Psychiatria Danubina, 2015; Vol. 27, No. 3, pp 278-279 *Case report*

PREGABALIN ABUSE OF BENZODIAZEPINE AND ALCOHOL ADDICTED PATIENT

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INTRODUCTION

Pregabalin (PGL) is a GABA-analog FDA and EMA approved for the treatment of partial onset seizures and neuropathic pain. The use of PGL for the treatment of generalized anxiety disorder (GAD) is only approved in European countries. It is categorized as a Schedule V drug (lowest potential for abuse) in the US Drug Enforcement Administration's Controlled Substances Act (Drug Enforcement Administration 2005). However, the chance of a possible addiction to PGL seems to rise notably among patients with past or current substance dependencies. Cases of PGL abuse or dependency have been reported since 2008, with a marked increase of such reports in the following years. In 2010, this led to a warning being added in the prescribing information stating that cases of abuse have occurred and that caution is needed with patients having a history of drug abuse. Conclusively, the patient should be observed for signs of PGL misuse or abuse (Prescribing information Lyrica 2011). Still, data on PGL abuse and addiction is scarce, most likely because PGL is not seen as a drug with high-abuse potential. There is one report summarizing a controlled study among patients in a detoxification ward for illegal drugs. 12.1% of all urine specimens from patients with opiate addiction were tested positive for PGL. None of these patients had a medical indication for using PGL (Grosshans et al. 2013). Male sex and a history of polysubstance abuse may be possible risk factors for the development of addictive behaviors related to PGL (Gahr et al. 2013).

PGL is an analog of γ-aminobutyric acid, a major inhibitory neurotransmitter in the brain. It does not bind directly to GABA-, benzodiazepine-, or opioidreceptors. Rather, PGL selectively binds to the α-2-δ subunit protein of voltage-gated calcium channels in various regions of the central nervous system, acting as a presynaptic inhibitor of the release of excitatory neurotransmitters in stimulated neurons. Because of PGL´s anti-glutamergic effects, which are similar to other GABA-like substances with dependency potential such as benzodiazepines and alcohol, an addictive potential is also to be considered with PGL.

We report the case of a male patient in his late twenties with GAD and past alcohol and benzodiazepine abuse who showed similar drug-seeking behavior with PGL.

CASE REPORT

Our patient (born in 1984) was first admitted to a psychiatric ward in 2006 because of major depression and GAD, and has returned a couple of times ever since. He has a long history of tranquilizer and alcohol dependency. He uses both substances to suppress conditions of agitation and anxiety. After a couple of detoxification treatments (both alcohol and benzodiazepines) with the following abstinent phase always only lasting short periods of time, the patient was first given PGL in a daily dosage of 300 mg to control his GAD in July 2012. As a result the patient reported improvement of mood, fear and agitation without further need of alcohol or benzodiazepines. Unfortunately, it soon came to an abusive use of PGL with an increase of dosage by the patient himself to an average of 750 mg per day with a daily intake up to 1050 mg in times of agitation. When there was no PGL available, it came to distinctive withdrawal symptoms including severe tension and anxiety, which led to excessive drinking and benzodiazepine relapses.

The first drug intoxication that required observation in an intensive care unit was in March 2013. The patient had taken a total of 20 pieces of PGL à 150mg in addition to 30 pieces of tramadolhydrochlorid à 50mg. One month later he was hospitalized following an overdose of benzodiazepines (diazepam). In July 2013 the patient once again was admitted to hospital because of drug intoxication. This time it was a combination of quetiapine, PGL and alcohol. A suicidal cause was assumed by us each time but had been denied by the patient every time. He claimed that taking the drugs in overdose was only meant for sedation but spiraled out of control.

By this time the patient had already lost control of his PGL consumption. He was not able to reduce the intake on his own, so he eventually had to undergo inpatient withdrawal treatment for PGL. While the intake of PGL was gradually decreased, withdrawal symptoms such as insomnia, nervousness, anxiety and sweating occurred. As supportive medication we used benzodiazepines (oxazepam up to 60 mg à day), which helped reducing withdrawal symptoms. Although the patient had not had any seizures in the past, anticonvulsive protection (levetiracetam in a daily dosage of 1,000mg) was administered, for there are reports that seizures can occur during withdrawal treatment even if seizures were

not the indication for establishing PGL before. Sleeping disorder could be eliminated by applying trazodone extended release 150 mg. All of the mentioned medications were gradually reduced to zero, too.

A year later the patient has continued to visit our outpatient clinic for regular check-ups. He has remained abstinent from PGL to this day.

DISCUSSION

In the described case the patient was not aware of the addictive potential of PGL. We could not find any guidelines referring to state of the art treatment of PGL-withdrawal. When we started to decrease PGL gradually, the withdrawal symptoms were severe and similar to those of alcohol or benzodiazepine withdrawal. So we were forced to offer a benzodiazepine to make the treatment bearable for him. At the end we were able to phase out PGL and oxazepam.

In the past the addictive potential of medical drugs has been underestimated e.g. in the case of benzodiazepines and zolpidem. For PGL some authors have already published data about cases with tolerance and addiction. Still, PGL causing addictive behavior is not common knowledge yet. Especially, doctors who do not mainly work in the field of addiction, but e.g. seizure disorders or pain treatment, often overlook the possibility of PGL-dependency.

Based on the neurobiological mode of action of PGL, individuals suffering from alcohol or benzodiazepine addiction may be more vulnerable to cross tolerance with PGL. In these cases the application of PGL should undergo a careful risk assessment. But even in the treatment of seizures or neuropathic pain patients need to be thoroughly informed about possible tolerance and addiction, for many clinicians underestimate the alcohol or benzodiazepine consumption of their patients. This is even more the case in the treatment of GAD.

The authors do not doubt that PGL poses an effective treatment for different indications. But more awareness of its addictive potential is necessary along with research about prevalence of PGL-addiction and appropriate treatment options. On the other hand, PGL´s application during tranquilizer or alcohol withdrawal could also be an interesting approach for clinical research.

CONCLUSION

In summary, this case illustrates the requirement for a heightened awareness when prescribing PGL to a person with alcohol or benzodiazepine addiction.

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