



# Pregabalin abuse among patients with chronic pain syndrome

Rania Kamal Hassan Hashish<sup>1</sup>; Tariq Elemam Awad<sup>2</sup>

<sup>1</sup>Department of Forensic Medicine and Clinical Toxicology, Faculty of Medicine, Suez Canal University, Ismailia, Egypt

<sup>2</sup>Department of Neurosurgery, Faculty of Medicine, Suez Canal University, Ismailia, Egypt

**\*Corresponding Author(s): Rania Kamal Hassan**

## Hashish

Department of Forensic Medicine and Clinical Toxicology, School of Medicine, Suez Canal University Hospital, 4.5 Kilo of the round road, Ismailia, Egypt 15213

Tel: 0020-128-2691-648, Fax: 0020-6439-23-439;

Email: Raniakhashish@yahoo.com

## Abstract

**Background:** Pregabalin abuse liability is underestimated and the evidence of abuse and dependence is emerging. It has many health and social consequences especially in patients with chronic pain syndromes. Pregabalin abuse has not been well studied among the Egyptian population.

**Purpose:** This study aims to estimate the prevalence and associated correlates of pregabalin abuse among patients with chronic pain syndromes in Egypt.

**Study design:** A descriptive cross-sectional study.

**Methods:** Two hundred patients with chronic pain syndrome were interviewed. Patients who fulfilled the diagnostic criteria for pregabalin dependence according to DSM 5 criteria for substance use disorders were enrolled in pregabalin abuse group. The study group was categorized into two groups; the control group (149 patients) and the pregabalin abuse group (51 patients). Participants were evaluated monthly for three consecutive months. History regarding pain medication usage was strictly taken. Pain was scored by 100 visual analogue scale for pain; additional information was asked from pregabalin abusers including dose, symptoms and dependence manifestations.

**Results:** Pregabalin abuse was more common among males, heavy manual workers, smokers and patients with other drug/substance abuse. Pain syndrome had more duration in pregabalin abuse group. The higher the pain intensity, the higher the direction for pregabalin abuse. The most common clinical symptoms of pregabalin abuse were fatigue, memory problems, dizziness and drowsiness.

**Conclusion:** Pregabalin has significant abuse potential, it is considered as an attractive drug to patients with chronic pain syndrome due to its sedating and psychedelic effects. Misuse of this prescription drug is a serious emerging issue which should be monitored carefully.

Received: Feb 24, 2020

Accepted: Mar 19, 2020

Published Online: Mar 23, 2020

Journal: Annals of Anesthesia and Pain Medicine

Publisher: MedDocs Publishers LLC

Online edition: <http://meddocsonline.org/>

Copyright: © Hashish RKH (2020). *This Article is distributed under the terms of Creative Commons Attribution 4.0 International License*

**Keywords:** Pregabalin; Abuse; Misuse; Dependence; Chronic pain syndrome



## Introduction

Abuse of prescription drugs is considered as a global problem, it is defined by the National Institute on Drug Abuse (NIDA) as “taking a medication in a manner/dose other than prescribed; taking someone else’s prescription, even if for a legitimate medical complaint such as pain, or taking a medication to feel euphoria” [1,2] Pregabalin is an analog of the neurotransmitter Gamma-Amino Butyric Acid (GABA), it act as inhibitory modulators of neuronal excitability, and it reduces the ectopic neuronal activation of hyper-excited neurons without affecting normal activation [3]. Pregabalin has been approved for the treatment of partial onset seizures, neuropathic pain, fibromyalgia, and general anxiety disorders [4-7]. Initially, it was thought that pregabalin has a low misuse potential and it was classified in the US as a schedule V drug (i.e. lowest potential for abuse) [5]. The reported euphoria - as an adverse event - that occurs in about 10% of patients is the suspected main cause of its abuse [8]. Pregabalin has a significant abuse potential [9], its misuse should be monitored carefully [10].

The serious emerging issue of pregabalin abuse is spreading in Egypt as well as many countries in the world. When this drug is taken in doses larger than its therapeutic doses; this might lead to very serious adverse effects and death [11,12].

To the best of our knowledge; there is not any study that explores and describes pregabalin abuse among chronic pain syndrome patients. This study aims to estimate the prevalence and associated correlates of pregabalin abuse among patients with chronic pain syndromes in Egypt. The pattern of pregabalin abuse was also studied.

## Patients and methods

This study was designed as a descriptive cross-sectional study. It was conducted between February 2017 and September 2019, at Suez Canal University Hospitals (Ismailia, Egypt). Ethical approval was obtained from Institutional REC.

Two hundred patients suffering from chronic pain syndrome were interviewed. Chronic pain is defined as pain that persists past normal healing time; lacks acute warning function of physiological nociception. Pain is considered as chronic when it lasts/recurs for more than 3 to 6 months [13].

