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World J Gastroenterol 2003;9(6):1365-1369
World Journal of Gastroenterology
 ISSN 1007-9327

• CLINICAL RESEARCH •

Prevalence of anti-ulcer drug use in a Chinese cohort

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Received: 2003-02-25 **Accepted:** 2003-03-16

Abstract

AIM: To estimate the age-specific prevalence of anti-ulcer drug use and to calculate the usage of different anti-ulcer drugs over 5 years within the universal health insurance program in Taiwan area.

METHODS: The National Health Insurance Research Database in Taipei supplied the cohort data sets of 200 000 people. The ambulatory and inpatient claims of the cohort from 1997 to 2001 were analyzed. The anti-ulcer drugs included all drug items of the group A02B (drugs for treatment of peptic ulcer) in the Anatomical Therapeutic Chemical classification system (version 2000). The amount of drug usage was measured in unit of defined daily dose.

RESULTS: Among the totally 13 034 393 visits with 56 672 631 ambulatory prescription items, there were 398 150 (0.7 %) prescribed items of anti-ulcer drugs in 378 855 (2.9 %) visits. Among the 107 649 admissions with 5 762 312 inpatient prescription items, there were 24 598 (0.4 %) prescribed items of anti-ulcer drugs in 11 548 (10.7 %) admissions. The annual prevalence of anti-ulcer drug use was 9.6 % in 1997, 11.6 % in 1998, 15.4 % in 1999, 14.5 % in 2000, and 15.9 % in 2001 respectively. The 5-year prevalence was 36.1 %. The age-specific prevalence among the people younger than 20 years was 9.2 % in 2001 and 23.7 % during the 5-year period. Cimetidine not only was the most popular ingredient among anti-ulcer drugs (57 634 cimetidine users in 70 729 all anti-ulcer drug users during the 5-year period) but also had the largest prescribed amount (42.3 % of DDDs for all anti-ulcer drug users during the 5-year period). The annually prescribed amount of anti-ulcer drugs had grown from 4.9 DDDs/1000 inhabitants/day in 1997 to 7.5 in 2001. This increase was largely attributed to H_2-receptor antagonists and the expanding number of users.

CONCLUSION: Prescribing of anti-ulcer drugs is indeed popular among the Chinese population in Taiwan area. The disproportionate use of anti-ulcer drugs by children demands further investigation.

Chen TJ, Chou LF, Hwang SJ. Prevalence of anti-ulcer drug use in a Chinese cohort. *World J Gastroenterol* 2003; 9(6):1365-1369
http://www.wjgnet.com/1007-9327/9/1365.asp

INTRODUCTION

In the past three decades, the invention of several revolutionary anti-ulcer drugs, *e.g.* H_2-receptor antagonists, synthetic prostaglandins, proton pump inhibitors, and cytoprotective agents, has changed the physicians' treatment patterns in gastroenterology and greatly improved the ulcer-healing rate of patients with peptic ulcer disease[1-6]. In spite of effectiveness and popularity, the cost of these drugs has also aroused concern in the health care systems of developed countries[7-11]. The concern has been aggravating in recent years because of expanding use of proton pump inhibitors in treating gastroesophageal reflux disease. Although prescribing of these potent acid-suppressing drugs is popular, their patterns of utilization have been infrequently documented in national surveys[12-21].

In Taiwan area, a single and universal health insurance program started in 1995 and covered nearly all inhabitants (21 653 555 beneficiaries at the end of 2001)[22]. The prescription drug benefits are included in the insurance. Because all claims data for the reimbursement purpose are in electronic form and available to researchers, we can perform a survey of anti-ulcer drug use among the Chinese population in Taiwan area.

The aims of this study were twofold: to estimate the age-specific prevalence of anti-ulcer drug use and to calculate the usage of different anti-ulcer drugs over 5 years within the universal health insurance program in Taiwan area. The strengths of our study were to use the longitudinal data sets of a representative cohort of 200 000 people and to adopt the unit of international standards in measuring the anti-ulcer drug usage.

