A 64-year-old white woman carries the diagnoses of bipolar II depression and complex regional pain syndrome. She has been followed at the outpatient clinic for more than 2 years, with stable and baseline depression, without suicidal intent or behavior. The patient’s medication for bipolar disorder has been stabilized on paliperidone, but her principal challenge initially was how to decrease her pain levels. When zolpidem was serendipitously introduced a year later to assist with sleep disturbances, the patient reported that the pain, which had been localized to the right arm, was significantly reduced in severity (from a score of 10 to a score of 5 on a scale in which 10 is the highest level of pain).

The psychiatry resident continued to follow up with the patient on a monthly basis in the outpatient setting, and continued her on the same pharmacotherapy. Due to the added benefit of pain reduction from the zolpidem, the patient started to take more than the prescribed amount. The psychiatrist subsequently referred the patient to a pain management physician and counseled that the side effects of zolpidem warranted a careful adherence to the prescribed dose of the medication. Trazodone was then prescribed for the patient for its sedative properties, and zolpidem was discontinued (due to the patient’s improper use of the drug).

Despite its sedating properties, trazodone failed to work in the same manner for the patient, and the severity of the patient’s pain increased to a score of 10 on the pain scale. Moreover, trazodone did not possess the same analgesic properties as zolpidem, which was distressing to the patient. For this reason, trazodone was discontinued and zolpidem was reinitiated, with the counsel to only take the prescribed dosage, regardless of the pain the patient was experiencing.
Up to the time of the writing of this article, the patient has been compliant with treatment and reports a consistent reduction of pain in her right arm. There appears to be a direct correlation between her pain and sleep cycle: when the patient sleeps well, her pain is significantly reduced; conversely, when she sleeps poorly, her pain is elevated.

**DISCUSSION**

The analgesic properties of zolpidem are unknown, but there are several hypotheses to explain their existence. One hypothesis focuses on the correlation between sleep and pain. If sleep is improved, either pain processing is improved or the pain threshold is increased, resulting in decreased pain. There appears to be a correlation between sleep and pain, but the exact interaction is poorly understood. Another of the current hypotheses is that pain has an arousal-enhancing consequence and therefore prevents the initiation or continuation of sleep. A third hypothesis is that there may be neurobiological connections between nociceptive pathways and sleep-wake pathways. Therefore, poor sleep would have a negative impact on pain processing, which would result in increased sensitivity to pain.

A recent survey showed that more patients with chronic pain conditions experience insomnia than patients who do not have pain. Studies have shown that sleep deprivation increases the sensitivity to pain in both animals and humans.

Two recent studies have tested the use of zolpidem in postoperative orthopedic patients after knee arthroscopy and anterior cruciate ligament repair, respectively, with the use of narcotic and nonsteroidal anti-inflammatory drug pain medication versus control and placebo. Both studies found that there was a significant improvement in pain and fatigue in patients given zolpidem compared with the control group, but not with the placebo group.

There was also a significant reduction in narcotic usage in patients given zolpidem compared with the control group, but again not with the placebo group.

Zolpidem may have either an agonist or antagonist effect on algesia and its inflammatory mediators, such as histamine, prostaglandins, or cytokines. Zolpidem has been shown to decrease total lipids, total cholesterol, and triglycerides in hyperlipidemia induced by administration of a non-ionic detergent (Triton WR-1339).

This effect is thought to be through stimulation of peripheral omega-3 benzodiazepine receptors that can be found in many peripheral organs, including the kidney, heart, endocrine glands, erythrocytes, and on the outer mitochondrial membrane of the central nervous system (CNS). These receptors have been shown to play a role in many different processes, including steroidogenesis, immunity, cell growth and differentiation, cholesterol metabolism, and modulation of gamma-aminobutyric acid in the CNS. It is possible that these omega-3 benzodiazepine receptors also play a role in the analgesic effects of zolpidem.

**CONCLUSION**

This case highlights the effect of zolpidem on pain reduction in a patient with chronic pain. The addition of zolpidem to the patient’s treatment regimen resulted in a consistent reduction in her pain.

It is still unknown whether zolpidem functions to reduce pain via reduction of inflammatory mediators or via its effect on sleep or pain pathways. Zolpidem shows promise as an analgesic and warrants further investigation.

**REFERENCES**