ORIGINAL ARTICLE

Drug-Induced Insomnia: Descriptive analysis of FDA Adverse Event Reporting System

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Abstract

Aim: Insomnia is one the most common problems encountered by the family physician and can occur due to several causes such as using some drugs. The present study aimed to describe the reports that were submitted to FDA Adverse Event Reporting System (FAERS) about drug-induced insomnia. **Materials and Methods:** The FAERS was used to conduct this retrospective study that comprised a descriptive analysis of all reported adverse events of drug-induced insomnia in the past 5 years. **Results:** During the study period from the beginning of 2017 to the end of 2021, there were 86918 reports about drug-induced insomnia submitted to FAERS. The most frequently reported drugs were levothyroxine sodium (3.85%), duloxetine hydrochloride (3.24%), adalimumab (3.08%), pregabalin (2.71%), etanercept (2.17%), and niraparib (2.04%). **Conclusion:** It is important to increase the awareness of healthcare workers about the medications that could cause insomnia. Moreover, health-care providers should educate the patients about the drugs that could induce insomnia, how they can manage insomnia, and how they can report these adverse effects.

Key words: Adverse event, FDA adverse event reporting system, insomnia, reporting

INTRODUCTION

Insomnia is a noticeable problem in modern 24 h society.[1] It is an unwelcome experience of difficulty sleeping-is common and can be acute, intermittent, or chronic.[2] Insomnia is defined by the American Academy of Sleep Medicine as the subjective perception of difficulty with sleep initiation, consolidation, duration, or quality that occurs despite adequate opportunity for sleep, and that results in numerous forms of daytime impairments.[3]

Numerous studies from throughout the world have revealed that 10–30% of the population, and in some cases even 50% or 60%, suffer from insomnia. Significant negative effects of insomnia include sadness, diminished work performance, work-or vehicle-related accidents, and a general decline in quality of life.[4]

There are various mechanisms involved in the induction of insomnia by medicines. Some medicines affect sleep negatively when being used such as anticonvulsants, antidepressants, steroids, and central nervous stimulant drugs such as amphetamine and caffeine, while others affect sleep and lead to insomnia when they are withdrawn.[5] Van Gastel reported that insomnia could be caused due to the interactions of medicine with any of the numerous neurotransmitters or receptors that are involved in sleep and wakefulness.[6]

The Food and Drug Administration (FDA) has launched a new interactive, web-based dashboard search tool for its FDA Adverse Event Reporting System (FAERS) database that improves access to data about adverse drug and therapeutic biologic products reported to FDA.[7] The FAERS is one of the largest government databases that includes reports on medication errors and adverse event reports that have been submitted to the FDA.[8] FAERS is known as an essential source of data in monitoring drug effects to identify and evaluate previously unreported adverse events.[9]

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There is a lack of data on the adverse events reports about drug-induced insomnia. Hence, the present study aimed to describe the reports that were submitted to FAERS about drug-induced insomnia.

MATERIALS AND METHODS

The FDA Adverse Event Reporting System was used to conduct this retrospective study that comprised a descriptive analysis of all reported adverse events of drug-induced insomnia in the past 5 years.

The study included all reports of drug-induced insomnia adverse events filed by healthcare providers or other workers between 2017 and 2021. Other adverse events that were reported were excluded from the study.

The present study looked at the number of drug-induced insomnia cases, the reporters' specialties, the gender of the patients, the ages of the patients, and the most reported drugs in drug-induced insomnia.

RESULTS

During the study period from the beginning of 2017 to the end of 2021, there were 86918 reports about drug-induced insomnia submitted to FDA Adverse Event Reporting System. Among these 86918 cases, 48365 were classified as serious cases (55.64%). More than 18000 reports were submitted in 2017 and 2021. The number of drug-induced insomnia cases during the study is shown in Table 1.

Table 2 shows the specialty of the reporters. Most of the reporters were not healthcare professionals (68.66%).

Table 3 shows the gender of the patients. More than 65% of the patients were females and 34.19% of them were males.

Table 4 shows the age of the patients. The age of about 63.77% of the patients was between 18 and 64 years and the ages of 30.90% of them were between 65 and 85 years.

Table 5 shows the most common medications that were reported in drug-induced insomnia reports. There are many medications that were reported, so Table 4 includes only the drugs that were reported in more than 1000 reports. The most frequently reported drugs were levothyroxine sodium (3.85%), duloxetine hydrochloride (3.24%), adalimumab (3.08%), pregabalin (2.71%), etanercept (2.17%), and niraparib (2.04%).

