The Turkish Journal of Pediatrics 2022; 64: 357-363
https://doi.org/10.24953/turkjped.2020.30

Case Report

Pregabalin abuse in adolescence: a case series

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ABSTRACT

Background. Pregabalin is an inhibitor of gamma-aminobutyric acid (GABA) and can be abused, especially by polydrug abuser adults. Drug abuse is one of the many risky behaviors that can be seen during adolescence. Here, three adolescents with pregabalin abuse were described.

Case. These adolescents abused pregabalin to cope with their depressive and anxiety symptoms, become tranquilized, boost other drug effects, and reduce withdrawal symptoms. Therefore, the risk factors should be assessed while pregabalin is prescribed to adolescents.

Conclusions. The cases were reported in order to increase awareness concerning the abuse risk of pregabalin among adolescents.

Key words: adolescent, pregabalin, substance use disorder, prescribed drug addiction.

According to a study from Turkey, the lifetime prevalence of tobacco and substance use among adolescents was 45.4% for hookah, 34.2% for alcohol, 24.4% for cigarettes, 4.9% for volatile substances, 3.8% for benzodiazepines, 2.9% for marijuana, 0.6% for cocaine, and 0.4% for heroin.[1] According to the Turkish National Monitoring Center for Drugs and Drugs Addiction (TUBIM, 2019), alcohol and cigarette smoking were the antecedents of using other drugs, and the marijuana trial was the most common one at the beginning.[2]

Gabapentinoids, (pregabalin, and gabapentin) are inhibitors of the presynaptic voltage-dependent calcium channels of gamma-aminobutyric acid (GABA). They are prescribed for partial-onset seizures, anxiety, restless legs syndrome, neuropathic and non-neuropathic pain.[3] However, they are also assumed to have the potential for abuse.[4] Here, three cases of pregabalin abuse with different clinical presentations will be discussed. The first case is an adolescent girl presenting pregabalin dependency. The second case is an adolescent boy who had been using pregabalin to overcome heroin withdrawal symptoms, and the last case, also an adolescent boy who had been using pregabalin to increase the hedonic effects of cannabis.

These cases aim to increase awareness concerning the use of pregabalin and its addictive potential. Informed consent was received from the cases and their families for this report.

Case 1

Sixteen years-8 months girl applied to the child and adolescent outpatient clinic with her mother due to pregabalin abuse. She had been taking 900-1500 mg/day pregabalin, smoking cigarettes (1 package/day) for two years and occasionally drinking alcohol in social settings. Her family was of low socioeconomic status. Her parents divorced when she was seven, and she has been living with her father and two sisters (15 years and 13 years, respectively).

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Received 6th January 2020, revised 19th June 2021, accepted 3rd July 2021.

The parents were not close with her. Instead, they blamed her 19-year-old boyfriend, who also suffered from substance abuse problems of synthetic cannabinoids and pregabalin.

She started using pregabalin two years ago, after her boyfriend was hospitalized because of a fight. At first, she was using pregabalin to tranquilize herself and help her sleep. Then she progressively increased pregabalin use when she was angry, unhappy and anxious, and described withdrawal symptoms of sweating, irritability, insomnia, and loss of appetite. Her longest period of abstinence from pregabalin was two weeks. No other substance use was mentioned.

She had repeated 9th grade two years ago due to truancy and academic failure, and she dropped out the year before. She did not have any plans or hobbies, was unemployed, and all her friends were using heroin and pregabalin. She reported being depressive and hopeless, feeling aimless, having concentration problems, and cutting herself, but she had no suicidal ideation. At her initial psychiatric assessment, although she described depressive symptoms, she was euthymic. She had no formal and content thinking problems. Her judgment, insight and motivation were poor. Physical and neurological examinations and laboratory investigations were normal. Besides truancy, her parents reported acting-outs, running away from home, lying, stealing money from home and self-harm behaviors. Family history was significant for substance abuse (her uncle), conduct disorder (her sister), and antisocial personality disorder (her uncle).

She was diagnosed with oppositional defiant disorder (ODD) with conduct problems, substance abuse disorder, and unspecified anxiety disorder. She was prescribed olanzapine and sertraline, which gradually increased to 7.5 mg/day and 100 mg/day respectively during weekly follow-ups. She had been spending her days doing nothing except being with her friends. During the follow-up, although she reported not using pregabalin, her parents stated otherwise. After separating from her boyfriend, she refused treatment, started cutting herself, and expressed suicidal ideation in her acting-outs. Her parents admitted her to social services. Approximately four months after the initial assessment, she dropped out of follow-up. Social services continued to follow her.

Case 2

Seventeen years-6 months boy applied voluntarily to the adolescent medicine clinic for poly-substance abuse. He had been smoking cigarettes since the age of 12 (currently, approximately 20 cigarettes/per day) and drinking alcohol occasionally for the last three years. He started using cannabis two years ago, and synthetic cannabinoids one year ago. He had only tried hallucinogens for once. Two months ago, he started inhaling heroin two or three times a week. When he could not find heroin, he used pregabalin 900-1200 mg/day to deal with depressive feelings, loss of joy, and exhaustion. He described his motives for substance use as self-medication, peer pressure, and impulsivity. He had not used any drugs for the last two days. He stayed at home under his father's supervision for these 2 days with some vegetative withdrawal symptoms such as sweating, tremor, and aggression and started feeling better at the current hospital visit. He had never undergone a detoxification trial before.

