〈Regular Article〉

Awareness-raising Activities for the Appropriate Use of Prescribed Medication for Insomnia to Reduce the Risk of Delirium

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ABSTRACT **Background**: The number of dementia patients is rapidly increasing in Japan, having reached approximately 4.43 million in 2022, with predictions suggesting it will rise to approximately 5.84 million by 2040. The onset of delirium in dementia patients adversely affects in-hospital prognosis and increases the consumption of medical resources. A dementia delirium care team (OP-CAST) has been established at our facility to provide appropriate care for dementia patients. Given the importance of selecting medication for insomnia, our team conducts awareness-raising activities for the medical staff. As part of this initiative, we published the "OP-CAST Newsletter" to provide information on the prevention of insomnia and delirium, with a particular focus on the selection of recommended medications for insomnia. Herein, we investigated changes in the prescribed medications for insomnia before and after the publication of this OP-CAST Newsletter.

Methods: The survey was conducted in two phases: three months immediately before the publication of the first issue of the OP-CAST Newsletter in January 2020 (October to December 2019, Phase 1) and three months during which the survey was conducted (January to March 2023, Phase 2).

We reviewed the medical records and retrospectively investigated the medications prescribed for insomnia in patients who were hospitalized during these periods.

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Results: The results indicated that the usage ratio of recommended medication (orexin receptor antagonists) increased from 49% to 91%, while the usage ratio of benzodiazepines (BZDs; zopiclone, zolpidem, etc.) decreased from 44% to 3%. These changes were statistically significant, confirming a marked increase in the usage of recommended medication.

Discussion: Awareness-raising activities regarding recommended medications for the treatment of insomnia, as disseminated through the OP-CAST Newsletter, have significantly increased medical staff members' awareness of medication selection and promoted the use of appropriate medication. In particular, orexin receptor antagonists have been shown to reduce the risk of delirium and falls more effectively than benzodiazepines (BZDs) and are therefore expected to improve patient prognosis. The OP-CAST Newsletter is visually accessible, and the results suggest that it serves as an effective awareness-raising tool that successfully engages staff interest.

Conclusions: Awareness-raising activities utilizing the OP-CAST Newsletter promoted the appropriate use of prescribed medication for insomnia and successfully reduced the utilization of BZDs. This is expected to decrease the risk of delirium and falls, thereby confirming the efficacy of the newsletter as an awareness-raising tool in medical settings.

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Key words：Dementia, Delirium, Insomnia, Orexin receptor antagonists, Benzodiazepines, Awareness-raising activities, Medication selection

INTRODUCTION

With the rapid aging of society in Japan, individuals aged 65 years and older are projected to account for over 30% of the population by 2025. According to a research group from the Ministry of Health, Labour and Welfare, there were approximately 4.43 million dementia patients aged 65 years and older in 2022, indicating a prevalence of 12.3%. This number is expected to rise to approximately 5.84 million (prevalence of 14.9%) by 2040 and to approximately 6.45 million (prevalence of 17.7%) by 2060[1]. These developments suggest that in the future, hospitalizations of dementia patients and individuals with decreased cognitive function will increase, leading to a higher number of delirium cases. The onset of delirium can have multifaceted effects, including prolonged hospitalization, which contributes to an increased financial burden on the healthcare system[2, 3]. To address the challenges posed by the rising number of dementia patients being hospitalized, the dementia care fee addition was established in 2016. In the same year, the Kawasaki Medical School General Medical Center (hereinafter referred to as "our center") formed a dementia delirium care team, which has actively addressed Behavioral and Psychological Symptoms of Dementia (BPSD) and delirium.

DEMENTIA DELIRIUM CARE TEAM

The medical fee revision in 2016 led to the introduction of the dementia care fee, which subsequently resulted in the formation of our team. This multidisciplinary team comprises psychiatrists, internal medicine physicians, certified dementia nurses, pharmacists, licensed psychologists, and social workers. The team conducts weekly conferences and ward rounds for patients requiring intervention and provides guidance on the treatment and medication management of individuals with

dementia and delirium.

When the team was first established, it was named the "Dementia Delirium Care Team". However, we considered adopting a nickname, as some team members felt that removing the terms "dementia" and "delirium" could help eliminate language barriers. In alignment with the "Orange Plan" dementia policy, we chose to incorporate "orange" as a key term. Additionally, we included "pink" because the English term "delirium" reminded us of the beer brand "Delirium Tremens", which features a pink elephant on its label. Consequently, we settled on the name "Orange Pink Care Support Team", abbreviated as "OP-CAST", and used it in general to enhance awareness of the team within our hospital.

