3-7-2016

Pharmacotherapy for Chronic Insomnia: A Brief Survey of PCP Attitudes and Preferences

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Sorscher et al., J Sleep Disor: Treat Care 2016, 5:1
http://dx.doi.org/10.4172/2325-9639.1000169

Journal of Sleep Disorders: Treatment & Care

Research Article A SCITECHNOL JOURNAL

Pharmacotherapy for Chronic Insomnia: A Brief Survey of PCP Attitudes and Preferences

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Abstract

Purpose: To examine primary care professionals' (PCP) attitudes and prescribing preferences toward hypnotic medications to treat chronic insomnia.

Methods: An online survey was sent to members of the Dartmouth CO-OP, a practice-based primary care research network in Maine, Vermont, and New Hampshire. The survey begins with a case vignette of a 64-year old woman suffering from chronic insomnia. Clinicians were then presented with eight questions about management of the patient and their attitudes toward prescribing medications, focusing on benzodiazepines/benzodiazepine receptor agonists (BDZ/BZRAs).

Results: 103 of 198 clinicians (52%) responded. Regarding choice of medication for the case vignette, 80% of respondents preferred the off-label use of hypnotics such as trazodone or melatonin; 11% stated they would choose BDZs and 21% would choose BZRAs. Strong majorities expressed that negative consequences would occur with use of BDZ/BZRAs, including tolerance (77%), dependence (68%), other side effects (53%), and addiction (51%). PCP preference for off- label prescribing was correlated to levels of concern about harms (addiction, dependence, tolerance, side effects) of BDZ/BZRAs as measured on a global medication risk score in this survey. In addition, 14% of respondents felt that pharmacotherapy was not an appropriate therapeutic option for chronic insomnia in the case vignette.

Conclusion: Most of the clinicians surveyed acknowledged a legitimate role for hypnotic medications in chronic insomnia but expressed reservations toward BDZ/BZRAs despite their FDA-approval and proven efficacy. There appears to be a gap between published guidelines for selection of sedative-hypnotic medications and PCP preferences.

Keywords

Chronic insomnia; Benzodiazepines; Benzodiazepine receptor agonists; Primary care

Introduction

Chronic insomnia, defined as difficulty obtaining adequate sleep despite making an opportunity for it with resultant negative daytime consequences, is a prevalent condition affecting an estimated 10% of adults in the U.S [1,2]. Because it frequently occurs along with other common conditions such as depression, chronic pain, and polypharmacy, primary care professionals (PCPs) encounter insomnia in even greater frequencies: it is estimated that 50% of people who present to primary care clinics have sleep complaints [3].

Treatment options for insomnia fall in to one of two categories: cognitive-behavioral therapies and pharmacotherapy. Cognitive-behavioral therapy for insomnia (CBT-I) is highly effective but there is a well-documented shortage of trained providers of that therapy [4-6]. Because of this, PCPs must frequently decide whether or not to offer sleeping pills for the treatment of chronic insomnia [4].

Use of hypnotic medications has increased dramatically in recent years: data from the NHANES (reflecting prescribing patterns in ambulatory settings) reveals a 29 % increase in prescriptions for hypnotic medications from 1999-2010 [7]. In 2010, there were 60 million prescriptions for hypnotic medications with sales of over $2 billion in the U.S [8,9]. While there appears to be an increasing use of hypnotic medications by health care professionals, some authors on this topic raise concerns about the use of sleeping pills, especially benzodiazepines/benzodiazepine agonists citing lack of effectiveness and possible side effects such as falls and the potential for addiction, tolerance, and dependence [7,10-12].

There has been only one study of provider attitudes toward the use of sleeping pills conducted in the U.S., and this was limited in scope. This report consisted of interviews with 33 physicians in the Philadelphia area regarding prescriptions of benzodiazepines for insomnia in elderly patients [13]. These physicians were generally supportive of using benzodiazepines citing their effectiveness and downplaying concerns about addiction. Interestingly, the authors of the study interpreted these "accepting" attitudes toward benzodiazepines to be evidence that the physicians were practicing substandard care and not properly appreciating the hazards of using these medications.

