



Contents lists available at ScienceDirect

Saudi Pharmaceutical Journal

journal homepage: www.sciencedirect.com

Original article

Pharmacists' interventions to reduce sedative/hypnotic use for insomnia in hospitalized patients

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ARTICLE INFO

Article history:

Received 2 January 2018

Accepted 19 July 2018

Available online 20 July 2018

Keywords:

Sleep disorders
Medication errors
Medication safety
Geriatrics
Internal medicine
Clinical pharmacy

ABSTRACT

Background: Hospitalization can contribute to insomnia in many patients and is usually treated symptomatically. However, sedative/hypnotic misuse is associated with complications in this population, especially in the elderly. Such complications include dizziness, falls and over-sedation. Due to the implicit dangers, widespread use of these drugs for insomnia, particularly in older patients, has been discouraged by many hospitals. The aim of this study was to review and evaluate prescribing patterns and to optimize the use of the sedative/hypnotic agents through daily pharmacy interventions at a community hospital. **Methods:** This was a biphasic before and after study. Data on sedative/hypnotic use was collected retrospectively for a 2-month period and a sample of 100 patients was randomly selected for analysis. A 2-month prospective phase followed, in which daily orders were reviewed by one pharmacy resident and recommendations made to discontinue any unnecessary, newly prescribed sedative/hypnotic orders when appropriate. Finally, results of both phases were compared for any differences in patient demographics, being prescribed more than one sedative/hypnotic, and complications documented. **Results:** During the prospective phase, pharmacist interventions led to the discontinuation of 25% of a total of 97 sedative/hypnotic orders in 97 patients. The number of patients receiving more than one sedative/hypnotic agents in the intervention group was significantly lower than the retrospective control group (15 Vs. 34, $P = 0.0026$). The incidence of complications was not significantly different between the control and intervention groups for the following: over-sedation, falls and delirium ($p = 0.835$, $p = 0.185$, $p = 0.697$, respectively).

Conclusion: This study suggests that the use of sedative/hypnotics in the inpatient units (excluding the critical care unit), is somewhat prevalent, and many patients may be on more than one sedative/hypnotic, which could potentially cause cumulative harm. During the intervention phase, 25% of the total in-hospital orders for sedative/hypnotics were discontinued following recommendations made by a pharmacist, and significantly lower number of patients receiving duplicate sedative/hypnotics was noted. Further efforts should be implemented to avoid unnecessary sedative/hypnotic initiation in hospitalized patients, and to ensure monitoring by pharmacists is optimized.

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1. Background

Insomnia is defined by the presence of an individual's report of difficulty with sleep (Roth, 2007). It is usually associated with poor

physical and mental quality of life (Bolge, 2009; Nagel, 2003). Many factors can precipitate insomnia in individuals who are predisposed to this disorder such as pain, chronic diseases, and psychiatric disorders (Ford and Kamerow, 1898; Katz and McHorney, 2002; Sasai, 2010). Hospitalization is another major cause of sleeping pattern disturbance, which can contribute to insomnia in many patients (Sasai, 2010; Frighetto et al., 2004). The most common causes of insomnia in hospitalized patients include the effects of illness, environmental noise, care-giver interruptions, pain, and depression (Frighetto et al., 2004).

Insomnia is usually treated symptomatically during hospitalization (Frighetto et al., 2004; Ochoa Mangado, 2010). However,

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Peer review under responsibility of King Saud University.



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sedative/hypnotic use, misuse or over-use is thought to be associated with complications in this acutely-ill population, (Ochoa Mangado, 2010; Foy, 1995; Lenhart and Buysse, 2001) especially in the elderly where it has been shown to increase morbidity and mortality (Shumate, et al., 2013; Richards and Rowlands, 2013; Kolla, 2013). The complications include cognitive impairment, dizziness, falls and over-sedation. (Lenhart and Buysse, 2001; Shumate, et al., 2013; Richards and Rowlands, 2013; Kolla, 2013; The American Geriatrics Society 2012 Beers Criteria Update Expert Panel, 2012; American Geriatrics Society 2015 Beers Criteria Update Update Expert Panel, 2015; Agostini et al., 2007).

There are currently no standard guidelines for managing acute in-hospital insomnia, which could lead to overt misuse or over-use of the sedative/hypnotic agents in this setting. Due to the implicit dangers, many hospitals have discouraged the widespread use of sedative/hypnotic agents for insomnia by eliminating certain classes from their formulary, instituting a prior approval process, providing computer-based alerts (Agostini et al., 2007), and/or excluding them from most order sets (Agostini et al., 2007; Eide and Schjøtt, 2001).

