Original Article

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Prescription Patterns of Hypertension – National Health Insurance in Taiwan

Chih-Chieh Chou[1]
Meei-Shynan Lee[2]
Ching-Hsing Ke[1]
Mieng-Hsian Chung[1]

[1] *Department of Family Medicine, Tri-Service General Hospital, National Defense Medical Center*
[2] *School of Public Health, National Defense Medical Center, Taipei, Taiwan, R.O.C.*

Key Words
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Background. Hypertension is a universal disease. Treatment patterns of hypertension provide valuable information for clinicians. Therefore, we present the patterns of antihypertensive medications in Taiwan by their pharmacological classifications, breaking down by patients' ages and genders.

Methods. A descriptive and cross-sectional analysis was performed. Claims from the National Health Insurance of Taiwan were used and included all ambulatory cares of 21 million people from July 1, 1997 to June 30, 1998. A total of 9,717,960 visits with 16,595,030 matched records of antihypertensive medications were obtained. Hypertensive medications were divided into 5 main categories; monotherapy and multiple therapy were defined and discussed separately. Frequency and proportion of utilization of antihypertensive medication were charted and figured.

Results. The most frequently prescribed antihypertensive medications were: calcium antagonists: 5,332,527 records (54.9% of enrolled visits); beta-blockers: 4,230,843 records (43.5%); angiotensin converting enzyme inhibitors (ACEIs): 3,057,009 records (31.5%); diuretics: 2,255,838 records (23.2%); and "others": 1,647,100 records (16.9%). Regardless of gender, the top 2 prescription patterns were calcium antagonists and beta-blockers for monotherapy, beta-blockers + calcium antagonists and ACEIs + calcium antagonists for multiple therapy.

Conclusions. Although Taiwan is a country with National Health Insurance, patterns of pharmacologic treatment of hypertension in Taiwan are close to those in the US, not to those of countries in Europe. Also, these treatments were tailored to the conditions of the patients.

Hypertension is a major health problem, and the expenses of its treatment are high. In the United States, approximately 50 million people have been diagnosed with hypertension, and half of them are treated with antihypertensive medications.[1] In 1986, the cost for treating hypertension was estimated to be 7.5 billion USD in the US.[2] In 1997, the sales of drugs related to cardiovascular disorders totaled 13.4 billion USD in North America, and 12.5 billion USD in the top seven European countries.[3] In 1999, the direct and indirect costs for treating hypertension escalated to 37 billion USD in the US.[4]

In the early 1980s, calcium antagonists and angiotensin-converting enzyme inhibitors (ACEIs) gained ground as the first-line antihypertensive drugs.[5] In the US, prescriptions of both groups of medications increased rapidly. Market share of calcium antagonists increased from 0.3% in 1982 to 27% in 1993; ACEIs, from 0.8% to 24%, respectively.[6] Meanwhile, the market share of diuretics decreased from 56% to 27%. Although calcium antagonists and ACEIs rapidly found acceptance in the US, diuretics and beta-blockers were prescribed more frequently in Canada, Finland, and England.[3,7,8]

Research in Finland indicated that as patients' ages increased, so did rates of prescription for beta-blockers, but ACEIs decreased.[3] The sources of data used in those studies came from either surveys or the data of their respective local areas. Interested in following these patterns in Taiwan, we accessed patient records for hypertension available through the National Health Insurance (NHI) Program of Taiwan. With claims available from 21 million people,[9] our analysis of hypertension prescription patterns in Taiwan was extensive and accurate, as the program is

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Correspondence to: Chih-Chieh Chou, MD, MPH, Department of Family Medicine, Tri-Service General Hospital, National Defense Medical Center, 325, Sec. 2, Cheng-Gong Road, Taipei 114, Taiwan.
Tel/Fax: +886-2-8792-7057; E-mail: shenchch@ndmctsgh.edu.tw

available to all residents regardless of age or income.

As with industrialized nations, demand in Taiwan for universal health care led to the creation of a NHI program in 1995.[10] Taiwan's government consolidated its social insurance programs and extended coverage to all legal residents (except servicemen and the incarcerated) beginning March 1, 1995. This insurance is nationwide and operates with a universal claim system. Several factors inherent in Taiwan's NHI program lend themselves to pattern analysis such as we have undertaken in this study. As with the Current Procedure Terminology (CPT) codes in the US,[11] Taiwan's NHI allocates unique code to each procedure and medication.[12,13] These codes facilitate pattern analyses in healthcare; 1 can accurately follow trends in treatment, ailment, and prescription by drawing on extensive records.