MATERIALS AND METHODS

Data sources

We obtained 4 cohort data sets (R01-4) from the National Health Insurance Research Database (NHIRD; http://www.nhri.org.tw/nhird/) in Taipei in November 2002. The total 200 000 people in these 4 cohort data sets had been randomly sampled from 23 753 407 people who were ever insured under the universal health insurance program in Taiwan area from March 1, 1995 to December 31, 2000. Not every person of the cohort was insured through the study period because of new birth, death, immigration, and emigration. The cohort data sets contained all insurance claims of 200 000 people from 1996 to 2001. The structure of the insurance claim files had been described in details in our previous study[23].

In the current study, we analyzed the ambulatory and inpatient files of the cohort data sets from 1997 to 2001. Totally, there were 13 034 393 visits, 56 672 631 ambulatory prescription items, 107 649 admissions, and 5 762 312 inpatient prescription items.

Besides, we obtained a complete file of 21 146 approved drug items of Western medicine in Taiwan area from the web site of the Bureau of National Health Insurance (BNHI; http://www.nhi.gov.tw/; accessed January 12, 2002). Each drug of different brand, strength and form was officially assigned a unique code for use in the claims file. The BNHI also offered a list of ATC codes (the Anatomical Therapeutic Chemical classification system, version 2000)[24] for each drug item.

Study design

The anti-ulcer drugs in our study included all drug items of the group A02B (drugs for treatment of peptic ulcer, renamed to ' drugs for peptic ulcer and gastroesophageal reflux disease'

in 2002) in the ATC classification system. This group of drugs has 5 subgroups of the fourth level: A02BA (H_2-receptor antagonists, H_2RA), A02BB (prostaglandins), A02BC (proton pump inhibitors, PPI), A02BD (combinations for eradication of *Helicobacter pylori*), and A02BX (other drugs for treatment of peptic ulcer, renamed to ' other drugs for peptic ulcer and gastroesophageal reflux disease' in 2002). A total of 428 anti-ulcer drug items, including the original brands and generics, have been registered in Taiwan area since 1995. Some drugs might be no more available on the market or not reimbursable by the insurance during the study period.

In estimating the age-specific prevalence of anti-ulcer drug use, we first identified the people receiving anti-ulcer drug items in each year. Because the number of people in the cohort fluctuated during the study period, we calculated the number of the denominator in each year by excluding those people who were not insured at any time of that year. A person' s age in a year was defined as the difference between her/his birthday and the end of that year. In estimating the 5-year age-specific prevalence from 1997 to 2001, we took December 31, 2001 as the index date to calculate a person' s age.

In describing the distribution of anti-ulcer drug prescriptions among the cohort, we calculated the number of recipients and the total prescribed amount for each ingredient (ATC 5th level) in each year. Supposed that the cohort did not take anti-ulcer drugs before the base year of 1997, the number of new anti-ulcer drug users was additionally computed for each year after 1997. The prescribed amounts of anti-ulcer drugs were measured in unit of defined daily dose (DDD) by ATC classification system[24]. The original dose of each prescription was converted to a number of DDDs according to the DDD of the ingredient. Some anti-ulcer drugs (e.g. cetraxate, urogastrone, and gefarnate) lacked either ATC codes or DDDs; we used the most commonly prescribed daily doses as their DDDs. For international comparison, the numbers of DDDs per 1,000 inhabitants per day were also computed.

Statistical analysis

The database software of Microsoft SQL Server 2000 was used for data linkage and processing. The regular statistics were displayed.

RESULTS

General information of the cohort

Among the 200 000-people cohort, only 195 971 people were eligible during the 5-year study period. The other 4 029 people who had dropped out of the insurance before 1997 would not be included in the following analyses. The number of eligible people varied from year to year (Table 1). There were more men than women (100 257 *vs.* 95 654), and the status of sex was unknown in 60 persons.

General information of anti-ulcer drug prescriptions

During the 5-year study period, 356 distinct anti-ulcer drugs had existed in the cohort data sets. The drugs belonged to 18 ingredients of ATC 5th level. At the ambulatory sector, there were 398 150 (0.7 %) prescribed items of anti-ulcer drugs in 378 855 (2.9 %) visits; at the inpatient sector, there were 24 598 (0.4 %) prescribed items in 11 548 (10.7 %) admissions.

