

Pattern of Hypnotic Drug Prescription in South Korea: Health Insurance Review and Assessment Service-National Patients Sample

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Background and Objective This study aimed to characterize patterns of hypnotic drug prescription based on age and gender using data from the Health Insurance Review and Assessment Service-National Patients Sample (HIRA-NPS) of South Korea.

Methods Using HIRA-NPS data, the “number of tablets of equivalent hypnotic drugs (TEQ)” was defined herein as the number of tablets of triazolam, zolpidem immediate-release form, or zolpidem extended-release form.

Results The proportion of hypnotic medication prescriptions, including triazolam and zolpidem, was 1.47% in the sample population. The proportion was significantly higher among women than men (1.63% vs. 1.29%; $p < 0.01$). In addition, the proportion of subjects who were prescribed hypnotic drugs increased with age. The mean TEQ per year was significantly higher among women in the 30–39 year old group ($p = 0.02$), but lower in women of the 70–79 year old group compared to men ($p = 0.04$). Of the subjects prescribed the drugs, 14.53% were prescribed at least 0.5 TEQ per day, while 5.0% were given at least 1.0 TEQ per day 0.6% at least 2.0 TEQ per day. Such cases were most common among middle-aged patients (30–59 years old).

Conclusions The proportion of hypnotic drug prescriptions increased with patient age and in females. However, the total amount of hypnotics prescribed per year was greatest among males and middle-aged patients. **Sleep Med Res 2013;4(2):51-55**

Key Words Hypnotics, Zolpidem, Insomnia, Dependence.

INTRODUCTION

Insomnia is a commonly reported clinical symptom. The annual prevalence of insomnia symptoms has been reported to range from 35–50% of the population,¹ including cases of insomnia disorders occurring at 10–22%,^{2,3} although the exact frequency depends on the diagnostic criteria applied. The prevalence of insomnia symptoms in Korea was reported to be 17–23%,^{4,5} including Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition diagnosis in 5% of the patients.⁴ Insomnia is predictive of psychiatric disorders, including depression, anxiety disorders, and alcohol or drug abuse, and is also associated with physical function and quality of life. The prevalence of insomnia is greater in the elderly population.^{4,5} Insomnia shows a female predisposition which is consistent and progressive with age, becoming more prevalent in the elderly.⁶ Additionally, it has been reported that chronic benzodiazepine or hypnotic drug users are most often elderly.^{7,8} The pharmacokinetics and clearance of hypnotic drugs may be altered in elderly individuals compared to younger individuals. It is well known that benzodiazepine, which has a long half-life, may be associated with an increased incidence of adverse events, such as confusion or falling down, among the elderly.⁹⁻¹¹

Several hypnotic drugs have been approved by the Korean Food and Drug Administration (KFDA). Physicians can also prescribe many hypnotic medications for insomnia without KFDA indication, including antipsychotics, benzodiazepine, and sedative antidepressants such as amitriptyline and trazodone antihistamine. Many people who suffer from sleep problems do not

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discuss them or their use of hypnotic drugs with their doctors. Currently, over-the-counter medications and alcohol are widely used as sleep aids. The potential for overtreatment with hypnotic drugs without proper sleep hygiene education raises health concerns in the population.¹² This study aimed to explore the patterns of hypnotic drug prescription according to age and gender using data from the Health Insurance Review and Assessment Service-National Patients Sample (HIRA-NPS).

METHODS

Patients

Data from the HIRA-NPS-2011 (serial number: HIRA-NPS-2011-0101) were analyzed to explore patterns of hypnotic medication prescription in South Korea. This study was approved by the Institutional Review Board of Asan Medical Center. The HIRA-NPS-2011 is a stratified random sampling for gender and age from the entire population enrolled in the Korean National Health Security System from January 2011 to December 2011. The total sample size was 1375832 people, which is 3% of the entire recorded patients.

Calculating the Number of Tablets of Equivalent Hypnotic drugs (TEQ)

Herein, the “number of tablets of equivalent hypnotic drugs (TEQ)” was defined as the quantity of triazolam, zolpidem immediate-release form, or zolpidem extended-release form tablets. Numerous studies have shown that 0.25 mg triazolam is comparable to 10 mg zolpidem in the immediate-release form,¹³⁻¹⁵ and that 10 mg of zolpidem in the immediate-release form is comparable to 12.5 mg of zolpidem in the extended-release form.^{16,17} The TEQ was calculated by summing the number of tablets of 0.25 mg triazolam, 10 mg zolpidem immediate-release form, or 12.5 mg zolpidem extended-release form prescribed per day. For example, if a subject was prescribed 0.125 mg of triazolam, 5 mg of zolpidem immediate-release form, or 6.25 mg of zolpidem extended-release form, the TEQ would be 0.5. If a subject was prescribed 0.25 mg of triazolam and 5 mg of zolpidem immediate-release form at the same time, the TEQ would be 1.5. The TEQ/year was calculated by summing the total number of hypnotic tablets prescribed in one year. If a subject was prescribed 0.125 mg triazolam for 30 days and 10 mg zolpidem immediate-release form for 30 days in a year, the TEQ/year would be 45.

