7% (1.8%)
Cetirizine 5 mg tab	407 (62)	1735	2142	19.0% (2.9%)
Cetirizine 10 mg tab	4112 (800)	15689	19801	20.8% (4.0%)
Loratadine 10 mg tab	2251 (430)	17421	19672	11.4% (2.2%)
Total	12267 (2196)	70264	82531	14.9% (2.7%)

Note: All values excluding those in the ''incidence'' column are the numbers of reported cases. ( ): cases in which the patient voluntarily reported ''sleepiness''.

Table 6. Major Reported Events Other than Sleepiness

	Events described by package inserts	Events not described by package inserts
Ebastine	• Thirst (117) • Malaise (47) • Gastric discomfort (24) (including gastric pain and heaviness) • Dizziness (9) • Diarrhea (including soft feces) (9)	• Muddled head (17) • Hard to rise in the morning (13) • Constipation (hard feces) (10) • Oral roughness (5) • Abnormalities in the eyes (4) (such as itching or pain)
Fexofenadine	• Thirst (131) • Malaise (61) • Headache (34) • Diarrhea (including soft feces) (19) • Dizziness (18)	• Gastric discomfort (74) (including gastric pain and heaviness) • Muddled head (29) • Constipation (hard feces) (18) • Oral roughness (11) • Dull headache (10)
Cetirizine	• Thirst (141) • Malaise (75) • Constipation (hard feces) (25) • Gastric discomfort (24) (including gastric roughness) • Insomnia (14)	• Muddled head (44) • Hard to rise in the morning (32) • Decreased concentration (6) • Bitter oral sensation (4) • Increased appetite (4)
Loratadine	• Thirst (111) • Malaise (52) • Gastritis (including gastric pain) (42) • Constipation (hard feces) (23) • Headache (21)	• Muddled head (26) • Hard to rise in the morning (10) • Oral roughness (9) • Itching (6) • Insomnia (6) (wake up in the middle of night)

Note: 1) For ''ebastine'' and ''cetirizine'', reports for both 5 mg and 10 mg tablets are combined and shown. 2) The top 5 items frequently reported are shown for each drug. Figures in ( ) indicate the numbers of reported cases. 3) The presence or absence of description in package inserts is based on package inserts as of October 2003.

''Sleepiness'' was selected as the theme because patients readily understand and often worry about this symptom. During the survey period, some community pharmacists reported by telephone that there are ''cases showing sleepiness in the initial stage of drug use but it seems to disappear with continuation of drug use.'' The JPA asked them to record these cases as cases of ''Became sleepy.''

As products for evaluation, 4 active ingredients (ebastine, fexofenadine hydrochloride, cetirizine hydrochloride, and loratadine) were selected under the following criteria: (1) drugs with common effects,

(2) absence of later products (''generic drugs'') at the time of the survey so that report forms can be simplified, and (3) drugs frequently used throughout the world.

2) Incidence of Sleepiness Table 5 shows the incidence of sleepiness in all reported cases irrespective of the presence or absence of concomitant oral drugs or the daily dose. These results are useful as information based on the administration status, but do not allow strict comparison of the incidence of sleepiness among drugs.

Table 7. Incidence of Sleepiness in ''Cases in which Reports Showed Alleged Absence of Concomitant Oral Drugs and Drug Use in Conformity with the Method and Dose in Package Inserts''

	Became sleepy	Did not become sleepy	Total	Incidence
Ebastine 5 mg tab	109	816	925	11.8%
Ebastine 10 mg tab	866	5224	6090	14.2%
Fexofenadine 60 mg tab	902	9357	10259	8.8%
Cetirizine 5 mg tab	62	336	398	15.6%
Cetirizine 10 mg tab	963	3732	4695	20.5%
Loratadine 10 mg tab	872	8521	9393	9.3%
Total	3774	27986	31760	11.9%

Note: All values excluding those for the ''incidence'' column indicate the numbers of cases. The χ^2-test using a 6×2 cross table (df=5) showed significant differences ($p<0.001$).

Therefore, statistical analysis was performed only in cases showing absence of concomitant oral drugs and drug use in conformity with the method and dose indicated in the package insert. Table 7 shows the results. In Table 7, the χ^2-test showed significant differences ($p<0.001$), confirming differences in the incidence of sleepiness among the survey drugs.