AWARENESS-RAISING ACTIVITIES

Although benzodiazepines (BZDs) are widely used to treat insomnia, they are associated with an increased risk of delirium, decreased cognitive function, and falls in elderly patients[4-6]. When treating insomnia in inpatients, the selection of medication plays an important role in mitigating these risks and in the overall treatment process. One alternative medication is orexin receptor antagonists. Orexin receptor antagonists target the orexin system, which regulates wakefulness, thereby enhancing sleep quality. This mechanism of action differs from that of conventional BZD sleep medications. While BZDs are highly addictive and heighten the risk of delirium and falls in elderly patients, research has shown that orexin receptor antagonists do not carry these associated risks[7, 8].

In recognition of the importance of medication selection, OP-CAST has been actively conducting awareness-raising activities related to medication selection for insomnia and delirium in inpatients. One such initiative involved providing information to medical staff through the issuance of the "OP-CAST Newsletter" starting in January 2020. The OP-CAST Newsletter was issued a total of five times: in January 2020, April 2020, May 2020, July 2020, and April 2021. These newsletters were distributed to doctors, wards, and medical departments to provide guidance on appropriate prescribing practices. Additionally, staff could easily access it via a link on the homepage of the electronic medical records system. The newsletter provided information regarding recommended medication selection during the onset of delirium, identified high-risk drugs for delirium, and suggested medications recommended for insomnia, among other topics, to raise awareness of appropriate medication use aimed at reducing the risk of delirium.

This study investigated changes in prescribed medications for insomnia before and after awareness-raising activities concerning recommended prescribed medications for insomnia using the OP-CAST Newsletter.

MATERIAL AND METHODS

The survey was conducted in two phases: three months immediately before the publication of the first issue of the OP-CAST Newsletter in January 2020 (October to December 2019, Phase 1) and three months during which the survey was conducted (January to March 2023, Phase 2).

We reviewed the medical records and retrospectively investigated the medications prescribed for insomnia for newly hospitalized patients during the investigation periods. We also evaluated the effectiveness of the awareness-raising activities by comparing the insomnia medications prescribed during each period. For statistical analysis, we used the chi-squared test to examine differences in the frequency of prescriptions for insomnia-related medications during each survey period. Statistical significance was determined using SPSS software (version 23), with a threshold set at $p < 0.05$ for all analyses. This study was approved by

the Kawasaki Medical School Institutional Review Board (approval no. 5555-02). It was conducted using only research funds from the university. No grants were received, and there are no conflicts of interest.

RESULTS

We surveyed 1,444 new inpatients in Phase 1 (October to December 2019) and 2,202 new inpatients in Phase 2 (January to March 2023). Table 1 presents the details of prescribed medications for insomnia during each period. Since lemborexant was not used during the first survey periods, we compared the frequency of different medications prescribed for insomnia across three categories: recommended medications (suvorexant, lemborexant, trazodone, and eszopiclone), BZDs (zopiclone, zolpidem, brotizolam, etizolam, and diazepam), and other medications (ramelteon and hydroxyzine).

The results showed an increase in the number of prescriptions for recommended medications. Specifically, the number of prescriptions for suvorexant decreased from 661 (Phase 1) to 440 (Phase 2), whereas lemborexant was prescribed 2,292 times in Phase 2. Trazodone prescriptions increased from 237 (Phase 1) to 1,597 (Phase 2), and eszopiclone prescriptions increased from 144 (Phase 1) to 1,293 (Phase 2). In contrast, the use of BZD medications considerably decreased. Zopiclone prescriptions decreased from 148 (Phase 1) to 28 (Phase 2), zolpidem prescriptions decreased from 583 (Phase 1) to 25 (Phase 2), brotizolam prescriptions decreased from 141 (Phase 1) to 93 (Phase 2), etizolam prescriptions decreased from 16 (Phase 1) to 8 (Phase 2), and diazepam prescriptions decreased from 38 (Phase 1) to 3 (Phase 2). For other medications, ramelteon prescriptions decreased from 39 (Phase 1) to 1 (Phase 2), whereas the number of hydroxyzine prescriptions increased from 258 (Phase 1) to 378 (Phase 2). In terms of percentages, the proportion of recommended medications among all insomnia prescriptions increased from 11,042/2,265 (46%) to 5,622/6,158 (91%), whereas the proportion of BZD medications decreased from 926/2,265 (41%) to 157/6,158 (3%). A chi-squared test applied to the cross-tabulation of insomnia prescriptions in Phases 1 and 2 revealed significant differences ($\chi^2(2) = 2,422$, $p < 0.01$, $v = 0.536$). A residual analysis showed that the adjusted residual value for recommended medications before publication was significantly smaller than the expected value (1792), and the adjusted residual value after publication was significantly larger than the expected value (4,872) (both $p < 0.01$). For BZD medications, the adjusted residual value before publication was significantly larger than the expected value (291.2), and the adjusted residual value after publication was significantly smaller than the expected value (791.8) (both $p < 0.01$). For the other medications (ramelteon and hydroxyzine), the adjusted residual value before publication was significantly larger than the expected value (181.8), and the adjusted residual value after publication was significantly smaller than the expected value (494.3) (both $p < 0.01$). This indicates that the number of prescriptions for recommended medications increased after publication, whereas the number of prescriptions for