Age specific prevalence of anti-ulcer drug use

In 1997, as high as 9.6 % (17 414/180 781) of eligible cohort received anti-ulcer drugs. The percentage increased by two-thirds to 15.9 % (29 181/183 976) in 2001. More than a third (36.1 %) of the cohort had ever received anti-ulcer drugs during the 5-year study period. Generally, the prevalence of anti-ulcer drug use increased with age. Another noteworthy finding was that anti-ulcer drugs had been prescribed to an appreciable percentage of children and adolescents (Table 1).

Recipients of anti-ulcer drugs by ingredient

Cimetidine was the most popular ingredient of anti-ulcer drugs among the cohort, followed by sucralfate, ranitidine, famotidine, omeprazole, pirenzepine, and lansoprazole (Table 2). The majority of new anti-ulcer drug users in each year were also attributed to cimetidine.

Table 1 Age distribution of patients receiving anti-ulcer drugs and age-specific prevalence of anti-ulcer drug use from 1997 to 2001

	1997	1998	1999	2000	2001	1997-2001
Sampling cohort						
0 – 19 years	57388	56427	55448	54684	51029	52103
20 – 39 years	62613	63765	64848	65219	63800	69425
40 – 59 years	39809	41420	42922	44241	45432	47663
60 years and older	20971	21836	22489	23093	23715	26780
Total	180781	183448	185707	187237	183976	195971
Patients with anti-ulcer drugs						
0 – 19 years	2965	3611	5171	4634	4712	12339
20 – 39 years	5345	6741	9249	8788	9673	23741
40 – 59 years	4933	6213	8277	8113	8664	20166
60 years and older	4172	4787	5905	5643	6132	14483
Total	17415	21352	28602	27178	29181	70729
Prevalence of anti-ulcer drug use						
0 – 19 years	5.2 %	6.4 %	9.3 %	8.5 %	9.2 %	23.7 %
20 – 39 years	8.5 %	10.6 %	14.3 %	13.5 %	15.2 %	34.2 %
40 – 59 years	12.4 %	15.0 %	19.3 %	18.3 %	19.1 %	42.3 %
60 years and older	19.9 %	21.9 %	26.3 %	24.4 %	25.9 %	54.1 %
Total	9.6 %	11.6 %	15.4 %	14.5 %	15.9 %	36.1 %

Table 2 Recipients of anti-ulcer drugs by main ingredient from 1997 to 2001 (number of new users in parentheses)

ATC[a] coding	Group / ingredient name	1997	1998	1999	2000	2001	1997-2001
A02BA	H_2 RA						
	01 Cimetidine	11538	15793 (11340)	22905 (14525)	22356 (10564)	24305 (9667)	57634
	02 Ranitidine	1588	1852 (1482)	2262 (1757)	2283 (1611)	2579 (1802)	8240
	03 Famotidine	974	1143 (953)	1401 (1113)	1526 (1216)	1669 (1232)	5488
	04 Nizatidine	187	255 (221)	295 (236)	199 (157)	137 (108)	909
	06 Roxatidine	89	98 (82)	87 (76)	83 (67)	97 (80)	394
A02BB	Prostaglandins						
	01 Misoprostol	128	145 (129)	156 (135)	150 (112)	88 (68)	572
A02BC	PPIS						
	01 Omeprazole	709	913 (807)	1168 (990)	1150 (917)	1445 (1156)	4579
	02 Pantoprazole	-	1(1)	84 (84)	147 (133)	273 (255)	473
	03 Lansoprazole	151	391 (365)	531 (459)	647 (537)	785 (643)	2155
	04 Rabeprazole	-	-	-	-	31 (31)	31
A02BX	Other drugs						
	01 Carbenoxolone	287	260 (219)	337 (271)	155 (105)	199 (164)	1046
	02 Sucralfate	3463	3192 (2510)	3107 (2301)	2390 (1506)	2173 (1390)	11170
	03 Pirenzepine	1177	1197 (937)	1181 (857)	731 (454)	625 (351)	3776
	05 Bismuth subcitrate	329	299 (266)	271 (223)	173 (141)	142 (111)	1070
	06 Proglumide	113	61 (53)	36 (34)	3 (3)	8 (5)	208
	07 Gefarnate	248	295 (270)	416 (363)	326 (265)	203 (161)	1307
	- Cetraxate	356	101 (81)	72 (59)	48 (40)	41 (37)	573
	- Urogastrone	192	46 (34)	42 (32)	14 (12)	6 (5)	275
Total		17415	21352 (14423)	28602 (16611)	27178 (11660)	29181 (10622)	70729

[a]ATC=Anatomical therapeutic chemical classification system.

