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Patterns and Costs of Antipsychotic Drug Use in Taiwan: 1997 to 2001

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ABSTRACT

The advent of atypical antipsychotics greatly changed the treatment pattern for mental illnesses worldwide. This study was designed to determine the trend in prevalence, prescribing pattern, and cost of antipsychotic agents in Taiwan from 1997 to 2001. Data were obtained from claims completed for a random sample of 200,000 people registered with the National Health Insurance program. The antipsychotics monitored included all group N05A drugs in the Anatomical Therapeutic Chemical classification system (version 2000). Conventional and atypical antipsychotics were handled separately. Of the 195,971 eligible registrants, 37,441 (19.1%) received any kind of antipsychotic during this 5-year period, but only 713 (0.4%) used atypical antipsychotics. The prevalence of conventional antipsychotic use during each successive year of this study was 5.2%, 5.7%, 6.6%, 6.2%, and 6.1% and 0.1%, 0.1%, 0.1%, 0.2%, and 0.3% for atypical agents. Although far fewer registrants used them, atypicals comprised 19.1% of all prescribed amounts measured in defined daily doses and 56.1% of the cost for all antipsychotics in 2001. During the 5-year study period, atypical antipsychotics were prescribed for 405 (57%) patients with schizophrenia, 132 (19%) with affective disorder, 128 (18%) with other psychiatric disorders, and 48 (7%) with a nonpsychiatric disorder. With the loosening of reimbursement restrictions in 2002, continued growth of atypical antipsychotic use in Taiwan might be expected.

Keywords: antipsychotics; cost analysis; drug utilization; pharmacoeconomics; prescribing

INTRODUCTION

The emergence of a revolutionary drug could change prescribing patterns and thus raise financial concerns among the authorities involved in

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health insurance and public health. The atypical antipsychotic is a good example, having caused such concerns in the past decade. Despite its clinical importance, literature about the utilization of drugs in this class are relatively scarce.[1-6]

The aim of this study was to analyze the prevalence, patterns, and cost of antipsychotic use during a recent 5-year period in Taiwan, with an emphasis on atypical antipsychotics. This trend analysis would help clarify the current status of treatment and the diffusion of new technology.

METHODS

Data Sources

The National Health Insurance program started in 1995 and enrolled nearly all the inhabitants of Taiwan (21,869,478 beneficiaries out of 22,520,776 inhabitants at the end of 2002).[7] The claims data were made available to researchers in electronic form under the National Health Insurance Research Database (NHIRD) project (http://www.nhri.org.tw/nhird/). Until mid 2003, the NHIRD offered dozens of extracted datasets. Patient and institutional identification data were encrypted to retain anonymity and protect privacy. The encryption was consistent in all datasets, so that the original identification numbers could remain unique and a longitudinal follow-up would be feasible.

The so-called "cohort" dataset was developed through person-based sampling. For each cohort dataset, the NHIRD initially developed a random sample of 50,000 people out of the 23,753,407 people insured between March 1, 1995, and December 31, 2000. All insurance claims belonging to these people were used to create one specific cohort dataset. NHIRD also planned to follow the cohort throughout the coming years.

The first 4 cohort datasets (R01–R04), which were based on claims completed between 1997 and 2001, were used for analysis. Not every one of the 200,000-person cohort was insured throughout the study period because of births, deaths, immigration, and emigration. These datasets contained 107,649 admissions, 5,762,312 inpatient prescription items, 13,034,393 visits, and 56,672,631 outpatient prescription items. The structure of the insurance claim files is described in detail on the NHIRD Web site and in other published materials.[8-12]

Additionally, a list of 21,146 Western drug items approved for use in Taiwan were downloaded from the Web site of the Bureau of National Health Insurance (http://www.nhi.gov.tw/, accessed January 12, 2002). Each brand, strength, and formulation of each drug had been assigned an official unique identifier for claims. The Bureau of National Health Insurance also offered a list of codes use in the Anatomical Therapeutic Chemical (ATC, version 2000) classification system.[13]

Study Design

The antipsychotics monitored in this study included all group N05A drugs listed in the ATC classification system. This group of drugs has 12 fourth-level subgroups: N05AA (phenothiazine with an aliphatic side chain), N05AB (phenothiazine containing a piperazine structure), N05AC (phenothiazine containing a piperidine structure), N05AD (butyrophenone derivatives), N05AE (indole derivatives), N05AF (thioxan-

thene derivatives), N05AG (diphenylbutylpiperidine derivatives), N05AH (diazepines, oxazepines, and thiazepines), N05AK (neuroleptics used in tardive dyskinesia), N05AL (benzamides), N05AN (lithium), and N05AX (other antipsychotics). A total of 384 antipsychotics had been registered in Taiwan. Some drugs might not have been available on the market or reimbursable by insurance during the study period.

