

## Use of Over-the-Counter Medicine, Complementary and Alternative Medicine, and Alcohol in the Treatment of Chronic Insomnia

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### Over-the-Counter Medicine

Americans spend billions of dollars each year on over-the-counter (OTC) medications, health foods, and dietary supplements,<sup>1</sup> yet there is little evidence on the efficacy of these substances. The assumption that OTC and nutritional supplements are safe just because they are not controlled is false. There are few rigorous scientific studies which support any beneficial effect of these unregulated compounds for the treatment of insomnia. Studies that have been done have used small samples, and at times, inadequate design, no statistical analysis, and few objective outcome measures.<sup>2</sup>

### OTC: H<sub>1</sub>-Receptor Antagonists

Histamine is a neurotransmitter with wake-promoting properties, and in animal models, suppression of histamine has led to sedation. Of the current U.S. Food and Drug Administration (FDA)-approved OTC sleeping aids, the most frequent active ingredients are diphenhydramine hydrochloride, diphenhydramine citrate, and doxylamine succinate. Since 1987, sales have steadily increased. Most recently, these antihistamines have been combined with analgesics (“nighttime analgesics”) with estimates that these medications are sold at twice the rate of the nonanalgesic sleeping aids.<sup>3</sup>

There are eight studies, with inconclusive results, concerning patients with sleep problems that examined efficacy of the H<sub>1</sub>-receptor antagonists that are still on the market. All were observational, patient self-report, or physician evaluation with no objective sleep measures.<sup>2</sup> Few were random, double-blind studies, and most had small sample sizes. While the reports on efficacy are inconclusive, there are reports that tolerability to the sedating effects of H<sub>1</sub>-receptor antagonists develops quickly.<sup>4</sup>

There are a variety of side effects reported, including sedation, diminished alertness, vomiting, depression, malaise, drowsiness, dry mouth, grogginess, weakness, headaches, gastrointestinal distress, impotence, and voiding difficulties.<sup>2</sup> They are contraindicated in patients with narrow angle glaucoma as these medications may increase intraocular pressure. In a study of hospitalized elderly, there was a 70 percent increased risk for impaired cogni-

tion, which was dose-related with the use of diphenhydramine for sleep.<sup>5</sup>

### OTC: Herbal and Nutritional Supplements

There are many herbal and nutritional substances sold for the treatment of insomnia, but there are almost no studies to support their efficacy or safety. The two most common are melatonin and valerian root.

### Melatonin

The FDA does not regulate melatonin, therefore formulations of it are not standardized and different preparations have been used in clinical trials. The few studies that compared effects of melatonin to other pharmacological agents in the treatment of sleep disorders found that melatonin was not as effective as either zopiclone or zolpidem. A major review of melatonin recently conducted by the Agency for Healthcare Research and Quality by the University of Alberta Evidence-based Practice Center concluded that, in general, studies have been of questionable quality.<sup>6</sup> The magnitude of the effects of melatonin appears to be of no clinical significance in insomnia. Short-term use of melatonin appears to be safe, but there are little data on its long-term use.

### Valerian Root

Valerian (*Valeriana officinalis*) root is an herb that is widely used to promote sleep with its sedative properties attributed to a benzodiazepine-like activity. Sales of valerian preparations totaled \$8 million in the United States between 1997 and 1998.<sup>7</sup> Over the past two decades, a number of controlled clinical trials have investigated the effects of valerian on sleep but mostly in normal subjects with inconsistent results. There is only one study of valerian in patients with insomnia. A single dose had no significant effect on sleep. A 14-day course was associated with shorter sleep latency and shorter latency to deep sleep by sleep recording, but there were no significant differences in subjective sleep quality or other objective sleep parameters. Adverse effects of valerian are rare and have been reported to be mild in general, including lightheadedness, headache, and “hangover.” However, there have been case reports of hepatotoxicity in individuals taking herbal products containing valerian and one report of heart failure and delirium following sudden withdrawal of valerian.<sup>2</sup>

**Disclosure:** Dr. Ancoli-Israel is a consultant, member of the speakers bureau, and/or member of the scientific advisory board for Neurocrine, King, Takeda, Sepracor, Sanofi-Aventis, and Cephalon.

## Other Herbal Products for Insomnia

There are many other herbal products that are sold for insomnia (e.g., passionflower, Jamaican dogwood, hops, chamomile, lemon balm, St. John's Wort, skullcap, California poppy, lavender), but there have been no studies of efficacy or safety.<sup>2</sup> The FDA issued an advisory statement for consumers regarding the potential risk for hepatotoxicity with kava kava.

## Complementary and Alternative Medicine Treatments

### LIGHT

Light treatment is recommended for depression and circadian rhythm disorders. Studies of insomnia have primarily been in older populations with and without dementia and include mixed results. Minor side effects have been noted, including eye irritation, headache, nausea, and dryness of eyes. Hypomania in patients with bipolar affective disorders is rare.<sup>8</sup>

### EXERCISE

A meta-analysis of the extant literature concluded that acute exercise had virtually no effect on sleep latency or wake time, a modest but statistically significant increase in total sleep time and deep sleep, and a significant increase in rapid eye movement latency and decrease in rapid eye movement sleep amount.<sup>9</sup> In general, studies of the effect of chronic exercise on sleep have not yielded compelling evidence that exercise promotes sleep. Much of this literature, however, has been limited to good sleepers.

### PASSIVE BODY HEATING

There have been a handful of studies showing that passive body heating (i.e., taking a hot bath for 30 minutes before bedtime) delays core body temperature and improves sleep efficiency in older patients with insomnia.<sup>10</sup>

### ACUPUNCTURE

In traditional Chinese medicine, acupuncture is used for the treatment of insomnia. One polysomnogram (sleep recording) study conducted before and after treatment showed a statistically significant effect on sleep in patients who received acupuncture versus placebo.<sup>11</sup>

### LOW ENERGY EMISSION THERAPY (LEET)

LEET delivers low levels of amplitude-modulated, radio frequency, electromagnetic fields. There have been very few studies on the efficacy and safety of LEET in patients with insomnia. The largest study in patients with chronic insomnia evaluated efficacy and found improvement in sleep with no rebound insomnia and no significant side effects.<sup>12</sup>

### ALCOHOL

About 30 percent of patients with chronic insomnia use alcohol to induce sleep,<sup>13</sup> but few studies have examined the effect on sleep in insomniacs. Roehrs et al.<sup>14</sup> found that 0.5 g/kg of alcohol improved sleep in patients with insomnia but not in age-matched normal controls.

In conclusion, most evidence does not support the use of OTC

or herbal preparations. More research is needed on the efficacy and, in some cases, on safety of OTC medications, complementary and alternative medicine, and alcohol in patients with insomnia. Specifically, randomized, placebo-controlled, objective sleep studies in patients with insomnia are needed, as are studies comparing the efficacy and safety of these substances to commonly prescribed hypnotics.

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