Patients who have predominant chronic pain syndrome due to degenerative or inflammatory process, and those with a proper diagnosis of the cause of pain according to proper investigations were included in the study.

Exclusion criteria ruled out patients with malignant causes of chronic pain, patients with psychological causes of chronic pains and those of vague causes of pain.

The patients were recruited from the Neurosurgery out-patient clinic at Suez Canal University Hospitals (Ismailia, Egypt). All patients filled out a pre-designed questionnaire, it includes socio-demographic data; data about history of their pains, investigations that had been performed; management offered and pain medication usage. Pain intensity was measured using 100 visual analogue score (VAS). Follow up visits were conducted monthly for three consecutive months. At each visit; pain medication usage was recorded via questionnaire and pain intensity was measured using VAS for each patient.

## Participants

A total of 200 patients (97 female, 103 male) of chronic pain syndrome were interviewed for pregabalin abuse. Patients who fulfilled the diagnostic criteria for pregabalin dependence according to DSM-5 criteria for substance use disorders were enrolled in pregabalin abuse group. Those patients should have one or more of the eleven abuse criteria in DSM-5 within the preceding 12-month period. The criteria are related to pregabalin hazardous use; social/interpersonal problem related to its use, legal problems, withdrawal symptoms, tolerance, use of larger amounts of pregabalin, repeated attempts to quit use, and physical and/or psychological problems related to pregabalin use [14].

The patients were categorized into two groups: Control group (149 patients) and Pregabalin abuse group (51 patients). To include patient in pregabalin abuse group, he/she should had been pregabalin dependent for at least 1 year, those who are not pregabalin abusers were enrolled in the control group for comparison.

In pregabalin abuse group, additional data were gathered including dose of pregabalin per day, symptoms of pregabalin abuse and dependence pattern of pregabalin abuse.

## Results

A total of 200 (97 female, 103 male) chronic pain syndrome patients with a mean age of  $44.8 \pm 20.1$  years (range 20–74) were interviewed for pregabalin abuse. The control group included 149 versus 51 patients in the pregabalin abuse group. The demographic data of both groups are presented in table 1, it shows that the two groups are fairly non homogeneous.

The mean age in the control group was  $45.3 \pm 13.6$  years in comparison to  $39.2 \pm 18.7$  years in the pregabalin abuse group. Pregabalin abuse was high in male gender 60.8% in comparison to 48.3% in control group. Also smoking was common in pregabalin abuse group 60.7% versus 24.8% in control group. Other drug/substance abuse was present in 39.2 % of the pregabalin abuse group in comparison to 4.7% in control group.

On average, patients had pain symptoms duration for 28 months (range 6 –54 months). Patients in the control group had mean pain symptoms duration for  $24 \pm 18$  months in comparison to  $32 \pm 18$  months in patients in pregabalin abuse group.

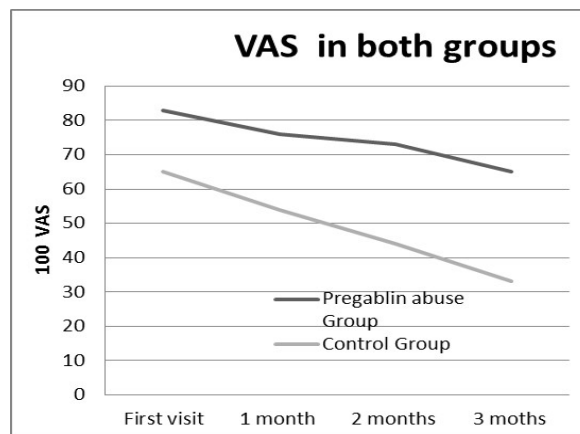
The diagnosis of patients in the study group was presented in table 2; it showed that both groups of patients were homogeneous in regard to the cause of chronic pain syndrome. Chronic low back pain and chronic radiculopathy were the most common causes of chronic pain syndrome (24.1 % and 22.1% in control group) versus (23.5.5% and 27% in pregabalin abuse group) respectively.

We used the 100 visual analogue scale (VAS) to assess and compare pain intensity in both groups of patients. The 100 VAS score for pain showed statistically significant higher values in pregabalin abuse group in comparison to the control group that was evident all over the follow up period (Figure 1).

More data was studied in the pregabalin abuse group to clarify dependence pattern. The average daily dose of pregabalin in pregabalin abuse group was 450-600mg in 25.5% of patients, 600-900mg in 31%.3 of patients and 900-1200mg in 21.6% of

patients. The clinical symptoms in pregabalin abuse group are presented in table 4. These include fatigue in 49 patients (96%), memory problems in 39 patients (76.5%), dizziness in 35 patients (68.6%), drowsiness in 33 patients (64.7%), Blurred vision in 32 patients (62.7%), tremors in 31 patients (60.7%), irritability in 29 patients (56.9%) vomiting in 20 patients (39.2%), and suicidal thoughts in 20 patients (39.2%).

