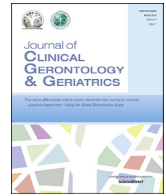




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Original article

Characterization of patients with duplicated z-hypnotic use: A population-based study in Taiwan



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ABSTRACT

Background/Purpose: A significant increase in the prescribing of nonbenzodiazepine hypnotic agents (z-hypnotics) has been noticed in the past decade. Several safety concerns have emerged after the excessive use of z-hypnotics. This study aims to characterize the z-hypnotics users with a focus on those with overlapping duration of z-hypnotics supply by using Taiwan's National Health Insurance Research Database.

Methods: Incident z-hypnotic users who received at least one z-hypnotic prescription from outpatient settings during 2001–2010 were identified and classified into three groups: duplicated users (those who received multiple z-hypnotic prescriptions on the same day), suspected duplicated users (those who received multiple z-hypnotic prescriptions with 7+ days of overlapping supply), and nonduplicated users. We examined the demographic profiles of these z-hypnotic users as well as z-hypnotics prescriptions (duration, daily consumption, and characteristics of providers).

Results: We identified 242,412 incident users of z-hypnotics with 2.4 million z-hypnotic prescriptions during the 10-year study. Almost 20% of them were duplicated ($n = 29,948$) and suspected duplicated users ($n = 16,899$). Duplicated and suspected duplicated users were more likely to be male and in their old age compared to the nonduplicated users. Approximately half of the suspected duplicated users (51.8%) and nonduplicated users (47.0%) received their z-hypnotic prescriptions from primary care clinics while duplicated users received their z-hypnotic prescriptions from metropolitan hospitals (29.9%) and academic medical center (26.2%). Duplicated z-hypnotic users were more likely to receive more days' supply and higher daily dose of z-hypnotics. Up to 31.0% of duplicated z-hypnotics users received > 1 defined daily dose/day if adding all prescriptions they received within 1 day.

Conclusion: Duplicated z-hypnotic users were more likely to receive prescriptions with long duration and high daily dose. Healthcare professionals and policy makers are recommended to put more efforts into dealing with this urgent drug safety issue.

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Introduction

A significant increase in the prescribing of nonbenzodiazepine hypnotic agents, the so-called *z-hypnotics*, has been noticed in the past decade.^{1–4} Compared to benzodiazepines (BZDs), z-hypnotics are considered as safer alternatives for insomnia due to their improved pharmacokinetic profile.⁵ However, several safety concerns have emerged after the tremendous use of z-hypnotics. Some

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studies have reported a high prevalence of inappropriate use of z-hypnotics, particularly long-term use in the elderly, which may result in adverse events.^{1,6} Another major safety issue is the *doctor-shopping* behaviors among insomnia patients and accompanying dependency of z-hypnotics.⁷ More empirical data regarding the quality of z-hypnotics prescriptions and characteristics of potential z-hypnotic-dependent users will help clinicians and policy-makers to identify *hot-spots* for rational use of z-hypnotics. Using Taiwan's National Health Insurance research database (NHIRD), this study examined the demographic profiles of z-hypnotic users as well as z-hypnotic prescriptions (duration and daily consumption) they received.

Methods

Data source

This retrospective cohort study used 12 years of data (1999–2010) from the National Health Insurance Research Database (NHIRD), a nationwide claims database from Taiwan's mandatory National Health Insurance program. The NHIRD contains anonymous eligibility and enrollment information, as well as claims for visits, procedures, and prescription medications for > 99% of the entire population (23 million) in Taiwan.⁸ Two subsets of the NHIRD, the Longitudinal Health Insurance Database (LHID) 2000 and LHID 2005, which contains a total of two million beneficiaries randomly selected from the NHIRD were used as our original cohort. The details of LHIDs and NHIRD were described in the NHI website and in our previous publication.^{1,9}

Study participants

Patients who received a prescription of z-hypnotics (zolpidem, zopiclone, or zaleplon) from an outpatient setting from January 1, 2001 to December 31, 2010 were identified as our study participants. The first prescription date of z-hypnotics was defined as the cohort entry date. To be eligible for the definition of incident z-hypnotics users, those who received z-hypnotics 1 year prior to the cohort entry date were excluded. The characteristics of z-hypnotic users were collected at the cohort entry date.

