LETTER TO THE EDITOR

Characteristics of Patients Who Were Able to Discontinue Lemborexant due to Improved Insomnia

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ABSTRACT

Objective: **There is little evidence of insomnia treatment, especially exit strategies for hypnotics. We examined on the characteristics of patients who were able to discontinue lemborexant due to improved insomnia.**

Methods: **Insomnia was assessed using the Athens Insomnia Scale (AIS). Efficacy outcome assessment was the Clinical Global Impressions-Improvement scale (CGI-I).**

Results: **Twenty-one patients, namely, 14 patients who newly started lemborexant and 7 patients who switched from benzodiazepine hypnotic monotherapy to lemborexant, were able to discontinue lemborexant due to improved insomnia. The time until lemborexant discontinuation due to easing of symptoms was 8.0 ± 3.6 weeks. The mean AIS total score was a significant improved (5.2 ± 2.7 to 2.6 ± 2.2) ($p < 0.01$). The mean CGI-I score was 2.7 ± 0.8.**

Conclusion: **The results of this study revealed improvements in subjective evaluation, and the patients were able to discontinue lemborexant at a relatively early stage. Therefore, these results indicate that the use of lemborexant may lead to treatment discontinuation, which is one of the exit strategies for hypnotics, and may in turn improve drug adherence.**

KEY WORDS

lemborexant, efficacy, treatment discontinuation, insomnia

INTRODUCTION

Benzodiazepine hypnotics have the risks of tolerance and dependence are high. Therefore, it is often difficult to reduce the dose of or suspend benzodiazepine hypnotics. On the other hand, the mechanism of the orexin receptor antagonist lemborexant has been shown to be effective for both difficulty falling asleep as well as nocturnal awakening. Furthermore, lemborexant has a low dependence potential, so that it can easily be discontinued; it therefore represents an insomnia medication that frees the patient from some problematic side effects of pharmacological treatment. Furthermore, there is little evidence of insomnia treatment, especially exit strategies for hypnotics. Here, we report on the characteristics of patients who were able to discontinue lemborexant due to improved insomnia.

METHODS

The patients had been diagnosed with insomnia disorder according to the DSM-V criteria. Insomnia was assessed using the Athens Insomnia Scale (AIS) (Soldatos *et al*., 2000). Efficacy outcome assessment was the Clinical Global Impressions-Improvement scale (CGI-I). This study was approved by the ethics committee of Fukui Kinen Hospital.

RESULTS

Twenty-one patients, namely, 14 patients who newly started lemborexant and 7 patients who switched from benzodiazepine hypnotic monotherapy to lemborexant, were able to discontinue lemborexant due to improved insomnia. The mean subject age and mean duration of illness were 39.3 ± 13.0 years and 47.6 ± 63.0 weeks. The average dose of lemborexant was 5.2 ± 1.1 mg. The time until lemborexant discontinuation due to easing of symptoms was 8.0 ± 3.6 weeks. The diazepam conversion amount of benzodiazepine hypnotics for patients who switched to lemborexant was 5.2 ± 0.6 mg and the administration period was 21.6 ± 28.6 weeks. The mean AIS total score was a significant improved (5.2 ± 2.7 to 2.6 ± 2.2) ($p < 0.01$). The mean CGI-I score was 2.7 ± 0.8.

DISCUSSION

Previous studies have found that withdrawal symptoms tend to occur when discontinuing multiple benzodiazepine hypnotics and/or after long-term administration for 6 months or more (Gorgels *et al*. 2006). Furthermore, there have been reports of difficulties in dose reduction or suspending treatment. The results of this study suggest that the smooth switching to lemborexant was because of the following: the administration period of benzodiazepine hypnotics is less than 6 months and they are used as a monotherapy. However, it should be thoroughly

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explained to the patient that since the sensation of falling asleep may differ from the one previous drugs evoked, the symptoms of insomnia might be temporarily aggravated. Furthermore, We attempted to mitigate their concerns and anxiety regarding sleep. On the other hand, long-term administration is not recommended due to various problems associated with benzodiazepine hypnotics, including physical dependence and adverse effects on cognitive function, and this leads to reduced adherence. Lemborexant does not act via the GABA receptors, and therefore, the risks of patients developing dependence and tolerance are considered low. Sleep-onset and sleep-maintaining effects have been reported by both short-term and long-term studies, via objective evaluation using polysomnography and subjective evaluation using sleep diaries (Rosenberg *et al*. 2019). The results of this study revealed improvements in subjective evaluation, and the patients were able to discontinue lemborexant at a relatively early stage. Therefore, these results indicate that the use of lemborexant may lead to treatment discontinuation, which is one of the exit strategies for hypnotics, and may in turn improve drug adherence.

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