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Short Communication

Suvorexant: something new for sleep?

Reddy A, Puvvada SC, Kommisetti S, El- Mallakh RS, Lippmann S. Suvorexant: something new for sleep?

Orexin, also called hypocretin, is a neuropeptide that acts on central nervous system receptors to promote arousal. Suvorexant, its receptor antagonist, generates interest as a medication to treat insomnia. Suvorexant helps in decreasing wakefulness by counteracting orexin activity. Its low side effect potential may offer considerable benefit. Compared with other sleep aids, diminished drowsiness and less cognitive dysfunction is an advantage. Now approved for clinical use, an apparent lack of rebound insomnia or drug dependence potential might make suvorexant a good choice pharmacotherapy for patients with insomnia.

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Significant outcomes

- Suvorexant is a potentially new pharmacotherapy for sleep that is an orexin receptor antagonist in the brain.
- It reduces alertness rather than causing sedation and appears to be safer and non-addictive, as compared with hypnotics.
- Now approved for use, suvorexant should be a valuable adjunct to counter insomnia.

Limitations

- Despite reported safety, suvorexant does result in some neurological side effects.
- New pharmaceuticals can induce unknown, unexpected adversities.

Insomnia

Insomnia is a complex issue in medical practice (1). Sleep disturbances are a problem for nearly a third of all people (2). Insomnia is associated with deleterious medical and psychiatric consequences for patients, and a challenge for clinicians. Inadequate sleep decreases cognitive function and increases cardiovascular risk (3). Sleep hygiene, regular exercise and treating the underlying causes of insomnia, which includes psychiatric conditions, would greatly benefit people having problems with sleep. Many current pharmaceuticals prescribed as sleep aids are associated with difficulties of cognitive disturbance, somatic side effects, and addiction or habituation (4).

Orexin

Discovery of the neuropeptide orexin and its receptors adds a new option for the management of insomnia (4). Orexin was discovered while investigating the etiology of narcolepsy (4). It is synthesised by neurons in the lateral and posterior hypothalamus, and it has potent effects on arousal and sleep. This peptide facilitates alertness by activating neurons in the locus ceruleus and tuberomamillary nucleus, basal forebrain, and cortex during wakefulness (5). The activity of orexins is mediated through the G protein-coupled receptors, OX1 and OX2 (4,5). They are normally at lower concentrations during sleep and are deficient in persons with narcolepsy (4). Similarly, exogenous orexin

injected into the brain, augments arousal at a cellular and behavioral level (5).

Suvorexant

This dual orexin receptor antagonist, suvorexant, has the potential to counter orexin activity (4). Initial studies suggest that it has efficacy in combating insomnia (6–8). Suvorexant works by diminishing alertness (4–8). In May 2013, suvorexant was approved by an advisory panel for the United States Food and Drug Administration (FDA) for the treatment of patients with sleep difficulties (9).

Suvorexant

Once orexin peptides were discovered, investigations began to develop an antagonist (4). Several researchers tried to discover different orexin receptor antagonists. Among them suvorexant is a potent and selective dual orexin receptor antagonist; this diazepine-based substance is the one most prominently considered (7–11). Orexin receptor antagonists counteract the effect of orexin at central nervous system receptors and might be advantageous for patients with trouble in sleeping (12).

Suvorexant is orally bioavailable, penetrates the blood–brain barrier easily, and occupies rat central nervous system orexin receptors (4). The estimated absolute bioavailability for 40 mg Suvorexant is ~47% (13). In humans, suvorexant reaches maximum plasma concentration in 3 h with dissipation of its effect in 9–13 h (12). The metabolism of suvorexant in humans is primarily by the hepatic cytochrome P450 3 A family and hydroxylation as the predominant metabolic pathway (13). Metabolites are then eliminated through faeces and urine (13). In May 2013, suvorexant was positively reviewed by an American advisory panel for the United States FDA in the treatment of patients with sleep difficulties (9).

Indications

Insomnia is the indication for prescribing suvorexant (6–12).

Reportedly, it does not have side effects of sedation or cognitive disturbances (12), which are associated with sedative hypnotics, including benzodiazepines and related drugs (4). Thus, suvorexant might offer an advantage in treating persons with the aforementioned adversities. These same properties might make it particularly desirable in patients with psychiatric illness, where the primary conditions, or their treatments, might be associated with inattention or reduced cognitive function. In addition, without sedative properties, it may be less likely to cause falling, especially in geriatric populations (11,12).

Studies

In animal research, suvorexant has less effect on reducing attention or memory as compared with benzodiazepines (4–14). In rodents, it reduced wakefulness and increased rapid eye movement (REM) and non-REM sleep (4).

Numerous clinical studies with suvorexant in humans, mostly in adults aged 18 to 65, document that it helps patients fall asleep with safety and long-term efficacy (7–13). It also decreases nocturnal awakenings (12). Subjects prescribed suvorexant do not exhibit rebound insomnia or evidence withdrawal upon abrupt discontinuation of the drug following 4 weeks of ingestion (6). Suvorexant usage does not induce disruption in sleep architecture nor sleep fragmentation (6–12).

Dosage

Suvorexant has been tested in several different strength versions; the manufacturer offered to market in tablets of 10, 15, and 20 mg formulations (6). The initial dosing regimens have been under review (4–15). In debilitated patients or those over age 65, the initial recommended dose should be 15 mg nightly. For healthy people under age 65, the initial dosage is 20 mg before bed time.

Adverse effects

The most common side effect of this pharmaceutical is somnolence, and that occurs in 7% of subjects prescribed 15–20 mg dosages (13). Undesired sleepiness is more prevalent as a complaint in about 11% of subjects prescribed quantities at or above 30 mg/day (13). Headaches have been documented in 8% of those receiving 15–20 mg daily (13). One case of hypnagogic hallucination and another of hypnopompic hallucination is reported at 15–20 mg dosage administrations (13). Suicidal ideation is 0.2% to 0.6% in patients on Suvorexant (13).

Drug interaction

Ketoconazole is not recommended for use along with Suvorexant. Diltiazem is to be used in lower dose, and Rifampin is to be used in maximum dose. There are no concerns for patients with hepatic or renal disease.

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Conclusion

Suvorexant is a potentially new drug for treating insomnia. Its mechanism of action renders a favorable side effect profile. FDA has recently allowed the drug to be marketed in the United States. Suvorexant is currently available as a new pharmaceutical means to counter problem sleep.

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Conflicts of Interest

This paper aims at informing physicians about suvorexant, a new sleep medication having a different mechanism of action when compared with other drugs. It could offer significant benefit to people with insomnia, perhaps without addiction or some of the many clinical difficulties associated with other medications that help in treating insomnia.

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