The NHI program's scope is wide, thus making detailed analysis of particular patterns in healthcare possible. In 1998, there were 21.1 million enrollees in Taiwan's health care program, accounting for 96.06% of the population targeted to receive the program's benefits.[9] Additionally, data gathered from Taiwan's NHI program is indicative of residents' needs and true health patterns. Prior to 1999, no prescription co-payment was required of patients, which implies that the cost of medication was not a factor for either patients or physicians in determining the course of treatment.[14]

METHODS

The present study was cross-sectional. Ambulatory Care Expenditures by Visits Files and Details of Ambulatory Care Orders Files were provided by authorities at the Bureau of NHI, Taiwan.[15,16] All claims submitted to NHI were collected between July 1, 1997 and June 30, 1998.

During the data-collecting period, 256 million visits were recorded; they were distributed quite evenly throughout the months in the year. We selected all claims with the diagnosis of hypertension (ICD-9CM: 401-405, WHO international code: A26) and gender information available. This yielded 12,880,142 visits (5.03% of all visits during the same period). Criteria for selection were patient age between 18 and 110, medicated with antihypertensive medication, and length of medication between 7 and 90 days. Therefore, there were 9,717,960 visits (75.4% of hypertensive visits) with 16,595,030 matched records of antihypertensive medications.

Patients' ages were divided into 5 groups, i.e., 18-39, 40-54, 55-64, 65-74, and 75 years or over. Descriptive analyses were performed. The top 5 prescriptive patterns were presented by patients' age and gender. Percentage was calculated as the number for each of these 5 categories divided by the total number of visits. Meanwhile, we also analyzed prescriptions by monotherapy and multiple therapy.

We found that there were more visits made by females than for males for hypertension-related issues: gender distribution was female 50.7% and male 49.3% from our selection (whereas for all enrollees in the NHI program, claims by females were 49.7% and for males 50.3%).[9] The average ages of female and male patients were 64.0 ± 11.5 and 64.0 ± 12.0 years, respectively.

Antihypertensive drugs were grouped into 5 categories, namely ACEIs, beta-blockers, calcium antagonists, diuretics, and others. The beta-blockers also included labetalol and carvedilol (alpha and beta-blockers). Diuretics included plain diuretics and diuretic-diuretic combinations. The "other antihypertensives" category included plain methyldopa, hydralazine, doxazosin, clonidine, terazosin, and prazosin.

Multiple treatments of antihypertensive medications fell into the aforementioned 5 main drug categories. If 2 or more drugs were in the same category in a visit, they were counted once. Fixed combined agents of 2 or more components were counted once for each class of which they were composed.

RESULTS

All antihypertensive drugs were divided into 5 categories. We counted all medication records in each major category regardless of the number of visits. They were as follows: ACEIs: 3,057,009 records (31.5% of all visits); beta-blockers: 4,230,843 records (43.5%); calcium antagonists: 5,332,527 records (54.9%); diuretics: 2,255,838 records (23.2%); and "others": 1,647,100 records (16.9%).

Once the medication records were tallied, we charted

prescription pattern for each visit. For monotherapy and all ages, we found that regardless of gender, the top 3 prescriptive patterns were ranked as calcium antagonists, beta-blockers, ACEIs (Table 1). These prescriptions accounted for 45.3% of antihypertensive treatments for males and 48.2% for females. For multiple treatments, 4 out of the top 5 prescriptive patterns were the same but ranked differently. These prescription patterns were beta-blockers + calcium antagonists, ACEIs + calcium antagonists, calcium antagonists + diuretics, and ACEIs + beta-blockers, respectively.