Statistical Analyses

The Stata program version 13.1 (STATA Corp, College Station, TX, USA) was used to select subjects who were prescribed any hypnotic drug. Patient medical records were merged (using a unique encrypted identification number) and the daily and annual TEQ was calculated. The Student's t-test for TEQ and

the chi-square test for the proportions of subjects who were prescribed hypnotic drugs were then employed for sex and age group comparisons. All statistical tests were two-tailed, and results were considered to be significant with p values < 0.05 .

RESULTS

Subjects Prescribed Hypnotic Drugs at Above 3 TEQ Per Day

From HIRA-NPS, 27 subjects (18 women and 9 men) were identified who were prescribed hypnotic drugs at above 3 TEQ per day during 2011. These 27 cases included 2 women in the 20–29 year old age group, 2 men and 7 women in the 30–39 year old age group, 2 men and 1 woman in the 40–49 year old age group, 1 man and 4 women in the 50–59 year old age group, 3 men and 1 woman in the 60–69 year old age group, and 1 man and 3 women in the 70–79 year old age group. Among these subjects, three were prescribed an unusually high amount of hypnotic drugs (3351, 5156, and 5305 TEQ) during 2011. These cases are further described below.

Case 1

A 26-year-old woman was prescribed 3351 tablets of zolpidem over 2011. On several occasions, she was prescribed 100 tablets of zolpidem over 5–8 day intervals.

Case 2

A 56-year-old man was prescribed 5156 tablets of triazolam in 2011. During this period, he was prescribed 100 tablets of triazolam for 21 and 28 days, respectively, and one tablet of triazolam per day for several months.

Case 3

A 57-year-old woman was prescribed 5305 tablets of hypnotic drugs (596 zolpidem and 4706 triazolam tablets) in 2011. This included prescriptions of 100 tablets of triazolam for 7, 14, and 21 days, respectively, 1 tablet of triazolam daily for several months, and 1 tablet of zolpidem daily for several months.

Patterns of Hypnotic Drug Prescription

Among the 1375832 subjects in the HIRA-NPS dataset for 2011, subjects under 10 and over 100 years old were excluded from statistical analyses. The 27 subjects who were prescribed more than 3 TEQ per day were also not included in the final analyses. Among the total HIRA-NPS cohort, hypnotic medications, including triazolam and zolpidem, were prescribed to 18,306 subjects (1.47%)(Table 1). The proportion of females who were prescribed hypnotic medication was significantly higher than males (1.63% vs. 1.29%; $p < 0.01$). The proportion of females who were prescribed hypnotic medication was significantly higher than men in the 30–79 year old groups, but

Table 1. Proportion of subjects prescribed a hypnotic drug (triazolam or zolpidem) in 2011 and the calculated TEQ

Age group (years old)	Total subjects (n = 1248874)		Men (n = 599625)			Women (n = 649249)		
	Subjects, n	Hypnotics users, n (%)	Subjects, n	Hypnotics users, n (%)	TEQ/year	Subjects, n	Hypnotics users, n (%)	TEQ/year
10-19	182053	181 (0.1)	94014	93 (0.1)	56.1 ± 99.0	88039	88 (0.1)	39.8 ± 87.9
20-29	182760	1032 (0.6)	87619	422 (0.5)	61.9 ± 108.0	95141	610 (0.6)	72.6 ± 127.3
30-39	221148	1834 (0.8)	107526	742 (0.7)	73.6 ± 139.0	113622	1092 (1.0)†	89.3 ± 146.1*
40-49	236928	3241 (1.4)	116043	1486 (1.3)	92.7 ± 157.2	120885	1755 (1.5)†	86.1 ± 144.4
50-59	200468	3964 (2.0)	97959	1728 (1.8)	83.5 ± 138.3	102509	2236 (2.2)†	78.4 ± 134.9
60-69	122270	3411 (2.8)	57709	1542 (2.7)	74.5 ± 133.8	64561	1869 (2.9)*	67.8 ± 120.3
70-79	76429	3223 (4.2)	31032	1224 (3.9)	74.2 ± 130.6	45397	1999 (4.4)†	64.9 ± 116.9*
80-89	24155	1295 (5.4)	7159	447 (6.2)	58.3 ± 117.3	16996	848 (5.0)†	53.1 ± 104.1
90-99	2663	125 (4.7)	564	39 (6.9)	76.4 ± 126.4	2099	86 (4.1)†	40.9 ± 84.9
Total	1248874	18306 (1.47)	599625	7723 (1.29)	78.0 ± 137.4	649249	10583 (1.63)†	73.4 ± 129.2*

TEQ, number of tablets of equivalent hypnotic drugs, calculated as the sum of the number of prescribed tablets of 0.25 mg triazolam, 10 mg zolpidem immediate-release form, or 12.5 mg zolpidem extended-release form per day.

