



## Tramadol-induced Seizure in a Nigerian Female Quarry Labourer: A Case Report

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### Abstract

*Tramadol is a centrally-acting atypical opioid-like analgesic with serotonin reuptake inhibition used in the treatment of pain. Seizure is one of its complications and can occur with its therapeutic use, abuse or overdose. Presented here is a 25-year old quarry worker who had seizure in two different occasions, each following increased dosage of oral tramadol being abused as an agent to reduce pain and increase the strength required to keep her menial job. The erroneous impression the father in-law had about seizure after the second episode led to patient coming to our facility. She was motivated to stop the drug and with psychotherapy, she stabilized and there was peace in the family. A continual public enlightenment aimed at educating people on drug abuse and reduction of the erroneous sociocultural beliefs about seizure is highly recommended.*

**Keywords:** *Tramadol, seizure, quarry worker, Nigeria.*

### Introduction

Tramadol is a synthetic analogue of codeine which acts as a pure opioid agonist and is known to exhibit its analgesic effect by inhibiting the reuptake of nor-epinephrine and serotonin endogenous neurotransmitters that modulate pain “Boostani & Derakhshan,<sup>(1)</sup>”.

The maximum recommended dose is 400 mg/day “Bamigbade & Langford,<sup>(2)</sup>” and doses above this have been associated with adverse effects such as respiratory depression, acidosis, hypotonicity, and seizures among others.

Seizures have been reported to occur both in overdoses and in recommended therapeutic doses.

The exact mechanism by which tramadol induces seizure is not yet clearly elucidated. However, it has been noted that in high concentrations tramadol exerts an inhibitory effect on gamma-aminobutyric acid (GABA) receptors “Rehni et al,<sup>(3)</sup>” and the inhibition of these receptors has been found to potentiate the severity of seizures in animal models “Sun et al,<sup>(4)</sup>”

Some studies have also demonstrated that tramadol-related seizures may occur especially in association with consumption of other drugs such as alcohol, selective serotonin reuptake inhibitors, tricyclic antidepressants, and antipsychotics “Ripple et al,<sup>(5)</sup>; De Decker et al,<sup>(6)</sup>”.

### Case History

Mrs PQR is a 25-year old married quarry worker who had abused pain relievers along with some other workers for over 5 years. They believed they needed pain relievers to sustain their hectic job. She started with paracetamol and later ibuprofen until two years ago when some of the men working with her in the same place introduced her to tramadol. She started with 200 mg a day and within twelve months, she had increased to 600 mg a day, taken in three divided doses – 200 mg in the morning before she leaves for work, 200 mg in the afternoon while at work, and 200 mg in the night before she goes to bed. Sometime in May 2018 she was reported to have convulsed in the workplace at about the time of closure of work. She was rushed to a nearby private hospital where she was observed over the night before she was discharged home. She later revealed that the previous evening, on her way from work, she bought the drug (having noticed that she was left with only the one tablet for that night). But she did not know that the make given to her was that of 400 mg strength against her usual 200 mg per tablet. So, the day she convulsed, she took 400 mg in the morning and 400 mg in the afternoon thinking she took 200mg in each circumstance. She had no past history of seizure or any form of head injury and no member of the family was known to have suffered from epilepsy. Though she was advised to stop tramadol after the convulsion, she had to continue with the drug as she believed that the drug made her not to feel the pain of the hectic job she was doing and she also argued that almost every of her co-workers was taking the drug but none had convulsed. She willingly stopped drinking alcohol some years earlier when she was pregnant of her first child and she never smoked or used tobacco or any other psychoactive substance in any form nor did she use any medication concomitantly.

In January 2019, there was a downward review of the salaries of the staff of the firm. To compensate for that, some of them had to work extra hours. She decided to increase the dosage of the tramadol

from 600 mg daily to 1000 mg in divided doses of 400 mg, 200 mg and 400 mg. On the second day of this increased dosage, she convulsed in the morning during Sunday church service while sitting down. It was gathered that she had a good night sleep the previous night and also ate well before leaving for the church that morning. Back from the church she was taken to a native practitioner for cleansing, on the directives of the father in-law who believed that the convulsion was as a result of her marital infidelity (notwithstanding that she maintained that she had never had any extramarital sexual relationship). She spent three days in the native practitioner's treatment home. While she was there she was given some local concoctions and reported to have had no other fit. On discharge, the father in-law insisted that she be taken to a hospital to be investigated for HIV and other sexually-transmitted diseases (STDs) and for the treatment of the bite she inflicted on her lips while convulsing (figure A). According to the father in-law, the native practitioner does not treat self-inflicted injuries on someone he considered unfaithful to the husband. Each of the seizure episodes was described to be tonic-clonic in nature. On their insistence, she and her husband were screened for HIV and other STDs with no remarkable finding. Her blood sugar and other haematological parameters yielded normal results. The father in-law, however, objected to electroencephalography; he argued that the patient's problem was not with her head or brain but with her sexual organs. Patient admitted that she was already dependent on tramadol but was prepared to do anything to stop it to avoid the false accusation from her father in-law and the kind of embarrassment she brought to herself when she convulsed in the church.