Dependence symptoms of pregabalin abuse are presented in table 5. Experiencing withdrawal symptoms when pregabalin use is stopped was present in 48 patients (94.1%). Believing that pregabalin has stopped working was present in 45 patients (88.2%). Trying to quit pregabalin but failing was present in 39 patients (76.1%).



**Figure 1:** Comparison of pain score in both groups all over 3 months follow up period using 100 visual analogue scale (VAS).

**Table 1:** Demographic data of the study groups

N (%)	Control group n=149	Pregabalin abuse n=51	Total N=200
	n(%)	n(%)	N(%)
Gender: Male	72 (48.3%)	31(60.8%)	103 (51.5%)
Female	77 (51.7%)	20 (39.2)	97 (48.5%)
Age, yr. Mean±SD:	45.3±13.6	39.2±18.7	44.8 ± 20.1
Range:	(21-74)	(20-72)	(20-74)
Age group			
Age 20 -	16 (10.7%)	7 (13.7%)	23(11.5%)
Age 30 -	40 (26.8%)	13 (25.5%)	53(26.5%)
Age 40 -	42 (28.2%)	14 (27.5%)	56 (28%)
Age 50 -	31(20.9%)	12 (23.5%)	43(21.5%)
Age 60 -	20 (13.4%)	5 (9.8%)	25(12.5%)
Occupation			
Heavy manual work	48 (32.2%)	28 (54.9%)	76 (38%)
Light manual work	101(67.8%)	23 (45.1%)	124 (62%)
Residence			
Urban	80 (53.7%)	28 (54.9%)	108 (54%)
Rural	69 (46.3%)	23 (45.1)	92 (46%)
Body mass index	29.9± 3.7	26.9±4.6	27.4±3.9
Positive smoking history	37 (24.8 %)	31 (60.7 %)	68 (34 %)
Other drug/substance abuse	7 (4.7 %)	20 (39.2 %)	27 (13.5 %)

**Table 2:** Diagnosis of chronic pain in patients of both study groups

	Control Group n=149	Pregabalin abuse Group n=51
Chronic Radiculopathy	33 (22.1%)	14 (27.5%)
Chronic Myelopathy	12 (8.1%)	3 (5.9%)
Chronic low back pain	36 (24.1%)	12 (23.5%)
Cervical Spondylosis	17 (11.4%)	4 (7.8%)
Failed Back Syndrome	13 (8.7%)	7 (13.7%)
Peripheral neuritis	29 (19.5%)	9 (17.6%)
Other Diagnosis	9 (6.1%)	2 (3.9%)

**Table 3:** Daily dose of pregabalin among pregabalin abuse group

Daily dose of pregabalin / mg N=51	n (%)
450- 600	13 (25.5%)
600-900	16 (31.3%)
900-1200	11(21.6%)
1200-1500	8 (15.7%)
> 1500	3 (5.9%)

**Table 4:** Clinical Symptoms of pregabalin abuse group.

* Clinical symptoms of pregabalin abuse n=51	n (%)
Fatigue	49 (96%)
Memory impairment	39 (76.5%)
Dizziness	35 (68.6%)
Drowsiness	33 (64.7%)
Blurry vision	32 (62.7%)
Tremors	31 (60.7%)
Irritability	29 (56.9%)
Vomiting	20 (39.2%)
Suicidal thoughts	20 (39.2%)

\*more than one choice are allowed

**Table 5:** Dependence symptoms among pregabalin abuse group.

*Dependence symptoms of pregabalin abuse. N=51	n (%)
Withdrawal symptoms when pregabalin use is stopped	48 (94.1%)
Believe that pregabalin has stopped working	45 (88.2%)
Try to quit pregabalin but failed	39 (76.1%)
Continue to take pregabalin despite unpleasant physical side effects, relationship problems, or issues at work	26 (50.1%)
Take pregabalin with alcohol or other drugs to cope with emotional pain or life circumstances	20 (39.2%)

\*more than one choice are allowed

## Discussion

Pregabalin is a gamma-amino butyric acid (GABA) analogue that increases neuronal GABA level and inhibits the release of excitatory neurotransmitters like glutamate, noradrenaline. Pregabalin has been approved for the treatment of partial onset seizures, neuropathic pain, fibromyalgia, and general anxiety disorders [5,6,7].

Pregabalin is one of the most commonly reported prescription narcotics that be abused worldwide [1]. Recent estimates suggest that 1% of the general population misuse pregabalin [15]. Reports of misuse normalized to prescription number suggest that drug dependence is reported with pregabalin [16]. Schwan et al reported that pregabalin misuse is increasing [8]. Grosshans et al reported that pregabalin have a high misuse potential due to its rapid absorption and fast onset of action [17]. Unsurprisingly, known substance misuse is associated with misuse of pregabalin [16-19].