*p < 0.05, †p < 0.01 for men vs. women.

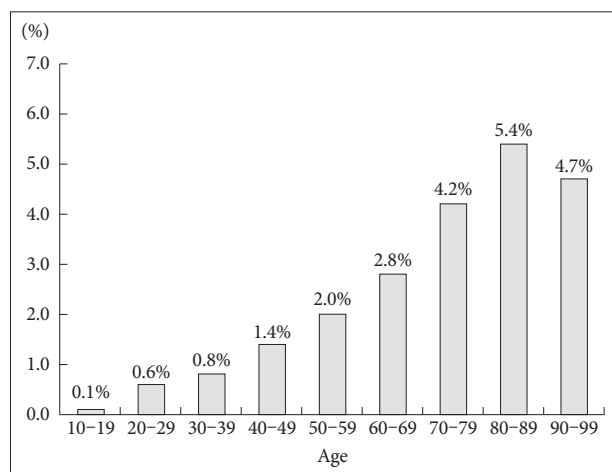


Fig. 1. Proportion of hypnotic drugs prescribed to patients by age group.

lower in the 80-99 year old group. In the 80-89 year old group, 5.5% of subjects were prescribed hypnotic drugs (Fig. 1). The rate was also high among the elderly population (70-99 years old). Triazolam was prescribed to 5152 HIRA-NPS subjects (0.41%) and zolpidem was prescribed to 14874 (1.19%) subjects. Among the men, triazolam was prescribed to 2063 (0.34%) and zolpidem to 6453 (1.08%) subjects. Among the women, triazolam was prescribed to 3089 (0.48%) and zolpidem to 8421 (1.30%) subjects.

The mean TEQ per year was significantly higher among women in the 30-39 year old group (p = 0.02), but significantly lower in the 70-79 year old group (p = 0.04) compared to men (Table 1). The proportion of subjects who were prescribed at least 0.5 TEQ per day was 14.5% (Fig. 2), and high rates were observed among the 40-49 (17.2%), 50-59 (16.4%), and 30-39 (15.9%) year old groups (Table 2). The proportion of subjects

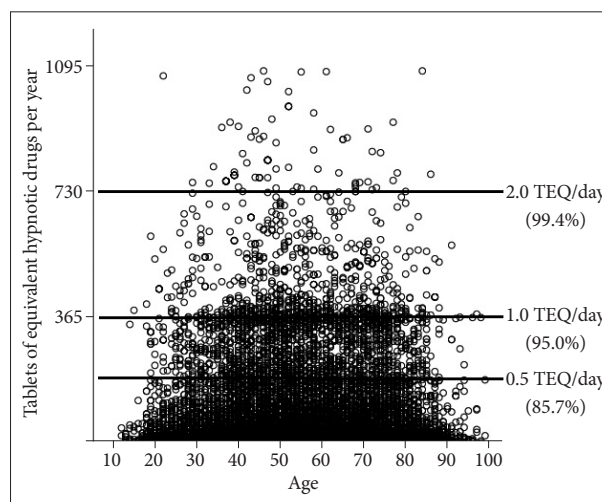


Fig. 2. Equivalent hypnotic drug tablets prescribed per year. Each open circle represents one patient. The 27 subjects who were prescribed 3 or more tablets of equivalence hypnotic drugs per day were not included in this figure. TEQ: tablets of equivalent hypnotic drugs.

who were prescribed at least 1.0 TEQ per day was 5.0%, and 0.6% received at least 2.0 TEQ per day. These instances were highest among the middle-aged (30-59 year old) groups.

DISCUSSION

In our current analyses, we observed the hypnotic drug prescription rate of 1.47% in South Korea, with the highest prevalence among the elderly. However, the total number of medications taken annually was found to be highest in 30-39 year old females and 70-79 year old males. Among patients who took any of the hypnotic medications, 5.0% took at least one hypnotic

Table 2. Number of tablets of equivalent hypnotic drugs (TEQ) prescribed by age group