The incidences of sleepiness stated in the package inserts may have been obtained by surveys under non-uniform conditions in the different drugs. Therefore, these incidences can not be directly compared. The present survey was performed under uniform conditions, and thus, the results are more useful. However, the obtained results may still contain some biases since the survey was performed by a question actively asked by pharmacists, and there was no guarantee that pharmacists who participated in the survey complied with the methods of the survey. In addition, there is a possibility that injected drugs were administered to some patients at hospitals or clinics. Therefore, ''absence of concomitant oral drugs'' does not always indicate that the patients used no drugs other than the survey drugs. Therefore, Table 7 does not show the real ''incidence of sleepiness'' but should be considered as results obtained under special conditions. In addition, since drugs may have adverse

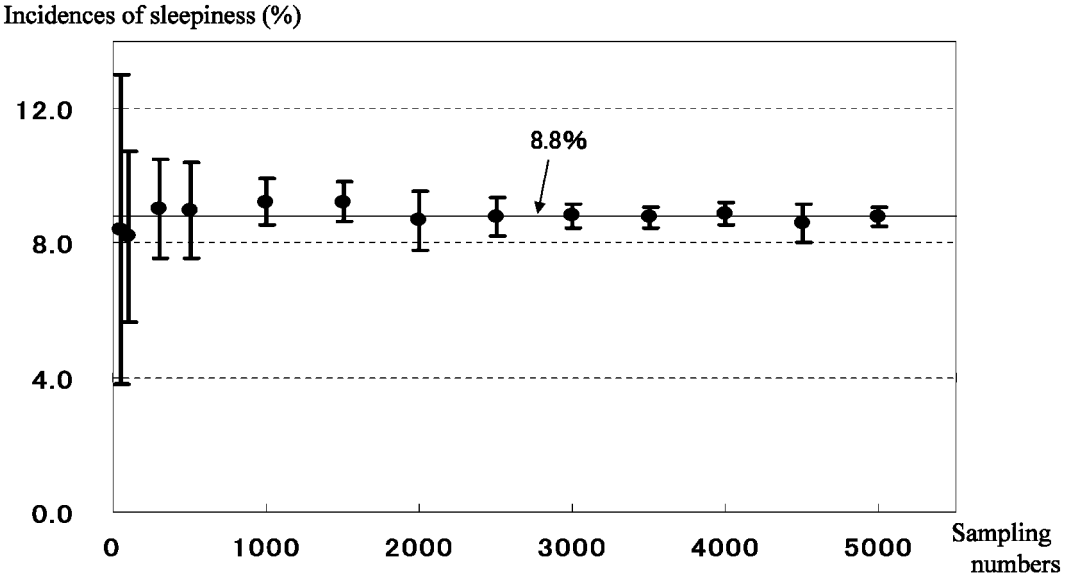

Fig. 3. Sampling Numbers and Incidences of Sleepiness

Note: Analysis was performed in 10259 cases using fexofenadine hydrochloride (60 mg tablet) in which reports showed alleged absence of concomitant oral drugs, and drug use in conformity with the method and dose in package inserts. For sampling, pseudorandom numbers were generated in the range of 1–10259 using a computer, and reported cases with the same register numbers as the obtained figures were selected. For each sampling number, 10 trials were performed. Each point indicates the mean±S.D.

effects other than ''sleepiness'', the results of this study do not determine the superiority of the drugs.

The obtained ''incidences of sleepiness'' (8.8—20.5%, Table 7) were higher than those indicated in each package insert (1.8—6.35%). This may be because the patients were informed of this adverse effect (sleepiness) at the time of medication counseling, and pharmacists actively asked the question, ''Have you ever become sleepy after taking this drug?'' Since 2.7% of all patients voluntarily reported sleepiness (Table 5), active interventions in patients by pharmacists may provide more information on the improvement of patients' QOL and safety.

3) Possibility of Obtaining Information on the Population There have been no nationwide surveys of the use of medicines in pharmacies. In other countries also, only a few studies have been performed on adverse drug events among outpatients.[10] In our study, 94256 cases were reported by pharmacies during a 4-week survey. Therefore, pharmacies may be useful for collecting information on the use of medicines in the future.

However, even if many cases are reported, correct information on the population is not always obtained. Therefore, whether information in the population can be estimated based on the results of this study was determined.

In this survey, 5234 pharmacies in 25 prefectures presented report papers. The total number of health insurance pharmacies in the 25 prefectures during this period was estimated to be 20770, and therefore, about 25% of all pharmacies participated in this survey. Since these pharmacies are considered to have voluntarily participated, random sampling was not performed for the selection of pharmacies. However, patients can freely choose pharmacies, and prior to the survey, the JPA requested that pharmacies should not intentionally select patients. Therefore, the pharmacies did not always select patients subjectively. Assuming patients were selected by random sampling, the relationship between the number of reported cases and the incidence of sleepiness was evaluated for fexofenadine hydrochloride (60 mg tablet), which was the most frequently reported. As shown in Table 7, 10259 cases were analyzed, and the results are shown in Fig. 3.

