Original Work

De-Prescribing of Non-Benzodiazepine Hypnotics in Older Adults Within an Ambulatory Care Setting

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Abstract

Objective: To assess the patient safety impact of a collaborative medication intervention of a deprescribing program for non-benzodiazepine (nBZD) sedative hypnotics in older adults within the Marshfield Clinic System.

Methods: A retrospective electronic chart review was conducted to assess nBZD sedative hypnotic use. The study population included adults aged 65 years or older with an active prescription for a nBZD sedative hypnotic (i.e. zolpidem, eszopiclone, or zaleplon) prescribed by a Marshfield Clinic provider between February 3, 2015, and November 2, 2015. The prescribing providers of the above patients were selected to receive a guidance statement on appropriate use of nBZD sedative hypnotics in elderly patients. The impact of this intervention was assessed after implementation through an electronic provider survey and electronic chart review.

Results: A total of 1318 patients were included. Approximately 65% of nBZD sedative hypnotic prescriptions were written for a day supply of 90 days or more. A total of 184 providers were identified for enrollment into the deprescribing program. At the 3-month follow-up, 556 patients were included in the chart review. nBZD hypnotics were deprescribed for 77 patients (14%). For providers who chose to continue prescribing nBZD sedative hypnotics, more than 50% had the following rationales: patient's unwillingness to discontinue the medication due to being a long-term medication user, or fear of inadequate sleep outweighing the risks of continued therapy.

Conclusions: Deprescribing of nBZD sedative hypnotics in older adults remains challenging despite increasing evidence of risks related to falls, fractures, carry-over sedation, and driving impairment. Considering patient's unwillingness to discontinue nBZD sedative hypnotics, patient-targeted education by providers on the risks and benefits of pharmacologic therapy compared with other modalities may increase the likelihood of appropriate deprescribing.

Insomnia contributes to over five million office visits per year in the United States, with an estimated 7% of adults developing short-term or long-term insomnia each year.[1,2] The prevalence and persistence of sleep disorders increase as the population ages, leading to a subsequent increase in sleep medication utilization.[3-5] The proportion of elderly patients using non-benzodiazepine (nBZD) sedative hypnotics (i.e. zolpidem, zaleplon, and eszopiclone) continues despite limited representation of older adults in clinical studies. A cautious approach to use of nBZD sedative hypnotics in the elderly similar to that of benzodiazepine (BZDs) hypnotics may be prudent given the increasing safety concerns (e.g. dependency/withdrawal, cognitive impairment, falls/fractures, driving impairment) and the paucity of long-term data on chronic use.[6-14] As more data become available regarding the safety of these agents in older adults, professional organizations are encouraging diligent medication use assessments by clinicians. The American Geriatrics Society 2012 Beers Criteria advised against chronic use (≥ 90 days) of nBZD sedative hypnotics in older adults due to the risks of falls, fractures, and cognitive and driving impairment.[15] In 2013, chronic use of nBZD sedative hypnotics was included in the Pharmacy Quality Alliance High Risk Medication Use in the Elderly criteria, a quality measure that was adopted by the Centers for Medicare & Medicaid Services. In 2015, the updated Beers Criteria advised against any use of nBZD sedative hypnotics in older adults, mirroring the same historic recommendation for BZDs.[16]

Methods

Study Design and Population

The intervention was conducted within Marshfield clinic, which is an interdisciplinary physician group practice with more than 50 clinic locations in central, northern, and western Wisconsin. This was a single-arm prospective study with three phases: A) a retrospective chart review, B) a physician-targeted intervention (i.e. deprescribing program) created by clinical pharmacists, and C) subsequent outcomes assessment. Deprescribing was defined as the process of discontinuing nBZD sedative hypnotic use by substituting a pharmacological alternative, tapering the nBZD sedative,

referring patients to psychotherapy as well as sleep specialists, educating patients on sleep hygiene, or any combination of these methods. The Marshfield Clinic's Institutional Review Board approved this study with waiver of informed consent.