There is evidence that when pharmacists monitor therapy, there is improved prescribing and administration of sedative/hypnotics in multiple settings. In nursing homes, a survey-based study examined pharmacist interventions that provided written and verbal drug information on the use of hypnotics (Eide and Schjøtt, 2001). Pharmacists' interventions reduced the use of benzodiazepines, especially long-acting agents such as diazepam and nitrazepam, increased the use of short-acting hypnotics as they were thought to be safe at the time, and reduced the administration of hypnotics before 9 pm as the administration of hypnotics very early in the evening increases the likelihood of long-acting compounds being preferentially prescribed (Eide and Schjøtt, 2001). Other studies emphasized the role of pharmacists in managing sedation in intensive care units (ICUs), where pharmacists' interventions improved adherence to sedation guidelines and resulted in a significant decrease in the duration of mechanical ventilation leading to shorter duration of hospital stay and lower drug costs (Marshall et al., 2008; Devlin et al., 1997).

However, there are no data on the impact of pharmacists' interventions on improving sedative/hypnotic use in the non-critically ill patients with acute hospitalization-induced insomnia. Therefore, the aim of this study was to review and evaluate prescribing patterns of the sedative/hypnotic agents, and to reduce the potential misuse or overuse of these agents through daily pharmacy interventions on medical wards.

2. Methodology

2.1. Design

This was a biphasic before and after single centered study conducted in a community hospital in Boston, Massachusetts. A retrospective phase included a chart review and analysis to serve as a control group. The prospectively phase included pharmacist interventions (intervention group) and comparison to the control group. The study was approved by the hospital institutional review board (IRB).

2.2. Study inclusion

Adults aged 18 years and older who were admitted and prescribed one or more agents in the following medication classes for the treatment of in-hospital insomnia were included: antihistamines, antidepressants, sedative-hypnotic benzodiazepines and benzodiazepine receptor agonists. Patients who were prescribed

any of medications in the above classes for reasons other than insomnia or admitted to critical care units were excluded from the study. Those who received sedative/hypnotics as continuation of their home medications were excluded also.

2.3. Procedures

During the retrospective phase, data on sedative/hypnotic use (according to the hospital's formulary) was collected using the inpatient electronic medical records (EMRs) from 1st September to 31st October 2014 (2-month period) to identify prescribing trends for the agents to establish the control group. A randomly generated sample of 100 patient EMRs were reviewed for inclusion, then subsequent sets of randomly generated EMRs reviewed until a sample size of 100 was met. The following data were extracted during this phase to review prescribing patterns of sedative/hypnotics: (1) patient's demographics; (2) sedative/hypnotic agent(s) ordered; (2) orders that are scheduled at bedtime; (3) orders written for as needed for sleep.

The prospective pharmacist-intervention phase ensued from 1st February to 31st March 2015, during which a hospital-wide daily orders report on sedative/hypnotic agents was generated and monitored. The report captured the list of the medications that were identified in the retrospective phase of the study when ordered as needed for sleep (prn insomnia). The pharmacist interventions were made and documented by a pharmacy practice resident training at the hospital. The intervention was performed during the days the pharmacy resident was physically at the hospital, and thus excluded weekends. The pharmacist interventions included recommending discontinuation of the newly prescribed sedative/hypnotics verbally during inpatient team rounds or by contacting the prescribing physicians via the hospital paging system that resulted in further discussions over the phone. A brief reasoning behind the recommendation was provided, emphasizing potential risks of these agents, before recommending discontinuation of the order. All interventions were documented and monitored for change 24 h post-recommendation. The following data were collected during this phase: (1) patients' demographic information; (2) presence of more than one sedative/hypnotic agent for sleep; and (3) any documented complications. Finally, the randomly-selected sample of the retrospective control group was compared to the prospective intervention group to detect any differences.

2.4. Outcome measures

The primary outcome was the association between pharmacist interventions and sedative/hypnotics prescribing pattern including: (1) number of discontinued sedative/hypnotic agents within 24 h after the pharmacist intervention, and (2) presence of more than one sedative/hypnotic agents as needed for insomnia before and after the pharmacist intervention. The secondary outcome was complication incidence, including any documented episodes of delirium, lethargy, confusion, falls, and/or over-sedation, before and after the pharmacist intervention.

2.5. Data analysis

Descriptive statistics were used to describe key patient characteristics of the control and intervention groups and compared using chi square analysis. A two-tailed chi square test was used to compare the primary and secondary outcomes between the two groups. A priori alpha of 0.05 was used for statistical significance. All analyses were conducted using SPSS (IBM Corp. Armonk, NY).