The ''mean value'' in Fig. 3 did not markedly differ among the sampling numbers. However, the standard deviation increased with a lower sampling number and decreased with a higher sampling number. When 1000 cases or more were sampled, no marked qualitative changes were observed in the standard deviation. These results suggested that the incidence of sleepiness after administration of fexofenadine hydrochloride (60 mg tablet) in the population was also about 8.8%.

For the cases using fexofenadine hydrochloride (60 mg tablet) shown in Table 7, statistical analysis was performed for each prefecture, and Table 8 was obtained. Some values were close to 8.8%. However, since the number of reported cases was mostly less than 1000, these values were considered to be incidental based on Fig. 3.

Therefore, at present, when DEM is performed in prefectures separately, information on the population can not be estimated based on the results of statistical analysis in individual prefectures. However, when statistical analysis is performed using all reported cases in the nation, it is possible to estimate information on the population.

4) Possibility of the Discovery of New Adverse Effects Table 6 shows major descriptions about ''events other than sleepiness''. Though the details are not described here, most adverse effects indicated in package inserts were reported. In addition, events not observed in package inserts were reported in 663 cases. This may lead to the discovery of new adverse effects. Community pharmacists appear to have a good opportunity to collect information.

The classification/organization of free description items may involve the subjectivity of the person who performs the statistical analysis. Reporting methods associated with fewer biases in statistics should be evaluated in the future.

CONCLUSION

This study was performed to determine whether community pharmacists can contribute to the improvement of the safety of medicines where drug prescribing and dispensing are separated.

A survey was carried out using the incidence of sleepiness after use of antiallergic drugs (4 active ingredients, 6 products) as the theme. During a 4-week survey period, 94256 cases were reported. The obtained incidence of sleepiness was different among the drugs and was higher than the incidence indicated by the package insert of each drug. This may be because pharmacists asked the patients whether sleepiness de-

Table 8. Number of Reported Cases and Incidences of Sleepiness According to Prefecture

Prefecture No.	Number of reported cases	Incidence of sleepiness (%)	Prefecture No.	Number of reported cases	Incidence of sleepiness (%)
1	2	0.0	25	116	7.8
2	4	0.0	26	124	10.5
3	26	7.7	27	139	8.6
4	29	13.8	28	146	13.0
5	31	0.0	29	149	10.7
6	31	6.5	30	151	4.0
7	34	0.0	31	174	6.3
8	34	8.8	32	273	7.7
9	39	10.3	33	274	8.4
10	41	4.9	34	283	5.7
11	43	11.6	35	288	12.2
12	49	18.4	36	289	9.7
13	53	5.7	37	352	9.1
14	57	8.8	38	358	7.0
15	57	5.3	39	373	7.0
16	60	6.7	40	379	11.6
17	66	4.6	41	386	6.2
18	75	12.0	42	479	9.6
19	80	8.8	43	610	7.5
20	81	9.9	44	690	8.4
21	83	16.9	45	795	9.6
22	101	12.9	46	1052	8.4
23	101	6.9	47	1100	9.6
24	102	14.7			

Note: Analysis was performed in 10259 cases using fexofenadine hydrochloride (60 mg tablet) in which reports showed alleged absence of concomitant oral drugs, and drug use in conformity with the method and dose in package inserts, according to the 47 prefectures.

veloped. These results suggest that active intervention by pharmacists can provide more information on the QOL of patients and safety. In the free description column, some events not described by the package inserts were reported, suggesting that new adverse effects could be discovered by community pharmacists. Therefore, community pharmacists can contribute to the improvement of the safety of medicines.

Although many cases were collected in this study, only about 25% of the pharmacies in the survey range participated in this study, and many pharmacists throughout the nation have not yet participated in DEM. Information applicable to the population could be estimated when statistical analysis was performed using reported cases from across the entire nation, but appeared to be difficult using reported cases from each prefecture alone. To simplify the contents of the survey, the presence or absence of drugs for injection or external use administered to the patients was not included in the survey items in this study. However, these items are also necessary. To obtain useful results of DEM conducted by the JPA in the future, more pharmacies should participate in DEM, and more cases should be collected. In addition, the contents of the survey should also be improved by including more detail.

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