A retrospective chart review was conducted to characterize the utilization of nBZD sedative hypnotics in older adults within the system and to identify providers for inclusion into the deprescribing program. All patients ≥ 65 years who had been prescribed a nBZD sedative hypnotic by a Marshfield Clinic provider between 12/1/2014 and 9/16/2015 through the electronic prescribing platform were included. Agents defined as nBZD sedative hypnotics included all brands, generics, and various dosage forms of zolpidem, zaleplon, and eszopiclone. Patients were excluded if they received two different nBZD sedative hypnotics during this time period.

The prescribing providers for the study patients were included in the deprescribing program if they wrote prescriptions for any nBZD sedative hypnotic with a total day supply including refills ≥90 days or any combination of nBZD sedative hypnotic and BZD for the same patient.

Study patients who met inclusion criteria were included in the 3-month follow-up chart review. Identified prescribers were offered the opportunity to participate in an electronic survey assessing physician satisfaction and assessing potential barriers to deprescribing of nBZD sedative hypnotics.

Intervention

The provider-targeted intervention was focused on providing education and a list of patients. Following a review of the current literature, and in coordination with sleep medicine and medication safety specialists, a guidance document (i.e. Drug Safety Alert letter and Sleep Fact Sheet) on the safety concerns and appropriate use of nBZD sedative hypnotics in older adults was developed. For each enrolled provider, a list of patients that had received those prescriptions identified in the retrospective chart review was generated. The guidance document and provider-specific patient lists were mailed to providers on 11/20/2015. The guidance document included options including 1) thoroughly assessing sleep and sleep medicine efficacy and safety and determining if a taper of the nBZD sedative hypnotic, and eventual discontinuation would be beneficial, 2) considering a consultation with Marshfield clinic Sleep Medicine for cognitive-based therapies in patients who require continued use of nBZD sedative hypnotic therapy despite other optimized therapies (e.g., sleep hygiene education, stimulus control, stress management), and 3) carefully considering risks and benefits of alternative medications before switching therapy; for example, it is not recommended to switch to a benzodiazepine product due to the proven risks of use in older adults.

Study Measurements

Data collected included patient demographic information and nBZD sedative hypnotic utilization information (e.g. medication name, dose, dosage form, frequency, quantity prescribed, refills prescribed, prescriber). The 2012 Beers Criteria recommendation to avoid use of nBZDs ≥90 days per year was used as a guide to determine chronic, potentially unsafe nBZD sedative hypnotic use. Zolpidem, zaleplon, and eszopiclone prescriptions that allowed a patient to use a nBZD sedative hypnotic ≥90 days within one year served as a surrogate marker for potentially inappropriate, unsafe medication use.

Data collected on enrolled providers included provider specialty, location, and the total number of patients included in the provider-specific patient list.

Outcomes were assessed three months after the intervention through an electronic chart review to identify any possible changes in prescribing of nBZD sedative hypnotics. Data reviewed included patient demographic information, provider medical record notes written after the intervention date, and medication records. The electronic chart review determined if the nBZD sedative hypnotic was discontinued, if an alternative agent was prescribed in addition to or in place of the nBZD sedative hypnotic, and if any concurrent BZD was discontinued in patients who were prescribed both agents. Reasons for discontinuation were also noted if identified in the medical record.

An online survey was sent to providers who were enrolled in the program via electronic mail. Questions were reviewed for bias and appropriateness by the Institutional Review Board. The survey was used to characterize potential barriers or opportunities for nBZD sedative hypnotic deprescribing and if the provider found the intervention helpful.

