The Place for Drugs in the Treatment of Insomnia

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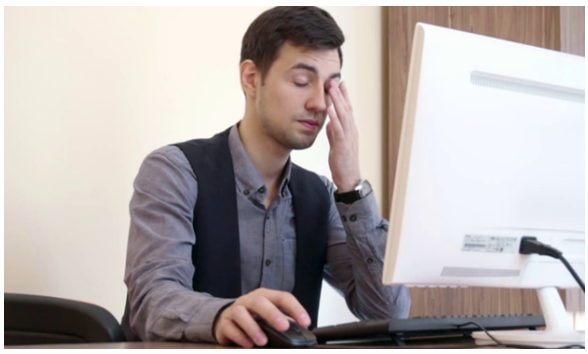

Insomnia can cause a lot of suffering and dysfunction. Insufficient sleep may lead to excessive daytime sleepiness that can make it hard to stay awake at work or while driving. This is potentially dangerous making short term treatment with sleeping pills quite appropriate if it is effective for that individual. Insomnia related fatigue and cognitive dysfunction can make it difficult to cope causing "molehills to turn into mountains" more easily, leading to anxiety, depression, and the feeling of being overwhelmed and incapacitated. The short-term use of an effective sleep agent can enable the patient to continue to function and maintain their occupation, while working towards a long-term solution to their insomnia.

Sleeping pills are typically recommended for so called "acute insomnia" or short-term insomnias related to sudden stresses like the death of a loved one, loss of job, marital breakdown or economic catastrophe. However, many of these life situations although sudden in onset are often not short-term in effect. Associated stress, anxiety or depression may become a major factor. Stress management strategies and treatment for anxiety and depression may become more important because they address aggravating causes of the insomnia.

For those who typically have trouble sleeping when away from home on vacation or business trips, you may find short-term use of sleeping pills appropriate. A vacation is not very enjoyable or rejuvenating if you cannot sleep. A business trip may not be as effective if you are irritable or cannot concentrate properly because you are sleep deprived. Sleeping pills can be useful and beneficial while traveling. On the other hand, many people who do not sleep well away from home are often not consistently good sleepers at home either even under more ideal circumstances. You can train yourself to become a better sleeper. Then, not only will you consistently sleep well at home, but you will also be able to sleep well away from home even under less than ideal conditions.

We will often use a sleeping pill in the sleep lab in patients who have insomnia or who are not consistently able to sleep well at home. Patients wonder if the sleeping pill will affect their sleep study. They are worried that we will not see them sleep "normally". I remind them

that nobody sleeps normally with wires glued to their head and a camera watching them all night. If they have insomnia, I already know that because they are awake when it is happening, and they can tell me about it. However, I need them to sleep to see if there is anything else going on in their sleep. If they do not sleep, we will not learn anything.

We tell the patient that a sleeping pill will be available for them if they need it. They just have to ask the technician. We use Zopiclone because it has been shown not to make sleep apnea worse unlike many other sedating medications. It works quickly and is short-acting so is normally worn off by the time they leave the clinic in the morning. The only thing is that some people notice a metallic taste in the morning. It may also reduce the amplitude of the brain waves resulting in less deep, slow wave sleep being scored. Overall, it does not really affect the results of the study. It just makes it easier for the patient to get to sleep and return to sleep during the night.

Zolpidem is in the same class of “non-benzodiazepine” type hypnotic agents as Zopiclone. Like Benzodiazepines, they also act on the GABA receptors which work to “turn off” the alerting parts of the brain. Unlike many of the sleep agents used and prescribed today, Zopiclone and Zolpidem have been designed just to be used as sleeping pills. They have all the qualities of a good sleeping pill. They are quick-acting and last just long enough to get through the night. They are usually worn off by morning and have very few side effects other than sedation.