Table 3 Total prescribed amount of anti-ulcer drugs by main ingredient from 1997 to 2001 (unit of measurement: numbers of defined daily doses [DDDs])

ATC[a] coding	Group / ingredient name	1997	1998	1999	2000	2001
A02BA	H_2 RA					
	01 Cimetidine	114145	151403	221528	198255	221836
	02 Ranitidine	57329	62357	69780	69954	88034
	03 Famotidine	33366	40063	51198	52852	53108
	04 Nizatidine	8943	12304	12282	8269	5305
	06 Roxatidine	3493	3057	3215	2847	4460
A02BB	Prostaglandins					
	01 Misoprostol	2244	3649	5594	4534	1941
A02BC	PPIS					
	01 Omeprazole	26635	33587	46429	43589	57193
	02 Pantoprazole	-	14	2593	4845	9276
	03 Lansoprazole	5840	14276	19624	24860	31023
	04 Rabeprazole	-	-	-	-	864
A02BX	Other drugs					
	01 Carbenoxolone	5708	4164	4768	1945	1918
	02 Sucralfate	26172	20170	15942	10960	9898
	03 Pirenzepine	7575	7378	5925	3868	3942
	05 Bismuth subcitrate	7999	6104	5213	2686	2754
	06 Proglumide	1010	459	198	12	31
	07 Gefarnate	14379	17859	26568	16682	8972
	- Cetraxate	4072	1254	849	615	657
	- Urogastrone	5067	1272	1151	232	32
Total		323976	379370	492856	447005	501243
	Ambulatory sector	297213	355837	465326	420144	470924
	Inpatient sector	26764	23532	27530	26861	30319
DDDs / 1000 inhabitants / day		4.9	5.7	7.3	6.5	7.5

[a]ATC=Anatomical therapeutic chemical classification system.

Total prescribed amounts of anti-ulcer drugs

Measured in unit of DDDs, cimetidine again had the largest prescribed amount (42.3 %) of all anti-ulcer drugs among the cohort during the 5-year study period (Table 3). It was then followed by ranitidine (16.2 %), famotidine (10.8 %), omeprazole (9.7 %), and lansoprazole (4.5 %). The majority of anti-ulcer drugs were used at the ambulatory sector (93.7 % of total DDDs).

The total prescribed amount of anti-ulcer drugs grew from 4.9 DDDs/1 000 inhabitants/day in 1997 to 7.5 in 2001 (Table 3). This increase was attributed to the expanded number of users because the average prescribed amount of anti-ulcer drugs per user in a year remained relatively stable (18.7±54.8 DDDs in 1997, 17.9±41.0 in 1998, 17.3±51.0 in 1999, 16.5±40.5 in 2000, and 17.3±40.8 in 2001).

On the other hand, H_2-receptor antagonists and proton pump inhibitors had contributed to the growth of the total prescribed amount of anti-ulcer drugs during the study period (Figure 1). While H_2-receptor antagonists had the largest share of growth, proton pump inhibitors had the highest growth rate. In the meantime, the usage of prostaglandins had remained stable, but other drugs for treatment of peptic ulcer had fewer users and smaller prescribed amount totally.

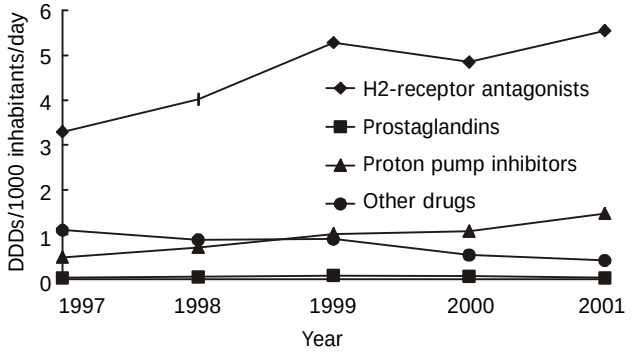

Figure 1 Trend of total prescribed amount of anti-ulcer drugs by pharmacological subgroups from 1997 to 2001.