The atypical antipsychotics included sertindole (N05AE03 in ATC), ziprasidone (N05AE04), clozapine (N05AH02), olanzapine (N05AH03), quetiapine (N05AH04), remoxipride (N05AL04), amisulpride (N05AL05), risperidone (N05AX08), clotiapine (N05AX09), zotepin (N05AX11), and aripiprazole (no ATC code had yet been assigned).[14] A total of 28 drugs had been registered.

The trend in prevalence, prescribed amounts, and cost of antipsychotic use during the 5-year study period was first stratified by category (conventional vs atypical) prior to analysis. Because the number of people in the cohort fluctuated during the study period, the denominator used to calculate the prevalence in each year included only those who were still insured that year. Prescribed amounts were measured in defined daily doses (DDDs) according to the ATC classification system. To facilitate international comparisons, the number of DDDs per 1000 inhabitants per day was also computed. The original monetary value in New Taiwan dollars in each year was uniformly converted into US currency based on the average exchange rate in 2001 (1 US$ = 33.8003 New Taiwan dollars, according to the Central Bank of China in Taiwan; http://www.cbc.gov.tw/, accessed February 6, 2003.)

To illustrate the distribution of each antipsychotic among the cohort, the number of recipients, the total amount prescribed, and the total cost for each ingredient (fifth-level ATC) in 2001 were calculated.

For atypical antipsychotics specifically, the demographics of new users in each year was computed. A new user in a year was defined as an individual who began to take atypical antipsychotics that year and did not take any in any previous year. All recipients of atypical antipsychotics in the base year (1997) were deemed new users. In addition to the sex and age of news users, the diagnostic distribution for atypical antipsychotic prescriptions was also calculated. Up to 5 diagnoses on an admission record and 3 diagnoses on a visit record were taken into account. The original codes from the *International Classification of Diseases, 9th Revision, Clinical Modification* were categorized into 4 groups in hierarchical order according to Hermann and colleagues: schizophrenia and other psychotic disorders (codes 293.81, 293.82, 295, 297, and 298), affective disorders (293.83, 296, 300.4, 301.13, and 311), other psychiatric disorders (290 to 319, excluding those in the former 2 groups), and nonpsychiatric disorder (excluding those in the former 3 groups)[4]; therefore, a patient with both schizophrenia and affective disorder would be categorized in the schizophrenia group.

Statistical Analysis

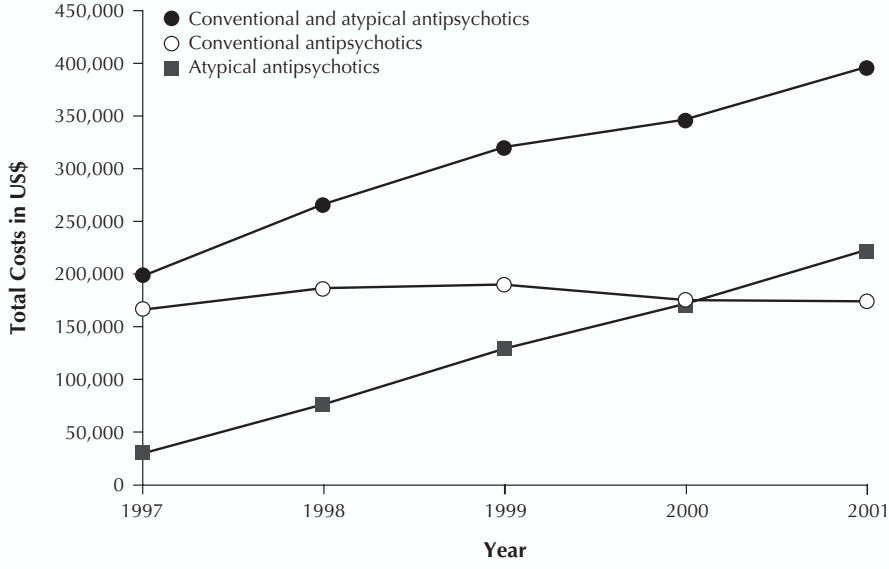
Microsoft SQL Server 2000 database software was used for data linkage and processing. The regular statistics were displayed.