In contrast to the lone report in the U.S., surveys of PCP attitudes and prescribing patterns for sleeping pills have been published in Europe as well as Canada, Australia, and Thailand. In general, these reports reveal significant ambivalence toward BDZ/BZRAs [14-23].

This study seeks to determine U.S. primary care professionals' (PCP) attitudes and prescribing preferences toward hypnotic medications to treat chronic insomnia. We focus upon benzodiazepines (estazolam, temazepam, triazolam, quazepam, flurazepam) and benzodiazepine receptor agonists (eszopiclone, zolpidem, and zaleplon) – families which comprise most of the hypnotic agents that are FDA-approved for the treatment of insomnia.

Methods

Study design

In this survey, we presented a clinical vignette of a middle aged woman with chronic insomnia without co-morbid illness that persists despite reasonable attempts to improve sleep hygiene: "Ms. D.C. is a 64-year-old woman who presents with a complaint of insomnia for the past 12 years, ever since menopause. She awakens "like clockwork" at 3 AM, her mind becomes active, and she can't

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Received: December 23, 2015 **Accepted:** March 02, 2016 **Published:** March 07, 2016

fall back to sleep for several hours. She pays meticulous attention to sleep hygiene (no caffeine, no TV in the bedroom, no napping in the daytime, etc.). Despite these measures, she only gets five hours of sleep and feels exhausted in the daytime. Her past medical history is negative".

Participants were then presented with a series of seven statements (responses on a 5-point Likert scale) about attitudes and behaviors toward prescribing medication for chronic insomnia (Table 1). In addition, an eighth statement was presented inquiring about the appropriateness of using pharmacotherapy to treat chronic insomnia.

Responses to four questions about attitudes toward BDZ/BZRAs (Q1-4) were summed to create a "global medication risk score" (range: 4-20), with higher scores representing greater concern about addiction, dependence, tolerance, and side effects with BDZ/BZRAs. Chi square and student's t-tests were used to analyze the categorical and global variables.

Participants/Procedure: An invitation to the survey link was sent out to members of the Dartmouth CO-OP Practice-based Research Network (PBRN). Membership consists of primary care providers in Maine, New Hampshire, and Vermont and includes family physicians, internists, and adult nurse practitioners and physician's assistants.

Survey data were collected and managed using REDCap electronic data capture tools hosted at Dartmouth-Hitchcock Medical Center. REDCap (Research Electronic Data Capture) is a secure, web-based application designed to support data capture for research studies [24].

After the initial invitation, the survey invitation was an iterative process for 10 weeks to non-responders. All survey responses were collected anonymously unless participants wished to have their name entered into a drawing for a $25 gift card.

The study protocol was approved by the Dartmouth Committee for Protection of Human Subjects.

Results

198 clinicians received invitations and 103 completed the survey, for a response rate of 52%. Demographics of the respondents are presented in Table 2.

14% of respondents expressed that sedative-hypnotics are not appropriate to manage chronic insomnia (agree/strongly agree). This left 58% who expressed that pharmacotherapy is a reasonable option and 26% who were neutral in their opinion on this matter (Q8).

Regarding choice of medication, 11% "agreed" that benzodiazepines were their first line therapy (Q5) and 21% endorsed benzodiazepine receptor agonists for initial therapy (Q6). In comparison, a stronger preference was found in favor of off-label use of sedating medications (such as trazodone and melatonin) with 80% of respondents expressing that they were likely to choose hypnotic medications from classes other than BDZ/BZRAs for the patient (Q7).

Strong majorities of respondents expressed that significant risks were either "likely" or "very likely" to occur with BDZ/BZRAs. This includes: tolerance (77%), dependence (68%), side effects (53%) and addiction (51%) (Q1-4). Concerns about tolerance, dependence, and side effects were raised equally regardless of respondents' age group, gender, and specialty. However, regarding addictive potential, we found a significant difference in attitude based upon training background: 85% of nurse practitioners and physician's assistants expressed significant concerns about addiction potential, far greater than respondents from family practice (43%) and internal medicine (38%) (chi-square, $p < .001$).