Most other medications used to help sleep are not actually sleeping pills but are medications taken for their side effects of causing sleepiness! For example, most over-the-counter sleep aids contain diphenhydramine which is a sedating antihistamine that takes a few hours to obtain peak blood levels and has a half life of 8 hours which is 4 times longer than Zopiclone and Zolpidem. This means that half of the medication is still in effect when you try to get up in the morning.

Most doctors are uncomfortable with prescribing sleeping pills long-term but they are comfortable prescribing antidepressant and antipsychotic medications long-term. Thus, many patients with chronic insomnia end up on sedating antidepressants like Trazodone, Mirtazapine (Remeron) and Amitriptyline (Elavil) or antipsychotic medications like Quetiapine (Seroquel). All of these medications are designed to be taken once per day and to have round-the-clock effects. Not only do patients tend to feel sedated during the day, there are also many other side effects such as constipation, fast heart rate, heat intolerance and weight gain to name a few.

Benzodiazepines such as Lorazepam (Ativan), Oxazepam (Serax), and Temazepam (Restoril)

are the other class of commonly prescribed sleep agents. Oxazepam and Temazepam were designed primarily to be used as sleeping pills. Although the half lives of these medications are relatively short, they have active metabolites with relatively long half lives of 10 – 17 hours. These medications may be a little better at helping patients stay asleep or return to sleep than Zopiclone or Zolpidem, but the effects are more likely to linger into the next day.

Melatonin is a common over-the-counter type sleep remedy. It may be helpful in children or adults with milder forms of insomnia. It is not as effective as a prescription sleeping pill. Melatonin is naturally produced by the pineal gland at the base of the brain. It is secreted into the blood stream about two hours before your normal sleep time triggered by your biological clock. It helps the body become biologically ready for sleep. Thus, taking supplemental melatonin at bedtime is not going to be as effective as taking it an hour or two before bedtime. However, the effectiveness is greatly influenced by the phase of your biological clock. It works best when taken about 2 hours before your normal biological sleep onset time and very ineffective when taken 6 hours before or after that time. If your biological clock is delayed by 6 hours (eg: you are normally not sleepy until about 4 am and you like to wake up around noon) then taking the medication at 10 pm may have almost no effect at all. It is not a great sleep aid. It is more useful for helping people deal with “jet-lag” or other circadian rhythm disorders by helping to change the “time zone” of the “biological clock.” The proper use of melatonin in these conditions is somewhat complicated and described elsewhere.

There are a number of new hypnotic agents under development and not yet released in Canada, but some have been recently released in the US. They work through novel mechanisms such as the Melatonin or Orexin neuropathways. Orexin (Hypocretin) is a neurotransmitter that helps the brain stay awake. It is deficient in certain conditions of excessive sleepiness such as Narcolepsy. Medications that block Orexin cause sleepiness and can work as hypnotic agents. These new sleeping pills are designed specifically for sleep, so you are not taking it for it's "side effect". They are not necessarily any more effective than current sleep medications, and because they are new, will initially be more expensive. For those with side effects, allergies, or resistance to Zopiclone or Zolpidem, these new classes of hypnotic agents may provide a viable alternative when they become available. However, keep in mind that none of these medications work on the cause of your insomnia. Addressing the cause is usually the best long-term solution.

Some patients have insomnia caused by factors that are not resolvable or treatable such as chronic pain or anxiety. They cannot remove or treat the cause of their insomnia. Some patients will have chronic insomnia despite their best efforts at non-pharmacological management and may benefit from long-term hypnotic therapy. One issue will be how quickly the medication will lose its effectiveness. When that happens, they can switch to a different class of medication that works through a different mechanism. Keep in mind that the benzodiazepines and the non-benzodiazepine medications of Zopiclone and Zolpidem all work on the same GABA receptors. Therefore, if the body becomes resistant to Zopiclone there is probably not much point in switching to Ativan or another medication in these two classes because the GABA receptors are most likely going to be resistant to all of these medications. After a two-week drug holiday on some other class of medication, then the GABA receptors will likely become sensitive again.