Next, we analyzed the prescriptive patterns by patients' age groups. Similar orders of prescriptive patterns were found regardless of gender and age groups. For monotherapy, beta-blockers were the most prescribed for people younger than 55. Then, they were ranked as follows: calcium antagonists, ACEIs, others, and diuretics (Table 1). For multiple therapy, beta-blockers + calcium antagonists and ACEIs + calcium antagonists were the top 2 patterns except for females aged 18-39. Mean-

Table 1. Top 5 prescription patterns of monotherapy and multiple therapy for all visits

Age (yrs)	Male				Female			
All		n = 2,171,201		n = 2,621,891		n = 2,372,273		n = 2,552,595
	C	38.8	BC	22.10	C	39.8	BC	23.6
	B	26.3	AC	13.78	B	28.5	AC	12.0
	A	21.5	AB	7.15	A	20.1	BD	7.6
	O	8.4	CO	6.89	D	6.2	CD	7.6
	D	5.1	CD	5.79	O	5.4	AB	6.7
18-39		n = 74,876		n = 77,105		n = 52,250		n = 47,525
	B	40.0	BC	27.0	B	43.3	BC	25.8
	C	28.0	AC	13.1	C	24.2	AB	11.0
	A	25.8	AB	11.5	A	22.8	AC	10.5
	O	3.5	ABC	7.4	O	5.9	BD	7.8
	D	2.6	BD	5.7	D	3.9	ABC	5.1
40-54		n = 407,332		n = 488,141		n = 456,267		n = 479,370
	B	34.8	BC	25.6	B	39.1	BC	26.3
	C	33.1	AC	14.0	C	31.2	AC	10.6
	A	25.0	AB	9.2	A	21.0	AB	9.1
	O	4.4	ABC	7.4	D	4.3	BD	9.0
	D	2.7	BD	5.3	O	4.3	ABC	5.3
55-64		n = 476,803		n = 587,020		n = 655,602		n = 696,982
	C	38.9	BC	22.9	C	38.5	BC	25.5
	B	28.1	AC	14.2	B	30.6	AC	11.8
	A	22.8	AB	7.1	A	20.4	BD	8.0
	O	6.3	ABC	6.1	D	5.3	AB	7.0
	D	3.9	BD	5.7	O	5.2	CD	6.5
65-74		n = 802,465		n = 999,776		n = 765,052		n = 860,529
	C	41.1	BC	20.1	C	43.2	BC	23.2
	B	23.6	AC	13.0	B	25.0	AC	12.3
	A	19.9	CO	7.0	A	19.4	CD	8.3
	O	9.8	CD	5.9	D	6.7	BD	7.3
	D	5.6	AB	5.6	O	5.7	AB	5.8
≥ 75		n = 409,725		n = 469,849		n = 443,102		n = 468,189
	C	41.6	BC	16.0	C	46.8	BC	18.7
	A	18.8	AC	12.3	A	19.6	AC	13.2
	B	18.4	CO	8.6	B	18.5	CD	11.4
	O	13.0	CD	8.0	D	8.8	AD	7.7
	D	8.2	AD	6.0	O	6.4	BD	6.2

All numbers indicate percentage; A = ACEIs; B = beta-blockers; C = calcium antagonists; D = diuretics; O = others.

while, proportionate use of beta-blockers + calcium antagonists decreased as patients' age increased, but not ACEIs + calcium antagonists. With increasing age of patients, monotherapy with diuretics and other increased for both genders except for females aged 18-39. Meanwhile, we found increasing proportion of calcium antagonist + diuretics for female after age 55.

The proportion of medication use was calculated according to patients' gender and age. For monotherapy, this lead to our finding that female and male patients used the 5 groups of antihypertensive drugs differently (Figs. 1 and 2). Females used more calcium antagonist as their ages increased, rising from 28% to 41.6% for age under 40 to over 75. For females, use of diuretics also increased from 3.9% to 8.8%, correspondent to the age of the patient. The use of beta-blockers decreased markedly, from 43.3% to 18.5%, as patients' age increased. Meanwhile, the use of ACEIs and "others" remained stable. Around 20% of females used ACEIs, and another 8% used "others." For males, calcium antagonists were used most frequently, and the proportion of use increased from 24.2% to 46.8% as patients' age increased from less than 40 to over 75. The same trends of increased utilization according to age were noted for "others" and diuretics. The use of "others" increased with age, increasing somewhat more than use of diuretics did. As with female prescriptive patterns, males used fewer beta-blockers as their ages increased. Also, the proportion use of ACEIs de-