Preference for either BDZ or BZRAs was significantly correlated with lower "global BDZ/BZRA risk" scores reflecting less overall level of concern about tolerance, dependence, addiction, and side effects (aggregate of Q1-4). PCPs who were likely to prescribe BDZs had a mean global medication risk score of 12.10 compared to 14.76 for those who would not prescribe them ($p < .002$). Those likely to prescribe BZRAs had a mean score of 13.19 compared to 14.82 for those who would not prescribe them ($p < .011$). Conversely, respondents who stated they would select non BDZ/BZRAs options exhibited significantly higher mean global medication risk scores for these medications (14.80 for BDZs; 13.26 for BZRAs, $p < .022$).

Discussion

The survey revealed an acceptance that hypnotic medications are a legitimate option to treat chronic insomnia with only 14% outright rejecting their use in the case vignette. This is in agreement with newer thinking about chronic insomnia that recognizes the important

Table 1: Participant Responses to Survey Questions.

		Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
Q1	Benzodiazepines/benzodiazepine agonists are likely to be addictive.*	3/103 (2.9%)	21/103 (20.4%)	25/103 (24.3%)	38/103 (36.8%)	15/103 (14.6%)
Q2	Benzodiazepines/benzodiazepine agonists may work initially, but tolerance will develop.**	0/103 (0%)	6/103 (5.8%)	17/103 (16.5%)	59/103 (57.3%)	20/103 (19.4%)
Q3	Benzodiazepines/benzodiazepine agonists may work, but dependence will develop.***	1/103 (1%)	14/103 (13.6%)	16/103 (15.6%)	51/103 (49.5%)	19/103 (18.4%)
Q4	Side effects to benzodiazepines/benzodiazepine agonists are likely to occur.	0/103 (0%)	20/103 (19.4%)	27/103 (26.2%)	46/103 (44.7%)	8/103 (7.8%)
Q5	I am likely to use benzodiazepines (e.g. temazepam) for this patient.	31/103 (30.1%)	47/103 (45.6%)	11/103 (10.7%)	11/103 (10.7%)	0/103 (0%)
Q6	I am likely to use a benzodiazepine agonist (e.g. zolpidem) for this patient	20/103 (19.4%)	38/103 (36.9%)	22/103 (21.4%)	22/103 (21.4%)	0/103 (0%)
Q7	I am likely to prescribe a different type of sleeping medication (melatonin, trazodone, etc.) for this patient.	2/103 (1.9%)	9/103 (8.7%)	8/103 (7.7%)	55/103 (53.4%)	27/103 (26.2%)
Q8	Prescribing sleeping pills is inappropriate – the patient needs to address her insomnia.	14/103 (13.6%)	46/103 (44.7%)	27/103 (26.2%)	11/103 (10.7%)	3/103 (2.9%)

* addiction: persistent drug-seeking behavior despite negative consequences

** tolerance: decreased effectiveness after repeated usage

*** dependence: physiological withdrawal will occur if medication is discontinued

Table 2: Demographics of Survey Respondents (n=103).

Gender	Male Female	46 % 54 %
Age	Average (range)	53 (23-76)
Year Completed Training for Primary Care Practice	Average (range)	1992 (1970-2013)
Specialty	Family Physician Internist Physician Assistant Nurse Practitioner	54 % 23 % 8 % 14 %

contribution of inherent "hyperarousal" physiology to this condition. Whereas in the past, expert opinion held that insomnia was always the result of some underlying condition that, if addressed, would cure the sleep complaint it is now understood that in many cases, chronic insomnia can occur without an underlying cause and may need specific treatment with either cognitive-behavioral techniques or pharmacotherapy [25].