Table 1: The number of drug-induced insomnia cases

Category	Number of cases	Percentage
2021	18,405	21.18
2020	16,477	18.96
2019	15,971	18.37
2018	17,156	19.74
2017	18,909	21.75
Total	86918	100.00

Table 2: The specialty of the reporters

Category	Number of cases	Percentage
Healthcare professional	27,020	31.34
Consumer	59,204	68.66
Total*	86224	100.00

*In 694 cases the specialty was not specified

Table 3: The gender of the patients

Category	Number of cases	Percentage
Female	52,041	65.81
Male	27,040	34.19
Total*	79081	100.00

*The gender was not specified in 7837 reports

Table 4: The age of the patients

Category	Number of cases	Percentage
0–1 month	19	0.03
2 months–2 years	250	0.46
3–11 years	779	1.44
12–17 years	724	1.34
18–64 years	34,471	63.77
65–85 years	16,706	30.90
More than 85 years	1,109	2.05
Total*	54058	100.00

*The age of 32860 patients was not specified

DISCUSSION

The most frequently reported drugs were levothyroxine sodium, duloxetine hydrochloride, adalimumab, pregabalin, etanercept, niraparib, lenalidomide, methotrexate, dalfampridine, oxycodone hydrochloride, tocilizumab, leflunomide, and abatacept. Sheehan stated that several medications can upset normal sleep patterns such as heart medications, asthma medications, depression medications, anti-smoking medications. attention-deficit hyperactivity disorder medications, thyroid medications, some analgesics, and herbal medications.[10] Neel Jr informed that the most common medication classes that may cause insomnia included alpha-blockers, beta-blockers, corticosteroids, selective serotonin reuptake inhibitors, angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, cholinesterase inhibitors, histamine 1 antagonists, glucosamine/chondroitin, and statins.[11] Malangu stated that several medicines affect sleep negatively such as steroids,

Table 5: The most common medications that were reported in drug-induced insomnia

Category	Number of cases	Percentage
Levothyroxine sodium	3,347	3.85
Duloxetine hydrochloride	2,819	3.24
Adalimumab	2,680	3.08
Pregabalin	2,352	2.71
Etanercept	1,882	2.17
Niraparib	1,774	2.04
Lenalidomide	1,712	1.97
Methotrexate	1,670	1.92
Dalfampridine	1,458	1.68
Oxycodone hydrochloride	1,408	1.62
Tocilizumab	1,405	1.62
Leflunomide	1,360	1.56
Abatacept	1,350	1.55
Tofacitinib citrate	1,340	1.54
Apremilast	1,311	1.51
Prednisone	1,291	1.49
Clonazepam	1,150	1.32
Aripiprazole	1,143	1.32
Rituximab	1,096	1.26
Sertraline hydrochloride	1,061	1.22
Acetaminophen	1,021	1.17
Gabapentin	1,001	1.15

anticonvulsants, central nervous stimulant drugs, and antidepressants.[5]

Gonçalves *et al*. informed that numerous drugs used in the treatment of chronic diseases have the ability to cause insomnia as adverse effects such as adrenergic beta-blockers, statins, theophylline, corticosteroids, tricyclic antidepressants, monoamine oxidase inhibitors, selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors, norepinephrine-dopamine reuptake inhibitors, norepinephrine reuptake inhibitors, maprotiline, lamotrigine, felbamate, pseudoephedrine, and stimulants such as methylphenidate, typical and atypical antipsychotics, anxiolytic drugs, and anti-Parkinson drugs.[12] Naeem *et al*. stated that the use of antihypertensive drugs may cause insomnia and other central nervous system adverse effects after prolonged use.[13] They also stated that the use of antihypertensive drugs especially beta-blockers connected with rest apnea in case of prolonged exposure and impacts the quality of sleep.[13]

It can be noted that the research about drug-induced insomnia focused on several drug classes such as antidepressants, antihypertensive agents, and steroids. However, the present study showed that most of the reports were related to other drugs that are used for treating arthritis, cancer, autoimmune diseases, and multiple sclerosis (such as methotrexate, etanercept, leflunomide, tofacitinib, apremilast, adalimumab, rituximab, tocilizumab, abatacept, dalfampridine, and lenalidomide). There is a lack of studying the effect of these drugs on sleep disorders, so further studies are needed to find their association with insomnia.

CONCLUSION

Many drugs are used in the treatment of chronic diseases such as levothyroxine sodium, duloxetine hydrochloride, adalimumab, pregabalin, etanercept, niraparib, lenalidomide, and methotrexate could cause insomnia as adverse effects. It is important to increase the awareness of healthcare workers about the medications that could cause insomnia. Moreover, healthcare providers should educate the patients about the drugs that could induce insomnia, how they can manage insomnia, and how they can report these adverse effects.

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