All z-hypnotic prescriptions received by our study participants in the outpatient setting between the cohort entry date and December 31, 2010 were retrieved from the LHID. Incident z-hypnotic users were then categorized into three groups based on how they received their z-hypnotic prescriptions. Those who ever received z-hypnotics on the same day were defined as the duplicated users while those who ever received z-hypnotics with ≥ 7 days of overlapping supply were defined as suspected duplicated users. For example, if a patient receives two prescriptions (both were 28-days of supply of z-hypnotic) on January 14 and January 26, respectively, then they are defined as the suspected duplicated user. Other z-hypnotic users were defined as nonduplicated users.

Measurements and statistical analysis

Demographics of z-hypnotic users including age and sex were collected. Providers' characteristics, including prescribing physicians and medical facilities, were further examined. Prescribing physicians were grouped by their specialties (e.g., psychiatry). Medical facilities were characterized by accreditation levels: medical center, metropolitan hospital, local community hospital, and clinic. Several measures, including prescription duration, daily pills, and daily dosage, were used to quantify the use of z-hypnotics among the three types of z-hypnotics users. The daily dosage of z-hypnotics was calculated by number of pills taken and defined daily

dose (DDD) and presented by per-prescription as well as per-patient. The numbers of z-hypnotics prescriptions received within a day by duplicated z-hypnotics users were also investigated.

All data are expressed as number with percentage or mean with standard deviation and compared using analysis of variance (ANOVA) or Chi-square test. The analyses were performed with SAS, version 9.2 (SAS Institute, Cary, NC, USA).

Results

We identified 242,412 z-hypnotic users and 2.4 million z-hypnotic prescriptions received by them over the 10 years of the study period. The characteristics of z-hypnotic users are shown in Table 1. Nearly one-fifth of z-hypnotic users ($n = 46,847$) had received at least one duplicated or suspected duplicated prescriptions during the study period. The proportion of men in duplicated (41.2%) and suspected duplicated z-hypnotic users (41.0%) were significantly higher than nonduplicated users ($p < 0.01$). Approximately one-third (31.6%) of duplicated and one-fourth (26.8%) of suspected duplicated z-hypnotic users were elderly.

Duplicated z-hypnotic users received higher number of z-hypnotics prescriptions (36.1 prescriptions/patient in average) compared to the other two groups. Duplicated z-hypnotic users were more likely to receive their z-hypnotic prescriptions from metropolitan hospitals (29.9%) and medical centers (26.2%), whereas other users mostly received their z-hypnotics from clinics (47.0% in nonduplicated and 51.8% in suspected duplicated z-hypnotic users). Duplicated z-hypnotic users were more likely to receive their z-hypnotics prescriptions from neurology specialist but less likely from physicians in internal medicine and family medicine compared to the other two groups (Table 2).

Approximately 90% of duplicated z-hypnotics users received a prescription of > 7 days of supply (89.0% of 8–30 days and 0.5% of > 30 days). The daily z-hypnotic consumption was higher among duplicated users. Nearly one-sixth (15.2%) of them received > 1 DDD/d per prescription (vs. 6.8% of nonduplicated and 12.9% of suspected duplicated z-hypnotic users). Up to 31.0% of duplicated z-hypnotics users received > 1 DDD/d if adding all prescriptions they received within 1 day (Table 3).

Approximately 60% (56.9%) and 40% (42.4%) of duplicated z-hypnotic users received two or three prescriptions within a day. However, we found that very few patients received more than three z-hypnotics prescriptions within 1 day (Table 4).

Discussion

This study is the first to investigate the characteristics of duplicated z-hypnotics users and their utilization patterns of z-hypnotics over the past decade in Taiwan. We found that duplicated z-hypnotics users were more likely to be male and of older age and to receive their z-hypnotic prescriptions from metropolitan hospitals and medical centers. In addition, duplicated z-hypnotic users were more likely to receive prescriptions with long duration and high daily dose compared to their nonduplicated counterparts.

Recently, potential drug abuse resulting from multiple providers and drug-driven shopping behavior has become a critical issue in many countries.^{10–12} Nevertheless, previous studies have focused on opioids but not in sedatives such as BZD and z-hypnotics. Identifying patients who have high possibility of duplicated z-hypnotics use can help to reduce the risks of z-hypnotic misuse and associated adverse events.

Under the universal healthcare insurance provided by Taiwan's National Health Insurance program, patients in Taiwan have very high accessibility to healthcare services with relatively low financial and referral barriers. It was estimated that 17.3% of outpatients

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