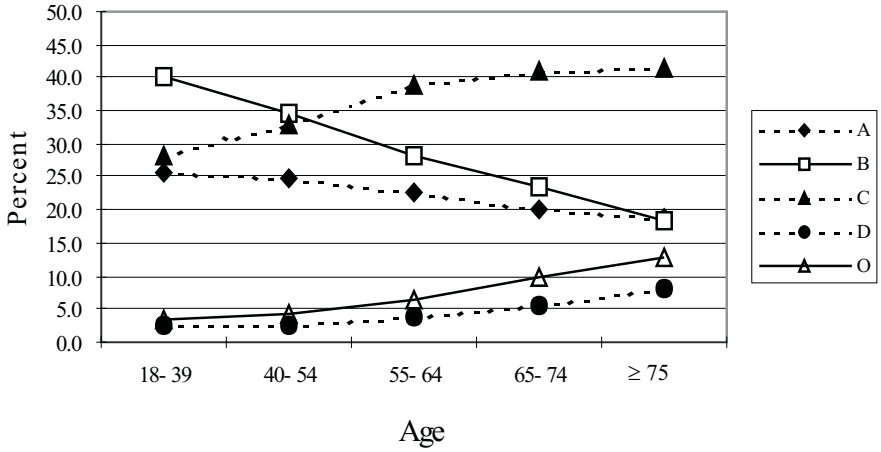

Fig. 1. Percentage of single treatment for males' orders, grouped by 5 main categories and age groups (A = ACEIs, B = beta-blockers, C = calcium antagonists, D = diuretics, O = others).

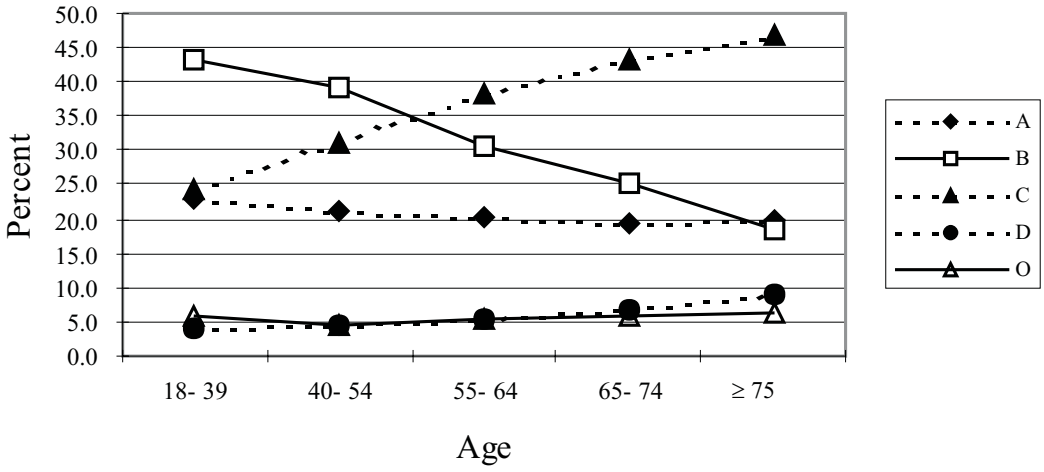

Fig. 2. Percentage of single treatment for females' orders, grouped by 5 main categories and age group (A = ACEIs, B = beta-blockers, C = calcium antagonists, D = diuretics, O = others).

creased more significantly for males than females.

As shown in Figs. 1 and 2, the difference between genders was in the "others" category; as they grew older, males used more "others" than females. Further, beta-blockers were prescribed more frequently than calcium antagonists for patients younger than 55 years old for both genders. The use of ACEIs stayed in the third place.

For multiple treatments (Figs. 3 and 4), trends of utilization were close to those of monotherapy. For males, calcium antagonists were the most used medications for patients older than 40. Unlike monotherapy, diuretics were used more frequently than others. For females, diuretics took the second place for females older than 75. Meanwhile, ACEIs were at the third place except in females' multiple treatment and age over 55. Proportionate uses of ACEIs were more frequent for males than females despite age and single/multiple treatments.

As diuretics were suggested for most patients, we tabulated the proportionate use of diuretics by gender, age, and places of prescriptions (Table 2). The use of diuretics increased with age increase; females were prescribed more frequently than males. Also, medical centers and primary care offices prescribed more diuretics than those of area hospitals and local hospitals, regardless age and gender.