TABLE 1. Baseline nBZD Sedative Hypnotic Utilization

Drug Name	*# Patients*
Eszopiclone	18
Eszopiclone (Lunesta®)	32
Zaleplon	27
Zaleplon (Sonata®)	11
Zolpidem	996
Zolpidem (Ambien® CR)	19
Zolpidem (Ambien®)	215
Total	**1318**

nBZD: non-benzodiazepine sedative hypnotics

Results

Baseline

A total of 1318 patients were prescribed nBZD sedative hypnotics at baseline and

TABLE 2. Baseline Day Supply of nBZD Sedative Hypnotic Prescriptions

Days Supply	*All Patients*	*nBZD Alone*	*nBZD and BZD*
< 90 day supply	455	390	65
≥ 90 - 180 day supply	327	251	49
≥180 day supply	536	456	107

BZD: benzodiazepine hypnotics; nBZD: non-benzodiazepine hypnotics

TABLE 3. Baseline nBZD Sedative Hypnotic Utilization by Age Group

Age	All Patients	nBZD Alone	nBZD and BZD
< 75	790	663	127
≥ 75	528	434	94

BZD: benzodiazepine hypnotics; nBZD: non-benzodiazepine hypnotics

were included in the initial retrospective chart review (Table 1). The average age was 74 years (SD 7.3), and 63% were female. The most commonly prescribed nBZD was zolpidem. During the study period, 17% (n=219) of patients received a prescription for both a BZD and an nBZD. For the subsequent analysis, patients were excluded if deceased or lost to follow up.

Approximately 65% of patients prescribed nBZD sedative hypnotics had prescriptions written for a day supply in excess of 90 days (Table 2). Of patients who received a nBZD sedative hypnotic prescription during this time period, 40% were 75 years or older (n=528; Table 3).

A total of 184 providers were identified for enrollment into the deprescribing program and were subsequently mailed the guidance document and prescriber-specific patient list.

Post-Intervention

At the 3-month follow-up, 556 patients remained in the study. The number of patients prescribed nBZD sedative hypnotics changed from 556 to 479 (14% decrease). The 14% discontinuation rate was consistent for both patient populations.

In the combination population, 20 patients (11%) had their nBZD sedative hypnotic discontinued without tapering, and 4 patients (3%) had both the nBZD sedative hypnotic and BZD discontinued without tapering. In the monotherapy population, 27 patients (7.1%) had the nBZD sedative hypnotic discontinued without tapering and without addition of another agent, while 20 patients (5.2%) were prescribed another agent for sleep after nBZD sedative hypnotic discontinuation (e.g. melatonin, trazodone).

Survey Results

A total of 24 providers (13%) participated in the online survey. For providers who chose to continue prescribing nBZD sedative hypnotics for patients on his or her patient list generated as part of the deprescribing program, more than 50% gave the rationale that the patient was unwilling to discontinue the medication, the patient was a long-term user of the medication, or the patient's perception of inadequate sleep outweighed the risks of continued therapy. When asked what factors in their practice positively affect their ability to deprescribe nBZD sedative hypnotics, more than 50% of providers surveyed stated patient willingness to discontinue nBZD sedative hypnotic therapy and the availability of sleep specialists played a role. Other notable responses included the availability of printed handouts regarding sleep hygiene, the lack of availability of other safe medications, and developing adequate patient rapport. When asked what factors in their practice negatively affect their ability to treat older adults with difficulty sleeping, more than 50% of providers gave responses related to limited resources (e.g. time), unwilling patients, or the difficulty of providing non-pharmacological care. Thirty-three percent of providers considered sleep specialists moderately inaccessible at their clinic locations, 63% agreed the formats of the Drug Safety Alert letter and Sleep Fact Sheet were appropriate to communicate the nBZD sedative hypnotic safety issue, 54% agreed the information provided was useful in guiding future nBZD sedative hypnotic use in their older patients (Table 5). Seventy-one percent of responders were aware of the 2012 and 2015 Beers Criteria concerning nBZD sedative hypnotic use.

Discussion

Our study showed that the use of nBZD sedative hypnotics was widespread in older adults and not in accordance with guidance by the 2012 or 2015 Beers Criteria. The effect of nBZD sedative hypnotic deprescribing intervention relative to other programs is difficult to assess due to the heterogeneity of interventions and the uniqueness of this study, but the discontinuation rate of approximately 1 per 10 prescriptions may be considered low compared to similar interventions (e.g. related to simvastatin drug-drug interactions or citalopram maximum doses) using Drug Safety Alerts at our institution.[21] This may be in part due to the short follow-up time of three months, as approximately 15% of patients were lost to follow up hence reducing the opportunity for the providers to discuss deprescribing with these patients.