3. Results

A total of 100 randomly-selected subjects made up the retrospective control group. As seen in Fig. 1, 158 patient EMRs were reviewed to include 100 subjects (63%) with 58 patients (37%) excluded for receiving sedative/hypnotics as continuation of their home medications.

A total of 97 patients (22%) met the inclusion criteria through the daily orders review of sedative/hypnotics during the 2-month prospective phase with 343 (78%) patients excluded for the following reasons: (1) received the medication for reasons other than insomnia (anxiety, itchiness, allergy and panic attacks; $n = 230$), or received medication as continuation of their home medications ($n = 113$) Fig. 1.

Baseline patient characteristics of the control group and intervention group are shown in Table 1, which were similar between the two groups. Thirty-four patients (34%) were 65 years and older in the control group compared to 24 (25%) in the intervention group ($P = 0.154$). The control group consisted of 54% male, while 55% of the intervention group were male ($P = 0.928$).

The study findings are shown in Table 2. For the primary outcomes, 25% of a total of 97 orders were discontinued within 24 h after pharmacist intervention during the prospective phase. The number of patients receiving more than one sedative/hypnotic agents was significantly lower in the intervention group compared to the control group (15 Vs. 34, $P = 0.003$). For the secondary outcomes, reported complications of over-sedation, falls, and delirium did not differ significantly between the two groups ($p = 0.835$, $p = 0.369$, $p = 0.745$, respectively).

4. Discussion

Although the use of sedative agents are protocolled in some hospital settings, such as the ICU, this is not generally the case when they are used to treat insomnia in the general medical wards. Active monitoring by a pharmacist can have a major impact on the safe use of sedative/hypnotics in this setting, thus circumventing potential deleterious effects. The current study compared the prescribing patterns of sedative/hypnotics before and after pharmacist interventions. The routine in-hospital prescribing pattern was interrupted by pharmacist interventions and reduced new orders for sedative/hypnotics by 25% in the 2-month period. Our analysis

Table 1
Baseline patient characteristics.

| | Retrospective control group (n = 100), N (%) | Prospective intervention group (n = 97), N (%) | p-value |
|-------------------------------|--|--|---------|
| Patient's demographics | | | |
| <i>Age</i> | | | |
| < Below 65 | 66 (66) | 73 (75) | 0.154 |
| < 65 and above | 34 (34) | 24 (25) | |
| <i>Sex</i> | | | |
| < Male | 54 (54) | 53 (55) | 0.928 |
| < Female | 46 (46) | 44 (45) | |

Table 2
Primary and secondary outcomes.

| | Retrospective control group (n = 100), N (%) | Prospective intervention group (n = 97), N (%) | p-value |
|----------------------------------|--|--|---------|
| <i>Primary outcome</i> | | | |
| On more than 1 sedative/hypnotic | 34 (34) | 15 (16) | 0.003 |
| <i>Secondary outcome</i> | | | |
| Over-sedation | 8 (8) | 7 (7) | 0.835 |
| Fall | 4 (4) | 1 (1) | 0.369 |
| Delirium, lethargy or confusion | 4 (4) | 5 (5) | 0.745 |
| None | 84 (84) | 84 (87) | 0.607 |

also showed that the pharmacist interventions led to a significant reduction in multiple sedative/hypnotics use for patients with hospital-induced insomnia ($p = 0.0026$).

Several recommendations emerged from the retrospective review of the sedative/hypnotic prescribing phase in the current study. As needed (PRN) use of sedative/hypnotics is encouraged over scheduled at bedtime (QHS) use. The latter could prompt over-sedation and increase potential risks from these medications. Thus, given the patient's vulnerability with hospitalization and potential for drug interactions, more serious side effects such as falls should be avoided.

A prospective cohort study conducted in hospitalized geriatric patients found that the risk of cognitive decline increased by 70%