RESULTS

Among the 200,000-person cohort, 195,971 had been insured at any time during the 5-year study period. The number of eligible people varied from year to year (180,781, 183,448, 185,707, 187,237, and 183,976 for each year from 1997 to 2001, respectively). A total of 37,441 registrants (19.1%) received any kind of antipsychotic during this 5-year period, but only 713 (0.4%) used atypical antipsychotics. The annual prevalence of conventional antipsychotic use was 5.2%, 5.7%, 6.6%, 6.2%, and 6.1%, for each year during this period; for atypical antipsychotics, it was 0.1%, 0.1%, 0.1%, 0.2%, and 0.3% for each year.

The total cost of antipsychotic use by the cohort in 1997 was US$196,129. The annual cost increased with time and doubled in 2001 (US$392,337). This growth was attributed almost entirely to atypical antipsychotics (Fig 1). In 2001, the cost of atypical antipsychotics exceeded that of conventional antipsychotics. On the other hand, the antipsychotics' share of the cost of all drug benefits increased from 1.3% in 1997 to 1.9% in 2001.

Fig 1. Trend in antipsychotic drug costs for the 200,000-person cohort in Taiwan from 1997 to 2001.



In contrast, the amount of antipsychotics prescribed remained relatively stable over the study period. The daily use was 4.2 DDDs/1000 inhabitants in 1997, 4.3 DDDs/1000 in 1998, 4.1 DDDs/1000 in 1999, 4.0 DDDs/1000 in 2000, and 4.3 DDDs/1000 in 2001. The increase in atypical antipsychotic use (from 0.2 to 0.8 DDDs/1000 inhabitants daily over 5 years) accounted for the reduction in conventional antipsychotics use (from 4.0 to 3.5).

Table 1 indicates the use of individual antipsychotics by the cohort in 2001. A total of 227 distinct antipsychotics had been prescribed, including 22 atypical antipsychotics belonging to 6 ingredients. Although a substantial number of people (11,446) received antipsychotics, the majority used prochlorperazine (7100) and sulpiride (3344). Only 464 registrants used atypicals, yet these drugs comprised nearly one fifth (19.1%) of all prescribed doses (in DDDs) and 56.1% of the cost of all antipsychotics. Among atypical antipsychotics, risperidone was used by the most registrants (n=236) and was prescribed in the greatest amount (18,552 DDDs).

Table 1. Distribution of Antipsychotic Drug Use by 183,976 Persons in 2001

Ingredient	ATC Code	Items, n	Recipients, n	DDDs, n	Total Cost, US$
Chlorpromazine	N05AA01	18	453	13,284	2083
Levomepromazine	N05AA02	3	8	50	56
Fluphenazine	N05AB02	6	34	8490	1239
Perphenazine	N05AB03	6	81	640	323
Prochlorperazine	N05AB04	16	7100	8442	3662
Trifluoperazine	N05AB06	9	119	11,918	2371
Thioridazine	N05AC02	15	165	6354	3891
Pipotiazine	N05AC04	1	26	1325	925
Haloperidol	N05AD01	52	883	76,890	33,902
Droperidol	N05AD08	2	35	207	47
Flupentixol	N05AF01	3	166	18,619	24,178
Clopenthixol	N05AF02	3	39	1275	5975
Chlorprothixene	N05AF03	1	7	403	668
Tiotixene	N05AF04	1	5	566	201
Zuclopenthixol	N05AF05	1	38	327	649
Pimozide	N05AG02	2	4	92	53
Loxapine	N05AH01	2	22	2479	2115
Clozapine*	N05AH02	7	72	13,017	55,881
Olanzapine*	N05AH03	2	69	9864	58,255
Quetiapine*	N05AH04	2	46	1716	13,068
Sulpiride	N05AL01	59	3344	70,924	82,075
Lithium	N05AN01	5	142	13,002	7892
Risperidone*	N05AX08	8	236	18,552	84,886
Clotiapine*	N05AX09	1	92	5375	3961
Zotepin*	N05AX11	2	53	7170	3981
Total		227	11,446	290,977	392,337
Antipsychotics					
Conventional		205	11,291	235,284	172,305
Atypical		22	464	55,692	220,032

*Atypical antipsychotics.