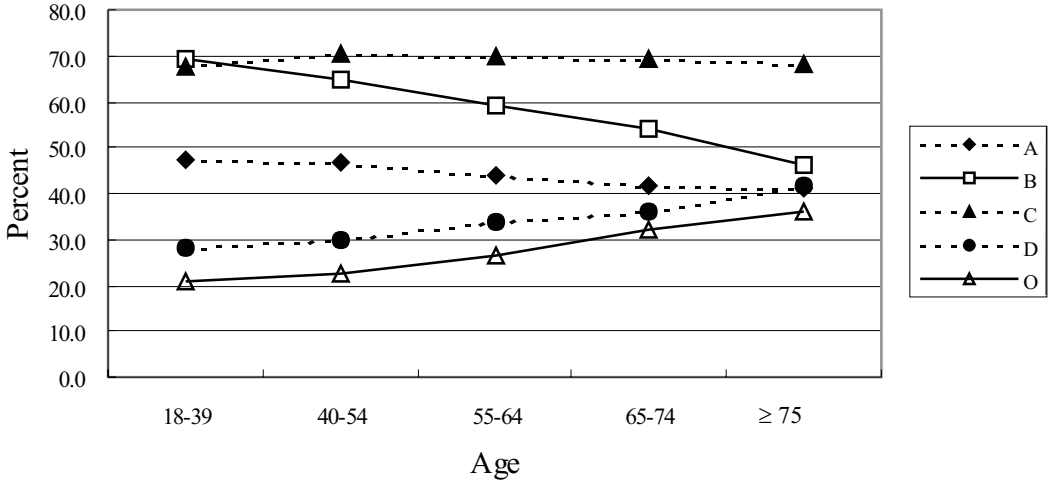

Fig. 3. Percentage of multiple treatment for males' orders, grouped by 5 main categories and age groups (A = ACEIs, B = beta-blockers, C = calcium antagonists, D = diuretics, O = others).

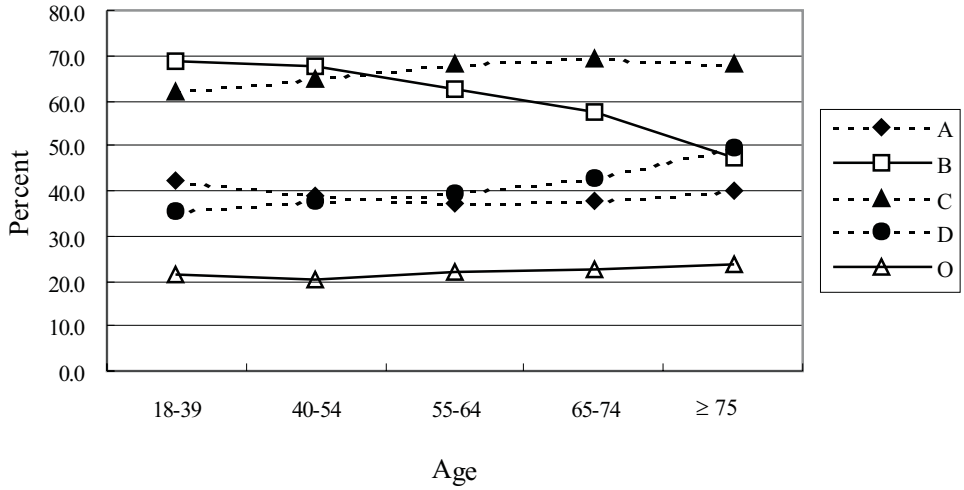

Fig. 4. Percentage of multiple treatment for females' orders, grouped by 5 main categories and age groups (A = ACEIs, B = beta-blockers, C = calcium antagonists, D = diuretics, O = others).

Table 2. Proportion of diuretic versus visits, by gender, age, and places of prescriptions

Gender	Age group	Medical center	Area hospital	Local hospital	Primary care
Female	18-39	20.2*	17.3	18.2	22.2
	40-54	22.0	20.7	21.5	24.0
	55-65	23.3	22.8	23.5	24.8
	65-74	27.7	25.9	26.1	27.5
	≥ 75	33.4	30.5	30.3	30.6
Male	18-39	16.2	13.5	15.9	17.9
	40-54	17.4	15.8	18.8	19.9
	55-65	20.4	19.3	21.2	22.6
	65-74	22.7	22.4	23.7	24.4
	≥ 75	27.7	27.4	26.8	26.4

*: percentage of records divided by visits.