Age group (years old)	Hypnotics users, n	Hypnotics users with the indicated TEQ/day			
		≥ 2	2 > and ≥ 1	1 > and ≥ 0.5	< 0.5
10–19	181	0 (0.0%)	3 (1.7%)	12 (6.6%)	166 (91.7%)
20–29	1032	2 (0.2%)	38 (3.7%)	87 (8.4%)	905 (87.7%)
30–39	1834	29 (1.6%)	55 (3.0%)	208 (11.3%)	1542 (84.1%)
40–49	3241	35 (1.1%)	172 (5.3%)	350 (10.8%)	2684 (82.8%)
50–59	3964	14 (0.4%)	220 (5.5%)	416 (10.5%)	3314 (83.6%)
60–69	3411	11 (0.3%)	145 (4.3%)	302 (8.9%)	2953 (86.6%)
70–79	3223	9 (0.3%)	128 (4.0%)	280 (8.7%)	2806 (87.1%)
80–89	1295	3 (0.2%)	35 (2.7%)	91 (7.0%)	1166 (90.0%)
90–99	125	0 (0.0%)	2 (1.6%)	9 (7.2%)	114 (91.2%)
Total	18306	103 (0.6%)	798 (4.4%)	1755 (9.6%)	15650 (85.5%)

TEQ, the number of tablets of equivalent hypnotic drugs, calculated as the sum of the number of prescribed tablets of 0.25 mg triazolam, 10 mg zolpidem immediate-release form, or 12.5 mg zolpidem extended-release form per day.

ic drug tablet every day annually.

Numerous studies have shown that the prevalence of insomnia is higher in the elderly,^{4,5} among whom it can often be a prodromal symptom for an underlying physical and/or mental illness.¹⁸ In addition, the elderly are more likely to take benzodiazepine hypnotics.¹⁹ Psychological problems, comorbid medical conditions, decreased physical activity, multiple usage of medications, and pharmacokinetics are contributors to the higher prevalence of insomnia and use of hypnotic drugs in the elderly.²⁰ In the current study, a high proportion of elderly subjects (70–99 years old groups) (Fig. 1) were observed to take hypnotic medication, which is in agreement with previous studies. However, the TEQ per year and the proportion of subjects who were prescribed at least one hypnotic drug tablet per day were higher among the 30–59 year old groups (Table 1, 2). We conclude from this that the elderly tend to take hypnotic drugs more frequently, but at a lower dosage.

In this study, the proportion of females who were prescribed hypnotic medication was significantly higher than males among the 30–79 year old groups. Numerous studies have reported the prevalence of insomnia to be higher in women,^{6,16} and that older women tend to use sedatives or hypnotics more frequently.²¹ Women are more vulnerable to stressful events or psychological stresses. Insomnia is a common complaint in various psychiatric disorders, especially depression and anxiety.²² In addition, greater bodily vigilance and awareness is found among women, and a socially sanctioned culture exists that encourages women to more readily express emotional distress and somatic symptoms.²³ Nevertheless, the proportion of the current study subjects who were prescribed hypnotic drugs was highest among men in the 80–99 year old group. This result could be a consequence of the low sample size of male subjects in this age group, or the exclusion of other hypnotic agents such as trazodone or various benzodiazepines from this study, which might have skewed the results. However, this finding indicated that much

older men tend to take hypnotic drugs more often.

Three subjects in the HIRA-NPS cohort for 2011 were found to have been prescribed “unusually” high amounts of hypnotic drugs for an unknown reason. However, we speculate that these individuals did not use the hypnotic drugs appropriately or just for sleep issues alone. Numerous studies have reported evidence of zolpidem abuse and dependence.^{24–26} In addition, history or abuse and underlying psychiatric diseases can increase the risk of zolpidem abuse.²⁷ Hypnotics impair cognition, memory, and performance, and also increase the risk of car accidents.²⁸ In addition, the sleep-promoting effects of hypnotics appear to be diminished with chronic use because of a build-up of tolerance.²⁹ In chronic insomnia patients for whom pharmacotherapy is unsuccessful, comorbid mental and physical factors indicate a sleep disturbance complexity that is unlikely to respond fully to medication.³⁰ We conclude from these findings that careful attention to the hypnotic drug use patterns is needed to prevent drug abuse and dependence.

In the present study, only the prescription rates for triazolam and zolpidem were estimated, and other hypnotic medications such as trazodone or various benzodiazepines were not included. Benzodiazepines, including clonazepam, are commonly used for sleep problems, while trazodone is widely prescribed for maintenance of sleep. It was not determined in this study whether trazodone or benzodiazepine was prescribed in the HIRA-NPS cohort for sleep problems or other symptoms, such as pain, anxiety, or movement disorders. This may have skewed our findings on the prescription rates of hypnotic agents. In addition, only the 2011 data from the HIRA-NPS was used, thus the long term use of hypnotic medications was not explored. Despite the limitations of this study, however, our findings demonstrated that the proportion of hypnotic drug prescriptions increased with age and was more common in females. Furthermore, the level of hypnotics used annually was greatest among males and in the middle-aged (40–59 years old) group of patients.

Conflicts of Interest

The authors have no financial conflicts of interest.

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