Table 2. Patterns of Atypical Antipsychotic Drug Use Among the 200,000-Person Cohort From 1997 to 2001

Characteristic	1997	1998	1999	2000	2001	Total
DDDs, n	11,396	21,807	32,848	41,036	55,692	
Recipients, n	111	183	250	337	464	713
New users, n						
Total	111	119	121	153	209	
Female	47	50	59	75	93	324
Male	64	69	62	78	116	389
Mean age, y (SD)	37.8 (12.6)	38.5 (16.7)	43.2 (20.6)	49.5 (22.4)	50.8 (22.9)	
Diagnostic distribution, %						
Schizophrenia	67	71	61	52	44	57
Affective disorder	24	18	18	14	20	19
Other psychiatric disorder	8	9	15	24	25	18
Nonpsychiatric disorder	1	3	6	10	11	7

SD=standard deviation

The demographic and diagnostic patterns of new users of atypical antipsychotics during the study period appear in Table 2. The number of new users increased 4-fold in 5 years. The proportion of men was larger than that of women each year. The mean age of new users increased from 37.8±12.6 years in 1997 to 50.8±22.9 years in 2001. Based on the claims diagnosis at initial use, atypical antipsychotics were prescribed to 405 patients with schizophrenia (57%), 132 with affective disorder (19%), 128 with other psychiatric disorders (18%), and 48 with a nonpsychiatric disorder (7%).

DISCUSSION

This study illustrated the trend in antipsychotic use during the period of 1997 to 2001 by a representative cohort in Taiwan. Besides revealing prevalence and cost statistics, the findings suggest that atypical antipsychotics might gradually replace conventional antipsychotics in patients with major psychotic disorders.

The annual prevalence of antipsychotic use in Taiwan was indeed high, ranging from 5.3% to 6.6%, with the 5-year cumulative prevalence reaching 19.1%. However, a detailed analysis of individual drug use suggested that most people did not receive antipsychotics for a psychiatric disorder. For example, prochlorperazine was also used for nausea and vomiting of various causes, and low-dose sulpiride was used for gastroenterologic disorders.

In a recent study of the use of antipsychotics in Australia,[6] investigators found an increase from 3.28 to 5.69 DDDs/1000 inhabitants daily from 1997 to 2001. During the same period, antipsychotic drug use in Taiwan remained relatively stable (range: 4.0–4.3 DDDs/1000 inhabitants daily) despite the increased use of atypical antipsychotics. Perhaps an excessive expansion of indications for atypical antipsychotics did not exist in Taiwan.

In this study, the author did not make a distinction between prescriptions made by psychiatrists versus nonpsychiatrists, especially prescriptions for atypical antipsychotics. Before 2002, National Health Insurance reimbursement guidelines limited the prescription of atypical antipsychotics to psychiatrists and made additional recordkeeping requirements. Such administrative barriers might explain the delay in the growth of atypical antipsychotics in Taiwan compared with other developed countries. The potential for the increased use of atypical antipsychotics in Taiwan can still be expected within the next years.

As an insurance claims study, this investigation had some unavoidable drawbacks. First, the limited number of unverified billing diagnoses made the study of off-label use difficult. Additionally, psychometric data were not available. Without knowing preexisting conditions and outcomes of therapy, it was almost impossible to evaluate the effectiveness of drug use. Finally, calculation of the total benefit of treatment is beyond the scope of insurance claims.

CONCLUSION

The use of atypical antipsychotics in Taiwan increased in terms of the number of recipients, prescribed amounts, and costs between 1997 and 2001. Because of prior reimbursement limitations by the National Health Insurance, an excessive use of atypical antipsychotics for off-label indications was not observed. The relaxation of these limitations in 2002 might promote the expanded use of atypical antipsychotics in the future.

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