DISCUSSION

These data were collected from claims of the NHI in Taiwan. NHI is a social health insurance and lays stress on its accessibility and equity. Therefore, NHI imposes very few restraints on treatment of hypertension. The only concern was that this study only chose those visits with diagnosis of hypertension. If a visit was not coded as hypertension, it would be discarded. Because certain antihypertensive drugs could be used for other diseases and there were no charts available for this study, we had to set selection criteria as presented above.

Hypertension and related diseases are major causes of mortality and morbidity in Taiwan, as well as in other countries. In Taiwan, antihypertensive drugs cost 35 million USD, 15.2% of all drug expenses in 1999.[17]

Prescription patterns differ regionally. We have demonstrated that in Taiwan, calcium antagonists were the most prescribed medications for hypertension. This is close to the pattern in the US.[6] However, in Britain, patients received diuretics most frequently.[8] It was also noted in Italy, Spain, South Africa, and Canada that diuretics were a popular treatment for hypertension.[3,18] In contrast, beta-blockers were the most prescribed medications in Germany, Slovenia, Hungary, Finland, Swaziland, and Hong Kong.[3,19] Klungel has proposed several reasons for these differences, including, age, side-effects, smoking, and marketing strategies.[20] Marketing strategies may influence physicians' prescriptions; however, patients can go to other clinics for refilling antihypertensive medications, without having to report to their insurer in Taiwan. This competitive and free market prevents certain marketers from controlling prescriptions.

In the 1980's, calcium antagonists and ACEIs were accepted as the first-line medications for hypertension. Market shares for both drugs increased significantly. In the US, calcium antagonists were the most frequently prescribed antihypertensive medications of which accounted for 38% of all prescription patterns in 1995. The second group of medications was the ACEI, 33%. In Taiwan, the prescription patterns in this study differed from those of other countries. Here, calcium antagonists were the most frequently prescribed antihypertensive medication, appearing in 54.9% of all prescriptions in 1998. The second was beta-blockers (43.5%), followed by ACEIs (31.5%), diuretics (23.2%), and "others" (16.9%).

When we analyzed the data by age and gender, calcium antagonists were the most frequently prescribed antihypertensive medications for patients 55 years old and over in Taiwan. Beta-blockers were used less frequently as patients' ages increased for both genders. In monotherapy, proportionate uses of ACEIs were about 20%, regardless of gender, and slightly decreased as patients' age increased. On the other hand, prescriptions of diuretics and others for both genders increased as age increased. The uses of diuretics for females were similar to those in Finland, but the uses of "others" for males were different from those in Finland.

Some studies suggested that aged patients are better in continuing to use the same medications as they received when they were younger. One would expect, if this were the case, that aged patients would use beta-blockers most

frequently. However, this pattern was not found in Taiwan. The proportional usage of ACEIs was about 31.5%, which was close to that in the US, at 33%. This might be related to the side-effect of cough that ACEIs are noted to cause, and patients might be more susceptible to cough in Taiwan. Although reported incidence of cough as a side-effect was 3-4%, it was estimated to be as high as 39%.[21] Further, cough occurs more frequently in women than in men, and in Asian than in Caucasian populations.[22] Therefore, in Taiwan, physicians would be less willing to prescribe ACEIs or have to discontinue ACEIs due to side-effect. Also, we found that ACEIs were less prescribed in females than in males despite age, both in monotherapy and multiple therapy. As a newer generation of ACEIs, with fewer side effects, was introduced to Taiwan, the proportional use of ACEIs might increase. The pattern of the prescription of beta-blockers, decreasing as patients' ages increased, was caused by their side-effects on lipid and heart rates. The increased uses of "others" for males, and of diuretics for females, might be due to certain age-related diseases or symptoms, such as hypertrophy of the prostate and pitting edema.

In comparison with the trends of monotherapy and multiple therapy, diuretics were prescribed much more often in multiple therapy. This implied that diuretics were used as adjuvant therapy. Also, ACEIs were prescribed less often in females in multiple therapy.

As NHI is a universal social insurance in Taiwan, the carrier imposed few restraints on the treatments of hypertension. Also, there was no co-payment for prescribed drugs in 1998. The pattern of prescription would present the real treatment profiles of hypertension, and this differed from those countries with national health insurance. Because this was a cross-sectional study, we need more longitudinal data to explore the trends of antihypertensive medications in Taiwan.

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