Prescribing alternative pharmacological agents for sleep after nBZD sedative hypnotic discontinuation occurred in 38% of the monotherapy population. A potential unintended consequence of this intervention was the initiation of BZD

TABLE 4. Total nBZD Sedative Hypnotic Use in the Pooled Monotherapy and Combination Populations Before Intervention Implementation and at 3-Month Follow-Up

nBZD Sedative Hypnotic	Before Intervention (n)	After Intervention (n)[1]	New BZD Prescription After Intervention
Eszopiclone	7	11	0
Eszopiclone (Lunesta)	21	13	2
Zaleplon	8	6	0
Zaleplon (Sonata)	5	4	1
Zolpidem	405	350	5
Zolpidem (Ambien CR)	10	9	0
Zolpidem (Ambien)	100	86	3
Total	**556**	**479**	**10**

nBZD: non-benzodiazepine sedative hypnotics
[1]Three months after communication of Drug Safely Alert and Sleep Facts Sheet

TABLE 5. Multiple Choice Survey Results (n=24)

	Inaccessible (1)	Moderately Inaccessible (2)	Accessible (3)	Moderately Accessible (4)	Very Accessible (5)	Did Not Answer Question
What is the level of access to sleep specialists at your clinic location?	2	8	6	4	2	2
	Strong Disagree	**Moderately Disagree**	**Agree**	**Moderately Agree**	**Strongly Agree**	**Did Not Answer Question**
The format (Provider letter and Sleep Fact Sheet) was appropriate to communicate this drug safety issue.	2	3	15	1	0	3
The information provided was useful in guiding future non-benzodiazepine hypnotic use in my older patients.	2	5	13	0	1	3

therapy in previously BZD-naïve patients, occurring in 9.6% of the population, though recommendations against switching patients to BZDs was included in the communication to providers.

As this intervention involved communication techniques centered on providers, it was important to gain provider perspective on deprescribing barriers and feedback on the intervention. Designing the intervention to be highly generalizable required the use of less resource-intensive strategies (e.g. development of patient specific recommendations, verbal contact with provider, implementation of electronic clinical decision support).The majority of providers reported the intervention to be appropriate for deprescribing of nBZD sedative hypnotics, despite the low discontinuation rates. This may be explained by the provider-identified barriers to deprescribing related to unwilling patients, patients already established on chronic nBZD sedative hypnotic use, and the inaccessibility of sleep specialists. The latter factor is concerning, as cognitive behavioral therapy for insomnia, the provision of which requires specialized training, is recommended as first-line treatment of chronic insomnia in older adults.[22]

Deprescribing of nBZD sedative hypnotics in older adults remains a challenge despite increasing evidence of risks related to falls, fractures, carry-over sedation, and driving impairment. Although there is considerable literature on the deprescribing of BZDs, there are few studies that focus on nBZD sedative hypnotics. Furthermore, the majority of studies published on deprescribing are highly specific to the institutions where they were conducted, limiting the generalizability of the results. Finally, inclusion of the very elderly (>74 years) in deprescribing programs is limited. This study focused on deprescribing of nBZD sedative hypnotics in a population wherein 40% were 75 years or older, using an approach that can be applied broadly across ambulatory care settings.

Deprescribing programs may experience greater success if they have a patient-centered component that educates patients on the potential risks and benefits of pharmacologic and non-pharmacologic treatments, as patient perceptions of nBZD sedative hypnotic use appeared to be a major determinant of deprescribing. Furthermore, close collaboration between providers of cognitive behavioral therapy for insomnia and primary care physicians is essential for a deprescribing program to ensure safe and effective transitions from pharmacologic therapy. Future investigation into the clinical pharmacist's role in educating patients with insomnia and facilitating collaboration between primary care providers and sleep specialists may ultimately improve methods or create new opportunities to support deprescribing programs.

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