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Review of the literature on the dangers of zolpidem use, its potential for abuse and addiction

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Abstract

Introduction and purpose of the work : Commonly Z-drugs, especially zolpidem , are considered safer than short-acting drugs benzodiazepines . Recently, more and more is said about the abuse of these relatively harmless drugs. The aim of this study is to collect scientific reports on the increasing abuse of these drugs.

State of knowledge: There are many reports of zolpidem abusers and addicts in the available literature . These people belong to three groups of patients: the first is people with insomnia who develop tolerance, the second is recreational use, and the third is people with mental disorders. Taking increased doses of zolpidem causes a psychostimulant effect, increased activity during sleep, up to

delusions and psychotic symptoms. Rapid discontinuation of high doses of the drug should be performed in a hospital setting.

Summary : Physicians should be advised to remain vigilant during therapy with group Z drugs and to check that the patient is not receiving the drug from multiple sources and is not taking zolpidem in supra-therapeutic doses.

Key words : zolpidem, drugs Z, substance abuse, addiction to hypnotics, insomnia

INTRODUCTION AND PURPOSE

Drugs from the Z-group are substances with a hypnotic effect and have been widely used since the 1980s. This group includes: zaleplon , zolpidem , zopiclone . [12] Zolpidem is an imidazopyrimidine , non- benzodiazepine drug that is an agonist of the A-acid receptor complex γ -aminobutyric acid (GABA), which binds selectively to the α_1 subunit (which is characterized by a hypnotic potential). [1, 7, 8, 13] The drug metabolism in the human body is mediated by CYP3A4. different sexes and due to their individual factors. [1]

The guidelines recommend taking zolpidem at a dose of usually 10 mg orally once a day at bedtime for several days, not longer than 4 weeks. [12] In the elderly, the recommended dose is lower, 5 mg. [12]

Characteristic features of zolpidem are: quick onset and short duration of action, lack of active metabolites and a relatively small number of side effects, which is why it is commonly considered a drug safer than benzodiazepines. As a result, it became the drug of first choice in the short-term treatment of insomnia [2, 7, 12]. Additionally, the advantage of zolpidem is the lack of characteristic side effects that have occurred in the treatment of sleep disorders with benzodiazepines (BDZ), such as sedation the day after taking the drug and somnolence. during the day, which gave the patients treated for insomnia hope to function normally during the day. [12, 13]

As it was commonly believed, the replacement of benzodiazepines zolpidem in the treatment of insomnia was supposed to reduce the risk of abuse and addiction to hypnotics, which was a common problem in people using benzodiazepines [1, 3].

In recent years, great attention has been paid to the fact that drugs from the group Z were not hastily recognized as safe. Many scientific reports challenge the thesis that zolpidem is a drug with low addictive potential, much less than in the case of benzodiazepines . [7] More and more often we find information about the abuse of this substance in over-therapeutic doses by patients and drug dependence syndromes from group Z, including the most commonly used zolpidem . [1, 3, 13]

The aim of this study is to collect and summarize information available in scientific publications on the growing abuse of Z-group drugs, especially zolpidem .

DESCRIPTION OF THE STATE OF KNOWLEDGE

Initially, when Z group drugs appeared on the pharmaceutical market, research was carried out on them, which showed their minimal potential for abuse. Years later, more and more reports of drug abuse in many cases appeared in more recent publications. [12, 16] Taking into account only scientific articles that appeared in the years 1966-2002, 36 case reports of

zolpidem dependence syndromes and 22 cases of addiction to other drugs from the "Z" group were found [11] Most patients with drug dependence syndrome She was also dependent on other psychoactive substances like alcohol, drugs or had other mental disorders. [11]

Scientific literature indicates that addiction and serious drug abuse occur in zolpidem therapy, but they occur less frequently than in the case of benzodiazepine treatment [1, 6] and that the relative frequency of reported addictions is lower than in the case of BDZ treatment. [11] Other studies report that zolpidem has a similar potential to cause abuse and addiction to benzodiazepines . [7, 9] Nevertheless, these drugs are potentially dangerous in terms of addiction, therefore their common use is controversial.