Two years ago, he first presented to the emergency department with visual hallucinations, drowsiness, and confusion after trying synthetic cannabinoids for the first time. His blood toxicology panel was negative at that time, and the urine toxicology panel was only positive for clomipramine (521 ng/ml). After the emergency room workup and treatment, he was consulted to the department of child and adolescent psychiatry and was discharged with a risperidone prescription. After a while he stopped using risperidone due to feeling drowsy all the time and dropped out of follow-up.

He had been living with his father and his eight years old brother in the family home. Family history was negative for substance use disorders. He had dropped out after finishing 8th grade due to academic failure. His academic performance was always poor. Due to difficulty focusing on lessons and impulsivity in elementary school, he was taken to a child and adolescent psychiatrist and diagnosed with attention deficit hyperactivity disorder (ADHD). He was prescribed methylphenidate but stopped taking this medication due to severe appetite loss, and he was never properly treated afterward. He had been working in a marketplace during night shifts as a porter for the last two years. According to his father, he had anger management issues where he harms himself and others during anger episodes. He was also engaged in several fights while attending school.

During the interview, he was slightly agitated. Physical examination and laboratory investigation were normal. Although he was consulted to the department of child and adolescent psychiatry, he refused to go. He was referred to a withdrawal center for further evaluation and detoxification.

Case 3

Fifteen years-9 months old boy applied voluntarily to the adolescent medicine clinic for his poly-substance abuse problem. He had been smoking cigarettes (6-7 cigarettes per day) and using cannabis regularly since he was 13. One year ago, after his cousin's death, who also had substance abuse problems, there was a 6-month long abstinence period for cannabis. However, after a while, he started using cannabis again, progressively increased the amount up to 3-4 times a week, and experimented with volatile substances such as paint thinner, lighter fluid, automotive fuel, and adhesives. He rarely consumed alcohol. For the last six months, he started taking pregabalin (900 mg/day) and phenprobamate (up to 4 grams) right after using cannabis to boost its euphoric effects. He reported that he had been using drugs to suppress his agitation, anger, depressive feelings and improve his mood. He had been using drugs mostly alone and sometimes with peers. He had been living with his parents and 18 years old brother. Other than his cousin, there was no family history of substance use disorders. His academic performance was good until last year. Then, he dropped out of regular school after 10th grade due to truancy and started attending an apprenticeship training school for the last three weeks.

On his first visit, he had been abstinent for one week. He had been evaluated at two child and adolescent psychiatry clinics during the past week, but was unsatisfied with the treatment. Other than these visits he had not received treatment for substance abuse before or had not been diagnosed with a psychiatric disorder. The physical and neurological examination and laboratory investigation were normal. The urine toxicology panel was negative. He was consulted to the child and adolescent psychiatry department.

In his psychiatric examination, he was dysphoric with blunt affect; his speech, formal and content of thinking was normal, but his motivation was poor. He was prescribed Quetiapine XR 150 mg/day and was referred to a withdrawal center for further evaluation and detoxification.

Discussion

In this article, three adolescents with pregabalin abuse are described: An adolescent girl with pregabalin use disorder who had many individual and environmental risk factors, an adolescent boy with multidrug abuse who had been using pregabalin to self-manage heroin withdrawal symptoms, and an adolescent boy using pregabalin to boost the euphoric effects of cannabis. Based on these cases, different aspects of pregabalin abuse in adolescence will be discussed and summarized in Table I.

Besides epilepsy, pregabalin can be used to treat anxiety disorders[5], alcohol, and

Table I. Different aspects of pregabalin abuse among the 3 adolescents.

Risk factors	Case 1	Case 2	Case 3
Sex/Age	Female/16 y 8 m	Male/17 y 6 m	Male/ 15 y 9 m
Smoking/Alcohol	One package/day for 2 years / occasionally in social settings	20 cigarette/day for 5 years / occasionally for 3 years	6-7 cigarette/day for 2 years /rarely
Academic performance	Dropped out of school because of truancy and academic failure	Dropped out of school due to academic failure	Good academic performance, but dropped out of school because of truancy
Family history	Low SES, divorced, antisocial uncle, drug-abuser uncle, sister with CD	Low SES, No history of drug abusers	Substance abuser cousin
Social setting	Drug-abuser friends and boyfriend	Drug-abuser friends	Drug-abuser friends
Pregabalin abuse duration	Two years	Two months	Six months
Pregabalin abuse doses	900-1500 mg/day	900-1200 mg/day	900 mg/day
Purpose of pregabalin abuse	To tranquilize and sleep, continue to use in order to reduce withdrawal symptoms	To deal with depressive symptoms and heroin withdrawal symptoms	To boost cannabis euphoric effects
Withdrawal symptoms	Sweating, irritability, sleep disturbances, loss of appetite	Sweating, tremor, aggression	None
Drug abuse other than pregabalin	None	Cannabis, synthetic cannabinoids, heroin	Volatile substances, phenprobamate
Comorbid psychiatric disorder	ODD, Anxiety disorder, Symptoms of depression and CD	ADHD, Depression	Depressive symptoms
Individual factors	Poor judgment, having no insight and any goal settings, poor problem solving skills	Impulsivity	Hopelessness, prolong mourning

