Are Sleeping Pills Good For You?

Pharmacists in the United States filled more than 56 million prescriptions for sleeping pills in 2008 at a cost of $4.5 billion, a startling 70 percent increase from 2002. They are among the most advertised, most prescribed and most profitable drugs. Although many prescriptions are given for short term use of about two weeks, two-thirds of all sleeping pills are consumed by chronic users who have taken hypnotics for an average of five years or more (1). Recently developed sleeping pills, including Lunesta (eszopiclone) and Ambien CR (zolpidem) are being promoted as effective for long term use. They have been demonstrated to produce on average a 10-30 minute increase sleep in total daily sleep time (2, 3) for up to six months, not a very large effect. But are these pills good for you?

Most sleeping pills (e.g., Valium, Ambien, Lunesta, Sonata) act on the benzodiazepine site or "receptor" in cell membranes When these drugs attach to this site, they mimic the effect of GABA, a ubiquitous brain chemical that decreases the activity of most brain cells. Contrary to some drug company claims, drugs acting on the benzodiazepine receptor do not "zero in" on and selectively decrease the activity of wake promoting neurons. Brain cells related to waking contain these receptors, but so do brain cells related to sleep, to heart and blood pressure control, sensory perception, motor control and the regulation of internal functions (4). The sleep inducing effect of sleeping pills is a result of the simultaneous inhibition caused by benzodiazepine receptors in all of these cell types, often working at cross purposes with regard to sleep (5). The state induced is not "natural" sleep.

Most sleeping pills are taken to relieve insomnia. According to several epidemiological studies, people with insomnia either do not have any marked shortening of lifespan relative to those reporting normal sleep or actually have a somewhat increased lifespan (see my prior blog "How Much Sleep Do We Actually Need").

Many cases of insomnia are linked to depression. However, studies in which insomnia subjects were randomly assigned to either placebo or benzodiazepine sleeping pills, reported that the rate of depression was doubled in those who took sleeping pills (6). Suicide rates are increased in those who had taken hypnotic mediations (7). Benzodiazepines were reported to have caused 3.8 percent of all deaths by drug overdose (8). Other troubling consequences of sleeping pill use are memory problems, falls, aggressiveness, and confusion. Sleepwalking, sleep eating and driving while not fully awake are common side effects (9, 10). Those taking sleeping pills can be expected
to feel a short term relief from insomnia when they first begin taking the pills. However, short term usage frequently leads to chronic usage and dependence (11).

The most troubling consequence of chronic sleeping pill is an apparent reduction in lifespan in chronic sleeping pills users relative to those reporting equivalent insomnia who did not take sleeping pills. Chronic sleeping pill use might be roughly comparable to cigarette smoking in its effect on lifespan. The life shortening effect of chronic sleeping pill usage has now been reported in at least 12 studies published in respected peer reviewed publications. Two studies have reported no effect of hypnotic usage on lifespan. No study has reported any lifespan or overall health benefit of chronic sleeping pill usage, which is striking considering that so much of the research on sleeping pills is funded by the drug companies producing them.

Despite the random assignment controls of some of the studies reporting adverse effect of sleeping pill usage, it remains possible that subjects staying in studies with benzodiazepine agonist use are inherently predisposed to die or develop certain diseases sooner, and that the pills are not the cause. At one point a similar argument was made for cigarette smoking, i.e. it was claimed that people inclined to smoke have a higher risk of lung cancer, but that this risk was not due to smoking. This contention was thoroughly disproved with the help of animal studies where all variables can be controlled. Such studies have not yet been done for hypnotic drugs.

How could these drugs cause the adverse effects that have been reported? In addition to their presence on a wide variety of brain cells controlling bodily systems, benzodiazepine receptors also exist in large numbers in bodily organs including the heart (12, 13), gall bladder, urinary bladder (14), thyroid, liver (15), lung, stomach (16, 17), testes (17), pancreas (16) and kidneys (16, 18) and are activated by many commonly used sleeping pills (19, 20). Benzodiazepine receptors are present on red blood cells, on tumors, as well as on cells of the immune system (5, 21-24).

Increased rates of infection have been reported with the use of hypnotics (25).

Sleeping pill use has been linked to cancer as well as cardiac death (7). In the periphery and to a lesser extent within the brain, activation of the benzodiazepine site directly affects the mitochondria (19, 23), the cell's energy machine which is involved in inflammation, cholesterol transport, adaptation to stress and cell death. When sleeping pills that attach to this receptor are taken at night, all of the benzodiazepine receptors are activated for hours, followed by withdrawal during the day. This cycle of activation-withdrawal of all of the brain and body's benzodiazepine receptors never happens in undrugged individuals.

Insomnia can be a devastating problem. In those cases where depression, chronic anxiety, pain or other medical problems cause insomnia, these underlying problems need to be treated rather than just addressing the sleep symptoms resulting from these problems.

There are non-drug treatments of insomnia that can be more effective than sleeping pill use. One pillar of these treatments is withdrawal from drugs, the most common of which is caffeine, present not only in coffee but in soft drinks, chocolate and many other foods. Maintaining regular sleep times seven days a week can also be helpful. Alcohol can induce sleep, but produces a rebound sleep disruption a few hours after sleep onset. The American Academy of Sleep
Medicine is a nonprofit medical organization which accredits and provides contact information for sleep disorder centers in the United States. The treatment of insomnia by cognitive-behavioral therapy and instruction in good sleep hygiene (26, 27) provides the benefits of drug treatment without the risks associated with their use, and with a better long-term outcome.

Reference List
18. T. Hauet et al., Transplantation. 74, 1507 (2002).