DISCUSSION

To the best of our knowledge, our study might be one of the few reports that surveyed the anti-ulcer drug use in the Chinese population. Only with the computerization of insurance reimbursement, pharmacoepidemiological studies of such a large scale could be feasible. Besides, the person-based sampling in our study could estimate both the total amount and prevalence of drug use among the population.

Our study revealed that prescribing of anti-ulcer drugs was indeed popular in Taiwan. Nearly a sixth of the population received anti-ulcer drugs covered by the health insurance in 2001 and more than a third of the population had been exposed to such drugs during the 5 years. But the total usage of anti-ulcer drugs in Taiwan was not high in international comparison. According to the statistics of the OECD (Organization for Economic Co-operation and Development), 8 countries supplied their national consumption of anti-ulcer drugs in 1998: Australia (38.8 DDDs/1 000 inhabitants/day), Sweden (29.0), Iceland (28.1), Denmark (16.5), Norway (16.0), Czech Republic (13.1), Finland (12.4), and Slovakia (8.7)[25]. In contrast, Taiwan had only 5.7 DDDs/1 000 inhabitants/day of anti-ulcer drugs in the same year. However, the statistics has not been adjusted by age.

In the 1990s, the developed countries experienced a drastic increase of anti-ulcer drug consumption since the introduction of proton pump inhibitors. For example, the national consumption of anti-ulcer drugs in Sweden increased from 9.2 DDDs/1 000 inhabitants/day in 1990 to 34.4 in 2000[25]. During the 5 years of our study, a growing trend of anti-ulcer drugs was also observed in Taiwan. But the increase was largely attributed to H_2-receptor antagonists and expanding user group. The explanation might be that the reimbursement policy of the health insurance in Taiwan limited the use of expensive proton pump inhibitors on the one hand and loosened the regulation over the much cheaper generics of H_2-receptor antagonists on the other hand.

While overuse of proton pump inhibitors has become a research topic[26,27], our study found that at least the children in Taiwan might be disproportionately exposed to anti-ulcer drugs. Because children were generally not able to receive upper gastrointestinal endoscopy, their use of anti-ulcer drugs could be seldom justified. It demanded further studies to explore such a situation in Taiwan.

Our study with insurance claims in Taiwan had some limitations. At first, the drug use outside the insurance was not included in the analysis. However, the majority of anti-ulcer drugs, including the low-dose cimetidine, were prescription-only drugs in Taiwan. Besides, the compulsory health insurance covered nearly all inhabitants in Taiwan and reimbursed most prescription-only drugs. The use of anti-ulcer drugs at the private market should be of a less significant scale.

Secondly, the actual duration of drug treatment was not computed in our study because of missing dosage frequency in the inpatient files of the NHIRD data sets. Instead, we calculated the cumulated numbers of DDDs for each person as a proxy of treatment duration. But the DDD is arbitrarily set for trend and international comparisons. It does not consider the dosing at the specific conditions of children, elderly, and other risk groups. However, our data showed that the yearly amount of anti-ulcer drugs per user was low on average. It might be inferred that most people took anti-ulcer drugs only for a short term.

Thirdly, the purpose of cohort data sets in the NHIRD was to trace a cohort retrospectively and prospectively. The people of the cohort were chosen in 2000 and it was planned to follow them up continuously in the next years. Thus, the data sets of 2001 did not include anyone born after December 31, 2000. The denominator in 2001 should be smaller than the actual number of people and the prevalence correspondingly became a little overestimated.

Finally, we did not analyze the distribution of diagnoses in our study because a claims diagnosis served for the purpose of reimbursement and was seldom verified. The NHIRD data sets did provide the information whether the patients had received the endoscopic or radiological examinations of upper gastrointestinal tract. But no laboratory findings were routinely transmitted to the insurer in electronic form. Conventional epidemiological surveys are still needed to understand the prevalence of peptic ulcer and gastroesophageal reflux disease in Taiwan.

ACKNOWLEDGMENTS

This study was based in part on data from the National Health Insurance Research Database provided by the Bureau of National Health Insurance, Department of Health and managed by National Health Research Institutes in Taiwan. The interpretation and conclusions contained herein do not represent those of Bureau of National Health Insurance, Department of Health or National Health Research Institutes.

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Edited by Xu XQ