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VARENICLINE SEIZURE: CASE REPORT AND LITERATURE REVIEW

VARENIKLIN NÖBETİ: VAKA RAPORU VE LİTERATÜR DERLEMESİ

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Abstract

Varenicline emerged as an efficient smoking cessation medication. However, little is known about its association with seizures. Here, we report a case of a young male who suffered a seizure on the day of the last dose of the suggested drug regimen. We argue that the Varenicline seizure was a result of withdrawal rather than a side effect. We therefore discuss several clinical, legal and legislative implications toward the drug prescription and dispensing.

Keywords: varenicline seizure; varenicline withdrawal

Özet

Vareniklin, etkili bir sigara bırakma ilacı olarak ortaya çıkmıştır. Ancak, nöbetlerle ilişkisi hakkında çok az şey bilinmektedir. Bu çalışmada önerilen ilaç dozajının son doz gününde nöbet geçiren genç bir erkek olguyu sunuyoruz. Vareniklin nöbetinin yan etkiden ziyade ilacın geri çekilmesi sonucu olduğunu düşünüyoruz. Bu nedenle, ilaç reçetesi ve dağıtımına ilişkin çeşitli klinik, yasal uygulamaları tartışıyoruz.

Anahtar Kelimeler: vareniklin nöbeti; vareniklin geri çekilmesi

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1. Introduction

In an era of self-awareness and empowerment, several medications helped smokers quit smoking. Varenicline emerged as an efficient smoking cessation medication, especially for relapsing prevention (Kaur et al. 2009). On a molecular level, it works as a partial agonist and antagonist agent, targeting dopamine activity, responsible for cravings and symptoms of nicotine withdrawal (Oncken et al. 2006, Coe et al. 2005). Moreover, Varenicline had an upper hand on the long-term cessation when compared to Bupropion; another commonly used smoking cessation medication (Cahill et al. 2016). However, little is known about Varenicline's association with seizures and hence several clinical, legal and legislative implications need to be elucidated. Here, we will report on a case of a young male who suffered seizure on the day of the last dose of the suggested drug regimen.

2. Case presentation

2.1. Patient information

A 26-year-old male, used to smoke a pack per day, for 10 years. He used the Varenicline regimen that is based on intake of 0.5 mg twice daily for 14 days, then 1 mg once daily for 28 days. He was brought to the emergency department after he had a first time witnessed seizure while driving. The seizure happened after he completed the first course of 0.5 mg Varenicline in a 14-day period. The dosing regimen for the drug was based on the direction of a general practitioner (GP) and was against the drug leaflet instruction.

The patient used the morning dose between 8-10 am and then suffered seizure at 6 PM, before using the second evening dose. However, the patient confirmed that he was not using the drug in a fixed interval; instead it was twice daily, with variable intervals.

The patient had no past medical history of epilepsy or childhood febrile seizures. There was no history of drug use or abuse, epileptogenic herbal or any other medication beside the Varenicline. He stopped smoking when he started to use Varenicline.

2.2. Clinical findings

His seizure commenced as a brief staring followed by a lower right limb jerky movement that became a generalized clonic seizure; it lasted for three minutes. His seizure was witnessed by a relative; an emergency physician; who was with the patient in the same car. The patient then regained consciousness with no post-ictal confusion or sleepiness. No prodromal symptoms. Upon arrival at the Emergency Department (ED) his Glasgow Coma Scale was 15/15 his pupils were reactive and a full neurological examination was normal.

2.3. Diagnostic assessment

His Blood glucose and his electrocardiograph (ECG) were normal. His basic lab results were all within normal range,

including complete blood count and electrolytes panel. The Computed Tomography (CT) brain scan revealed no intracranial insult and was within normal range.

2.4. Therapeutic interventions

The patient was observed for four hours during the ED stay with no recurrence noted and was advised to return to the ED if another seizure occurred.

2.5. Follow up and outcomes

A telephonic follow up was after 18 months, and revealed that the patient was in good health, and the seizure did not recur.

We utilized the Naranjo nomogram (Naranjo et al. 1981) to determine whether the seizure was actually attributed to the drug being studied; rather than other confounders. The patient's total score was six, signifying that our patient's seizure was probably related to the drug Varenicline. Table (1) illustrates the Naranjo nomogram score for our patient.

Table 1: The Naranjo nomogram probability scale for Varenicline seizure.

Item	Our patient	Interpretation
Are there previous conclusive reports on this reaction?	Yes	+1
Did the adverse event appear after the suspected drug was given?	Yes	+2
Did the adverse reaction improve when the drug was discontinued or a specific antagonist was given?	Yes	+1
Did the adverse reaction appear when the drug was readministered?	Not done	0
Are there alternative causes that could have caused the reaction?	No	+2
Did the reaction reappear when a placebo was given?	Not done	0
Was the drug detected in any body fluid or toxic concentrations?	Not done	0
Was the reaction more severe when the dose was increased, or less severe when the dose was decreased?	No	0
Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	Not done	0
Was the adverse event confirmed by any objective evidence?	No	0
Total score		6

3. Discussion

Because the medication is renally eliminated in approximately 24 hours, (Faessel et al. 2006) this raises a question of whether the seizure was a withdrawal symptom rather than a side effect. In a support of a withdrawal theory, one patient suffered a seizure during the phase of dose reduction from 2 mg to 1 mg per day (Serafini et al. 2010). In addition, the variability in the timing of each dose may in fact support the previous notion in the case of our patient. Aligning with that; neither the previous patient nor our patient suffered seizures after the cessation of medication during follow up.

From another perspective; the Varenicline regimen failure and hence the abrupt cessation was noted due to nausea. This is the most common and earliest side effect and hence, further explains why most seizures, noted during the first month of treatment (Oncken et al. 2006). On the whole we support the notion that Varenicline seizures are a withdrawal symptom rather than a side effect.

In addition, a history of seizures were noted as a risk factor based on the drug manufacturer's website <https://www.chantix.com/support-for-taking-chantix/chantix-savings#important-safety-information>. However, our patient neither had a history, nor family history of seizures and he was not sleep deprived and was not using any other medications. The fixed-dosing regimen that our patient followed may seem a risk for a seizure, nonetheless, seizures were reported by the manufacturer despite their suggested gradual regimen. From the literature review, we were unable to infer risk factors that are prone to develop seizures. Therefore, all users are at risk and should be cautioned. Further studies are suggested.

From a legal perspective; patients with epilepsy are prohibited from driving based on several countries' legislation. Similarly, it should be stated clearly that driving should be prohibited during the Varenicline withdrawal phase, whether at the end of the regimen or during dose reduction. This prohibition should also advocate those operating risky professions, like pilots and also those performing risky activities like diving. We believe, this is the healthcare provider's responsibility to caution users, whether primary physicians or pharmacist as the drug is sold over the counter.

In conclusion, despite the glamorous efficiency of Varenicline, it possesses a risk of seizure. Healthcare providers should convey information of the risk to patients during smoking cessation counseling. Patients at risk during dose reduction and medication cessation should not drive or engage in risky activities. Those working crucial safety occupations like pilots should be strictly off Varenicline and preferably during the whole course of treatment.

The case report has written in an anonymous characteristic, hence, detailed information about the patient was removed.

We declare no conflict of interest.

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