Table 1. Changes in Prescribed Medications for Insomnia

Medication for Insomnia	Phase 1	Phase 2
Suvorexant	661 (cases)	440 (cases)
Lemborexant	Not adopted	2,292
Trazodone	237	1,597
Eszopiclone	144	1,293
Zopiclone	148	28
Zolpidem	583	25
Brotizolam	141	93
Etizolam	16	8
Diazepam	38	3
Ramelteon	39	1
Hydroxyzine	258	378

※Phase 1: October to December 2019,
Phase 2: January to March 2023

BZD medications and other medications decreased after publication (Table 2).

DISCUSSION

OP-CAST plays an important role in improving care for dementia patients and addressing the needs of those experiencing delirium and insomnia. As part of this initiative, the team implements awareness-raising activities regarding the recommended medications for treating insomnia to prevent delirium. In Japan, suvorexant was the first orexin receptor antagonist approved as a treatment for insomnia in 2014, followed by the approvals of lemborexant and daridorexant. Numerous reports have indicated that orexin receptor antagonists may contribute to the prevention of delirium[9–11]. We conducted awareness-raising activities by publishing in the OP-CAST Newsletter that orexin receptor antagonists with these features should be the first-choice prescription for insomnia. In this study, the use of recommended medications significantly increased from Phase 1 to Phase 2, whereas the number of BZD prescriptions for insomnia significantly decreased. Additionally, the number of prescribed medications for insomnia significantly increased from 2,265 before the intervention to 6,158 after the intervention. This increase is primarily attributed to the standardization of how these prescriptions were recorded following the intervention. Specifically, before the intervention, the method of recording prescribed medications for insomnia varied among attending physicians, with some issuing only one instruction while others issued multiple instructions. In contrast, the OP-CAST Newsletter presented three recommended instructions for prescribing medications for insomnia, which physicians began to reference when issuing prescriptions. As a result, the number of prescribed instructions increased.

Table 2. Changes in Prescribed Medications for Insomnia

Medication Category	Phase 1	Phase 2	p-value
Recommended Medications	1,042	5622	< 0.05
BZD Medications	926	157	< 0.05
Other Medications	297	379	< 0.05

※Recommended Medications: Suvorexant, Trazodone, Eszopiclone (Phase 1); Suvorexant, Lemborexant, Trazodone, Eszopiclone (Phase 2).
※BZD Medications: Zopiclone, Zolpidem, Brotizolam, Etizolam, Diazepam.
※Other Medications: Ramelteon, Hydroxyzine.

In Phase 1, there were 2,265 prescribed instructions for insomnia among 1,444 hospitalized patients, averaging approximately 1.6 instructions per patient. In contrast, in Phase 2, there were 6,158 prescribed instructions for insomnia among 2,202 hospitalized patients, averaging approximately 3.0 instructions per patient. This suggests that the introduction of standardized prescribing instructions influenced the standardization of prescription practices.

This increase is largely attributed to the awareness-raising activities of the OP-CAST Newsletter, although several other factors may have also influenced these changes.

First, direct recommendations from the OP-CAST to physicians may have had an impact. The team provided guidance on the selection of insomnia prescriptions to attending physicians through ward rounds and conferences. This may have prompted attending physicians to prescribe the recommended medications suitable for individual cases. Additionally, educational activities for residents were also an important factor. Residents are known to be strongly influenced by their supervising physicians regarding their prescription choices, and those who received education from the OP-CAST may have actively used the recommended medications.