ADHD: attention deficit hyperactivity disorder, CD: conduct disorder, ODD: oppositional defiant disorder, SES: socioeconomic status

benzodiazepine dependence.[6] The therapeutic doses of pregabalin are between 150-600 mg/day, and the risk of abuse increases at high doses as its dose-dependent anxiolytic, euphoric and dissociative effects increase along with the risk of withdrawal symptoms.[7] Pregabalin abuse can be seen especially in individuals with a history of polydrug misuse or addiction.[8,9] In a qualitative research from Jordan, some participants described combining pregabalin with other substances, mainly hashish, and caffeinated sweet beverages, to enhance the euphoric effects.[10] The use of pregabalin to induce the anxiolytic, sedative, or euphoric effects of other substances such as alcohol[11], opioids[12], benzodiazepines, cannabis, and amphetamines[7,13,14] was also reported previously. In literature, the treatment of pregabalin withdrawal symptoms has not been fully established yet.[15] Physicians should be careful about the withdrawal symptoms, including insomnia, headache, nausea, anxiety, depression, diarrhea, flu syndrome, and convulsion.[16] Benzodiazepine use for pregabalin withdrawal symptoms can be controversial in terms of abuse risk.

Self-medication is defined as using drugs to self-treat a medical problem without receiving healthcare providers' advice. The risks of self-medication have been well documented, leading

to a delay in seeking medical advice, excessive dosages or prolonged drug-use duration, and drug abuse.[17] Appropriate treatment of psychiatric conditions could have prevented the use of pregabalin in our cases. Substance abuse, especially opioid abuse, is associated with anxiety disorders.[18] Also many pregabalin abusers have comorbid anxiety problems.[19] Self-medication is highly prevalent among adolescents with psychiatric disorders[20], so screening for self-medication is recommended.

Pregabalin might potentially be used to treat opioid, benzodiazepine, nicotine, cannabinoid, and alcohol abuse withdrawal symptoms. However, there is limited evidence for the efficacy and safety of pregabalin.[6,21] Evidence for the use of pregabalin to treat opioid addiction is based on case reports.[22-24] On the other hand, the abuse potential of pregabalin makes prescription controversial.[8,25] In a study of 124 patients with opiate dependency syndrome, 12.1% of urine samples were tested positive for pregabalin, suggesting pregabalin has a potential of abuse among individuals with opiate addiction. It can act as a weak rewarding substance in patients with long-term opioid tolerance.[9] A systematic review of 59 studies estimated the prevalence of gabapentinoids abuse to be 1.6%. However, the prevalence increases from 2% to 68% among patients with opioid abuse.[26] A study investigating the postmortem toxicology results of medico-legal deaths demonstrated that 91.4% of cases with pregabalin abuse also were using opioids.[27] Additionally, a case study reported an opioid dependent patient using pregabalin to reduce the opiate withdrawal symptoms.[22] Instead of an intention to experience its hedonic effects, opioid-addicted patients might use pregabalin to self-treat symptoms of opiate withdrawal syndrome. In a qualitative study analyzing the online reports of pregabalin, gabapentin and clonazepam users through Google search revealed that some cases were using pregabalin to overcome heroin withdrawal symptoms and cravings.[7] In the presence of sedative drug abuse, clinicians should be careful about the possibility of additional pregabalin abuse, as the risk of overdose and death increases with their combination.[28]

Pregabalin has been perceived as an easily accessible drug that can be abused to induce euphoria.[29] Pregabalin rarely causes a mild, dose-dependent euphoria effect.[30] Patients increasingly had been using higher than the recommended doses of pregabalin to achieve these euphoric effects.[26] Other than taking orally, pregabalin might also be abused rectally, intravenously, and with inhalation.8 Pregabalin has been hypothesized to have euphoric effects due to its direct or indirect effect on the dopaminergic reward system.[31]

Being easily accessible can make pregabalin addiction is increasing among adolescents. Abuse of over the counter and prescription drugs is a global problem.[32] Previously, pregabalin could be obtained through a regular prescription written by any physician from pharmacies in Turkey. However, the Turkish Ministry of Health upgraded the prescription category of pregabalin as a psychotropic drug with a potential of abuse that can only be obtained through special prescription recently. Therefore, physicians should carefully assess the risk factors for drug abuse when they are prescribing pregabalin.

Author contribution

The authors confirm contribution to the paper as follows: Evaluation and treatment of all 3 patients. BEA, MPK and SA; draft manuscript preparation: BEA, MPK. All authors reviewed and approved the final version of the manuscript.

Conflict of interest

The authors declare that there is no conflict of interest.

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