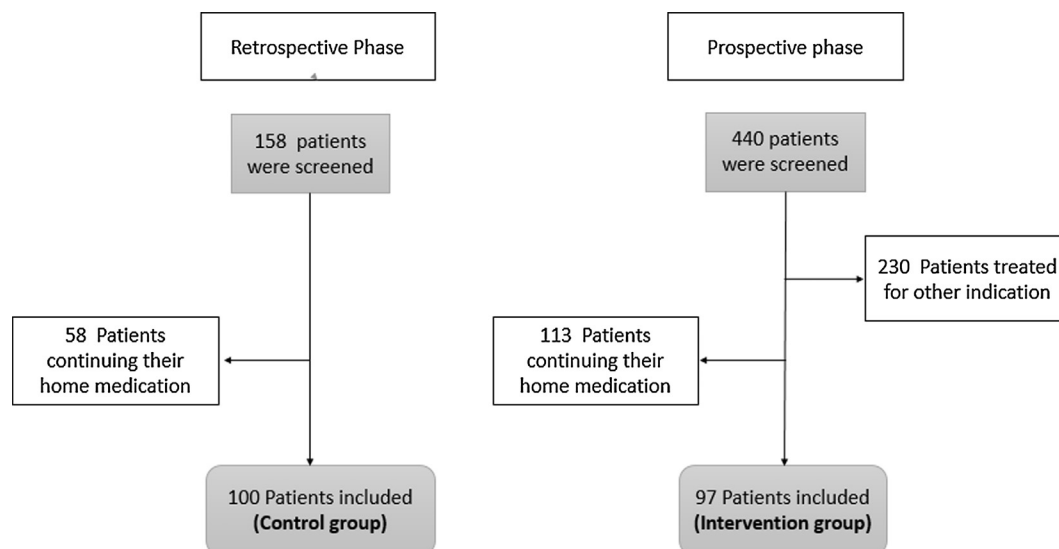


Fig. 1. Prospective and retrospective data sampling for control and intervention groups.

in elders who received diphenhydramine compared to 24% in elders who did not receive diphenhydramine (Agostini et al., 2001). Elders on diphenhydramine more often suffered from complications related to anticholinergic side effects (e.g., behavioral disturbances and urinary catheter placement) which can worsen patients' condition at the hospital and increase their length of stay. Diphenhydramine is listed in the AGS 2015 Beers Criteria for Potentially Inappropriate Medication Use in Older Adults due to increased risk of confusion, dry mouth, constipation and other anticholinergic side effects. (The American Geriatrics Society 2012 Beers Criteria Update Expert Panel, 2012; American Geriatrics Society 2015 Beers Criteria Update Update Expert Panel, 2015) Because of its anticholinergic effects, diphenhydramine should not be used as a hypnotic in hospitalized patients, particularly in the elderly population. (Agostini et al., 2001) A multicenter randomized placebo-controlled trial by Hatta et al. found that ramelteon was associated with lower risk of delirium ($P = 0.003$) when administered nightly to elderly patients admitted to the hospital (Hatta, 2014). Thus, the utilization of ramelteon in the elderly patients at risk for delirium should be encouraged.

To our knowledge, this is the first study to evaluate pharmacist interventions on sedative/hypnotic use in a general medical unit. All of the interventions were made by a single pharmacist to reduce potential variation and ensure consistency. However, if the elements of the intervention were standardized and implemented as a pharmacy-run program hospital-wide, the impact would be exponentially greater.

This study has several additional limitations. The limitation inherent in the before and after study design is present including random selection of patient charts, and the lack of randomized comparison groups and blinding. The study neither sub-analyzed among medication groups to assess whether the complications were caused by a particular agent over another nor stratified patients to determine if those on more than one sedative/hypnotic were more prone to experiencing complications. The study also did not look into age susceptibility to these complications, i.e., if patients over 65 years experienced more complications. Randomized controlled studies with larger sample size are needed to address these limitations.

This study highlights the important role, inpatient pharmacists can play in discontinuation of unnecessary sedative/hypnotic agents and decreasing multiple sedative/hypnotic exposure in hospitalized patients. Pharmacist interventions on sedative/hypnotic use among patients in the hospital wards should be promoted.

5. Conclusion

The study findings suggest that the use of sedative/hypnotics in the inpatient units (excluding the critical care unit), is somewhat prevalent and that many patients may be on more than one sedative-hypnotic agents. Twenty-five percent of the total in-hospital orders for sedative/hypnotic agents were discontinued following pharmacist interventions with significant reductions in multiple orders, though complication rates did not differ. Further efforts should be implemented to optimize the use of sedative/hypnotics in hospitalized patients especially when they are being introduced for the first time, including active monitoring of these medications by pharmacists.

6. Funding

The authors whose names listed certify that they have NO affiliations with or involvement in any organization or entity with any financial nor any conflict of interest in the subject matter or materials discussed in this manuscript.

7. Poster presentation

- (1) Presented in the annual 2015 ASHP midyear meeting as an abstract (no results were presented).
- (2) Presented as an abstract with results and conclusion at the hospital where it was conducted (Saint Elizabeth's Medical Center, Boston, MA, USA).

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