Furthermore, trends across the entire medical field may have had an impact. In recent years, awareness of the risks associated with BZD medications has increased, particularly regarding prescriptions for the elderly. Against this backdrop, there has been

an increasing tendency for physicians to choose safer alternatives. This possibly contributed to the increased use of recommended medications. In summary, in addition to the effects of the OP-CAST Newsletter, the interactions among several factors, such as advice to attending physicians, education for residents, and changes in prescription trends in the medical field, possibly increased the use of recommended medications. Moving forward, analyzing the influence of these factors in more detail is necessary to promote the appropriate use of medications.

Our hospital is a medical university hospital with 647 beds, comprising 21 treatment departments and 198 physicians on staff (as of April 1, 2024). Raising awareness regarding recommended medications for insomnia can be challenging in a large university hospital characterized by a high turnover rate of doctors and numerous departments. However, successful strategies have been documented in hospitals of a similar scale. Takasago *et al.* reported that the introduction of a flowchart for recommended prescription medications for insomnia (suvorexant and eszopiclone) led to an increase in the prescription rate of these medications over one year, rising from 25.3% to 52.8%[12]. Egusa *et al.* also reported that having pharmacists implement in-hospital sleep workshops, which involved changing prescribed medications for insomnia to suvorexant, resulted in a decrease in BZDs being the first choice for patients, from 81.0% to 19.1% and an increase in the use of suvorexant, from 11.4% to 53.9% over a period of two years[13]. Reviews of recommendations for drugs prescribed for insomnia, aimed at preventing adverse events such as delirium and falls, are being conducted at various facilities; however, the approaches differ. By distributing the OP-CAST Newsletter, we successfully reduced the frequency of BZDs prescribed for insomnia and significantly increased the prescription rate of recommended insomnia medications. The OP-CAST Newsletter features a vibrant design, which we believe contributed to its effectiveness in raising awareness. Given that studies have indicated that visual abstracts are more effective than conventional text-based approaches in promoting awareness of suicide prevention research results[14], we believe that the visual elements of the OP-CAST Newsletter played a significant role in its impact. Our awareness-raising method using a newsletter proved effective, requiring minimal expenditure on our part as we distributed it through a paper medium and facilitated access via electronic medical records. Therefore, this effective and efficient approach should continue to be utilized in the future.

Many cases of delirium develop during hospitalization for physical diseases and are associated with a poor prognosis. Delirium can lead to falls, secondary complications, increased mortality rates, and long-term cognitive decline[14]. Sasaki *et al*. reported that recommending suvorexant over BZDs as the first-line treatment for insomnia resulted in a decrease in falls from 329 to 266 over a six-month period following the implementation of this initiative[15]. Given that the increase in prescriptions of recommended insomnia medications at our hospital may have also contributed to a reduction in falls, we plan to investigate the effects on fall rates moving forward.

LIMITATIONS AND CHALLENGES OF THE PRESENT STUDY

This study was retrospective, and as such, there are limitations in assuming causal relationships. While changes in the number of insomnia prescriptions during the survey period were largely attributed to the publication of the OP-CAST Newsletter, determining the extent of its independent effect was difficult as the timing of the publication coincided with the increasing awareness of the risks of BZD medications and benefits of orexin receptor antagonists in the entire medical

field. Additionally, OP-CAST activities included not only publication of the newsletter but also direct guidance to attending physicians on recommended prescriptions for insomnia and educational instructions given to residents on recommended prescriptions. This may have also influenced the increase in the number of recommended insomnia prescriptions. Moving forward, we will focus on conducting a questionnaire survey to investigate whether prescribing physicians had read the OP-CAST Newsletter and whether it influenced the prescriptions, in addition to determining whether these results correlate with prescription trends.

In this study, we evaluated the impact of recommended insomnia medications on prescription choices, but we did not assess their effectiveness, particularly changes in the incidence of delirium and in-hospital fall events. Therefore, whether the increased use of recommended medications led to improved patient outcomes remains uncertain. Therefore, the clinical effectiveness, including changes in the risk of delirium and falls, still needs to be verified.

CONCLUSIONS

Awareness-raising activities using the OP-CAST Newsletter promoted the appropriate prescription of recommended medications for insomnia and significantly reduced the frequency with which BZDs were prescribed for insomnia. These results suggest that increased usage of recommended prescribed medications for insomnia could reduce the risk of delirium and falls. Awareness-raising activities, such as the OP-CAST Newsletter, appear to be a straightforward and effective approach that could be implemented in medical settings.

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