Regarding the specific choice of pharmacotherpeutic agent, respondents in this survey expressed substantial reservations toward BDZ/BZRAs. Similar levels of distrust of BDZ/BZRAs are found in the European reports on this topic [19]. The present survey also found twice as many practitioners willing to prescribe BZRAs compared to BDZs. This is similar to a preference for BZRAs (compared to BDZs) found in European reports such as from Germany and the United Kingdom [16,19]

We found that antipathy toward BDZ/BZRAs and the tendency to recommend off-label use of other sedating medications was associated with concerns about dependence, side effects, addiction, and, especially tolerance. Some of these attitudes are not borne out by the scientific literature. For example, studies of eszopiclone and zolpidem have both indicated that tolerance is unlikely, at least over 1 year of nightly usage [26,27]. Other reports indicate that rates of dependence are only 10-30% in chronic benzodiazepine users. And although BDZs are well known to have an addictive potential, reports such as that by Mahowald and Schenck indicate that the rates of addiction are very low in people with no prior history of substance abuse. As one consensus conference of experts in insomnia concluded: "Insomniacs tend to show therapy-seeking,rather than drug-seeking behavior, and patients without histories of drug abuse are unlikely to self-escalate dosage of currently available hypnotics [28-30].

PCPs from all specialties in this survey strongly preferred off-label use of medications such as trazodone and melatonin compared to BDZ/BZRAs. Of concern, neither of these choices has as strong an evidence base to support their use as BDZ/BZRAs. Furthermore, trazodone often engenders side effects due to its anticholinergic activity. As for melatonin, data to support its effectiveness, proper dose, and even purity is in question. This viewpoint is expressed in the Medical Letter summary of pharmacotherapy for insomnia [31]

There are some limitations to this exploratory survey, such as the sample size and limited geographic reach (northern New England providers). The findings in this survey need to be repeated in larger populations of PCPs with greater geographic variation in the U.S. in order to determine how commonly held these attitudes are. Also, the survey is based upon a single vignette, that of a middle-aged woman with chronic insomnia without other stated comorbidities. No doubt, responses would vary depending upon the presence of other co morbidities such as chronic pain, mental health disorders, or substance abuse that frequently co-occur with insomnia. Additionally, for brevity, the survey used "trazodone and melatonin" to stand broadly for all non BDZ/BDZA choices and thereby did not allow for analysis to compare these and other agents that are sedating but used less frequently such as ramelteon, doxepin, and atypical antipsychotics. In defense of this, we note that amongst prescription hypnotics, trazodone is far more widely prescribed than any of the non BDZ/BZRA choices just cited and melatonin, available without prescription, is used even more commonly than trazodone [7,32].

While cognitive-behavioral therapy remains the preferred initial treatment for chronic insomnia, [6] there has been growing acceptance from expert panels and consensus conferences for the use of pharmacotherapeutic agents to treat this disorder [30,33]. This survey reveals that PCPs are increasingly willing to use pharmacotherapy for chronic insomnia but frequently choose off-label use of sedating antidepressants such as trazodone and other non FDA approved medications such as melatonin. We found that these preferences are driven by concerns about addiction, dependence, tolerance, and side effects from BDZ/BZRA medications. These views stand in contrast to treatment guidelines from the American Academy of Sleep Medicine and the Medical Letter that propose BDZ and BZRAs, as first line treatments for chronic insomnia [31,34].

Support

Research reported in this publication was supported by The Dartmouth Clinical and Translational Science Institute, under award number UL1TR001086 from the National Center for Advancing Translational Sciences (NCATS) of the National Institutes of Health (NIH). The content is solely the responsibility of the author(s) and does not necessarily represent the official views of the NIH.

Acknowledgements

We thank members of the Dartmouth CO-OP Primary Care Research Network for their participation in the survey.

Conflict of Interest Statement

Adam J Sorscher has served as a consultant to Pernix Pharmaceuticals that markets Silenor, a medication for insomnia. The other authors of this paper report no conflicts of interest.

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