In 2001, zolpidem was placed on the list of drugs causing addiction in Schedule IV of the 1971 Convention. giving as the reason the high frequency of its abuse and addiction to a degree similar to that of benzodiazepines. [14, 15]

Benzodiazepines and group Z drugs has been created in Great Britain . Among the items included there was the question of what is the main reason for taking the above-mentioned drugs. The collected data showed that the respondents most often used medication due to the need to help with falling asleep (66.4%), coping with stressful situations (37.1%) and improving well-being (31%). [12, 17]

Research published so far lists categories of zolpidem abusers who may become addicted. The first is patients who start zolpidem therapy to treat insomnia. Therapy is extended beyond the recommended duration, patients develop tolerance to the sedative effects and gradually increase the dose taken until they become abused and addicted. These are often elderly people who have symptoms of depression and anxiety. Zolpidem in higher doses has an anxiolytic effect , therefore this group is highly exposed to addiction. The second group are people who previously abused psychoactive substances such as alcohol and drugs and consume zolpidem because of its euphoric effect for recreational purposes. [12, 16, 26] The last group consists mainly of women with iatrogenic insomnia or secondary to mild psychiatric disorders who abuse zolpidem [12,27,28]. The Z-drugs, along with benzodiazepines , are the drugs most frequently detected in suicide toxicology studies in the causes of death registries in Norway and Sweden. [12, 18]

Regardless of the dose, zolpidem is not effective in the long-term treatment of insomnia. [1] Scientific literature provides numerous descriptions of clinical cases, when patients gradually increased the doses of zolpidem without medical supervision , obtaining drugs from several sources at the same time. [7, 12] Taking zolpidem in higher than recommended doses (600-2000 mg daily) resulted in psychostimulatory effects in patients. Symptoms such as improved well-being, euphoria, increased energy, sociability and talkativeness were observed. [12, 19, 20] Other disturbing behaviors were also observed after high doses of the drug, such as walking in sleep, bizarre behavior, psychomotor agitation, disorientation at night, driving in sleep, eating disorders related to sleep, falls at night or other complex activities during incomplete awakening from sleep. [7, 12, 21, 22] There are also reports of delusions and psychotic symptoms after taking high doses of zolpidem [12, 23, 24]. The intake of long-term increased doses of zolpidem resulted in severe thirst and inability to stop taking the drug. [12, 25]

Although zolpidem is rapidly metabolized and does not accumulate metabolically active breakdown products, rapid drug withdrawal is associated with serious side effects. Symptoms of withdrawal include increased insomnia, headaches and muscle aches, confusion, increased anxiety, and irritability.

Patients who have experienced abuse and dependence on zolpidem are often the first to try to limit their use of zolpidem themselves. In this they replace it with another sleeping drug, often from the group of over-the-counter drugs. This leads to an overuse of OTC drugs, which are more readily available than Z-drugs. [7] It should be remembered that over-the-counter drugs can serve as an aid in the transition phase and that those who are prone to overuse of psychotropic drugs may be susceptible to substance abuse. [7, 10]

Treatment of addiction to hypnotic drugs from the group Z should take place in a hospital setting. Reports show that rapid rinsing of zolpidem in doses above 160 mg / day may cause severe withdrawal symptoms such as seizures and psychosis. [4, 5] Rapid withdrawal of high doses of zolpidem should be performed under medical supervision and cross-treatment alternating with long-acting benzodiazepines should be used. The preferred drug for this type of therapy is clonazepam. It has the effect of reducing the risk of side effects. [1, 7] Discontinuation therapy was started with a reduction in the dose of zolpidem for 14 days, gradually adding other sedatives and hypnotics. A substance that may be helpful in weaning zolpidem is melatonin. Together with zolpidem, they share the same target points in the brain, ie they act on GABA, therefore there are recommendations for the use of melatonin as an aid in reducing drug abuse [12, 29].

CONCLUSION:

The above-mentioned scientific studies prove the danger of using zolpidem in an uncontrolled manner, for a long time and in higher than recommended doses. It is very important to prescribe zolpidem with the same caution as benzodiazepines, especially in geriatric patients and those struggling with other addictions. [12] It should be emphasized how important it is to draw the attention of clinicians and general practitioners who issue prescriptions for sleeping medications. They paid attention to all medications that are prescribed to the patient, also by other doctors, in order to detect duplication of prescriptions by several doctors and misuse of sleeping pills. [7]

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