**FIGURE A: SEIZURE-RELATED MOUTH/LIP ULCERS**

An assessment of the patient with the Naranjo scale - an Algorithm or Adverse Drug Reaction Probability Scale which is used to assess whether there is a causal relationship between an identified untoward clinical event and a drug using a simple questionnaire to assign probability scores “Naranjo et al<sup>(7)</sup>” - yielded a score of 8, suggesting strongly the probability of the seizure being as a result of the tramadol consumption.

The lip injury was attended to. She had some sessions of individual psychotherapy aimed at encouraging her to sustain her zeal for abstinence. Subsequently, family sessions were organized. She has remained abstinence and seizure-free for over six months, coping very well with her job without taking any drug; and the views of the entire family members appeared to have changed as at the last contact when a home visit to the family was undertaken.

### Discussion

Patient PQR is a female. Studies have shown that there is a high prevalence of tramadol use and seizures among males compared to female “Boostani & Derakhshan,<sup>(1)</sup>; Taghaddosinejad et al<sup>(8)</sup>”. This case is one of the few cases that support that females equally abuse the drug and can as well come down with its complications.

The patient reported here sustained trauma (tears and abrasions) on the face. An Iranian study to determine the prevalence, type and site of the injuries due to tramadol-induced seizure reported that the commonest site of trauma was the face with abrasion as the commonest type of trauma “Farajidana et al<sup>(9)</sup>”.

The two seizure episodes in this patient occurred within 24 hours of increased doses of the drug. This finding is in line with many reports where seizure secondary to tramadol use occurred few minutes after tramadol intravenous injection “Usmani & Azmat<sup>(10)</sup>” or few hours after oral ingestion “Majidi & Fard<sup>(11)</sup>”.

Though this patient had taken tramadol for over 2 years, she never developed seizure until she took a dose higher than 400 mg a day. This supports the views of many researchers that the side effect (seizure) is dose-dependent “Taghaddosinejad et al<sup>(8)</sup>” though some researchers think otherwise “Talaie et al<sup>(12)</sup>” but it has been observed that the most common dose range of tramadol in individuals with seizure is 500–1000 mg “Talaie et al<sup>(12)</sup>”.

The seizure noticed in this patient was of the generalized tonic-clonic type which has been reported as the commonest type of tramadol-induced seizure “Boostani & Derakhshan,<sup>(1)</sup>”.

The intake of tramadol by Mrs PQR was intentional. In an Iranian study to examine the relation between seizure and plasma tramadol concentration in patients with tramadol poisoning it was noted that intentional overdose was the most common mode of poisoning “Taghaddosinejad et al<sup>(8)</sup>”.

In most reported cases of seizure associated with tramadol, there is either a history of seizure and/or a co-administration of another drug such as a selective serotonin reuptake inhibitor (SSRI), an antidepressant, or an antipsychotic “Usmani & Azmat<sup>(10)</sup>” but the case reported here is a clear case of seizure related to only tramadol use, an uncommon finding just as earlier reported by Decker and team “De Decker et al,<sup>(6)</sup>”.

The patient had the first episode of seizure when her daily dose was mistakenly increased from 600 mg to over 800 mg. A further attempt to increase the dose above 600 mg led to the second episode of seizure, supporting the report that for patients who have had a tramadol-induced seizure, the likelihood of recurrent seizures is high “Shadnia et al<sup>(13)</sup>”.

The belief about the aetiology of epilepsy has been a concern globally. In many communities, people with epilepsy are still seen as having low social value and they face social rejection, as evidenced in this case from the attitude of the father-in-law to her.

### Conclusion

Tramadol is a novel centrally acting analgesic beneficial in the treatment of mild to severe pain. Its abuse in recent times in Nigeria has been reported to be on the increase. Seizure is an unfortunate complication, especially when taken high doses. The current efforts by the Nigerian government to curtail the importation and abuse of opioid pain killers should be encouraged and strengthened. Public enlightenment aimed at educating people on drug abuse and reduction of the erroneous sociocultural beliefs about seizure is recommended.

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