To date, there is little data about pregabalin abuse in Egypt. The current study highlighted the problem of pregabalin abuse in Egypt; it also provided an overview about the problem of its abuse.

The present study showed that pregabalin abuse was more common among males, this result is similar to that of other studies which consider being a male as a risk factor for the addictive behavior [1,20], it showed also that pregabalin abuse is more common among heavy manual workers; this can be explained

by its highly sedative effect that encourage heavy manual workers to misuse it.

The present study also reported that pregabalin abuse is more common among smokers and patients with other drug or substance abuse. This result agree with that Al-Husseini et al, 2017 who reported that pregabalin abuse is common among cigarette smokers and poly-drug users [21]. This can be explained by that some pregabalin abusers mix it with other drugs like tramadol and synthetic cannabinoid to potentiate its effect [21].

Chronic pain syndrome had more duration in pregabalin abuse group. Our study showed that the cause of chronic pain syndrome is not associated with pregabalin abuse. It may be postulated that neuropathic pain may predispose to pregabalin abuse but this was not evident in our study.

Our study showed that the higher the pain intensity in chronic pain syndrome, the higher the direction for pregabalin abuse. This can be explained by that these patients try to use higher than the prescribed dose to obtain more sedating effect. The average daily dose of pregabalin abuse was 450-900mg in 56% of patients. The most common clinical symptoms of pregabalin abuse include fatigue, memory problems, dizziness and drowsiness.

Our data suggest that pregabalin is liable to be abused among individuals with chronic pain syndrome. Thus, vigilance and caution are called for when patients are exposed to treatment with pregabalin to limit the possibility of its misuse

## Conclusion

Pregabalin has significant abuse potential and is an attractive drug to patients with chronic pain syndrome. Misuse of this prescription drug is a serious emerging issue which should be monitored carefully.

## limitations of the study

Pregabalin abuse group was small in number, the study was conducted only upon patient admitted Suez Canal university Hospital in Ismailia city, It is recommended to conduct further future studies in other cities .

## Disclaimer

The authors had not got any financial support and have no financial interests concerning the submitted article.

Ethical approval was obtained from the Institutional REC.

Authors declare that they have not any conflict of interest

## References

1. Al-Husseini A, Abu-Farha R, Hout MC, Wazaify M. Community pharmacists experience of pregabalin abuse and misuse: A quantitative study from Jordan, Journal of Substance Use. 2018; 24: 273-279.
2. Lessenger JE, Feinberg SD. Abuse of prescription and over-the-counter medications. The Journal of the American Board of Family Medicine. 2008; 21: 45-54.
3. Papazisis G, Tzachanis D. Pregabalin's abuse potential: A mini review focusing on the pharmacological profile. International Journal of Clinical Pharmacology and Therapeutics. 2014; 52: 709-716.

4. Bandelow B, Wedekind D, Leon T. Pregabalin for the treatment of generalized anxiety disorder: a novel pharmacologic intervention. *Expert Rev Neurother*. 2007; 7: 769-781.
5. Boomershine CS. Pregabalin for the management of fibromyalgia syndrome. *J Pain Res* 2010; 3: 81-88.
6. Brodie MJ. Pregabalin as adjunctive therapy for partial seizures. *Epilepsia*. 2004; 45: 19-27.
7. Tassone DM, Boyce E, Guyer J, Nuzum D. Pregabalin: a novel gamma aminobutyric acid analogue in the treatment of neuropathic pain, partial-onset seizures, and anxiety disorders. *Clin Ther*. 2007; 29: 26-48.
8. Schwan S, Sundström A, Stjernberg E, Hallberg E, Hallberg P. A signal for an abuse liability for pregabalin--results from the Swedish spontaneous adverse drug reaction reporting system. *Eur J Clin Pharmacol*. 2010; 66: 947-953.
9. Millar J, Sadasivan S, Weatherup N, Lutton S, Lyrica N. Recreational Pregabalin Abuse in an Urban Emergency Department. *Emerg Med J*. 2013; 30: 874.
10. Moore RA, Straube S, Wiffen PJ, Derry S, McQuay HJ. Pregabalin for acute and chronic pain in adults. *Cochrane Database Syst Rev* 2009: CD007076.
11. Drug Enforcement Administration, Department of Justice. Schedules of controlled substances: placement of pregabalin into schedule V. Final rule. *Fed Regist*. 2005; 70: 43633-5.
12. Filipetto F, Zipp C, Coren J. Potential for Pregabalin Abuse or Diversion After Past Drug-Seeking Behavior. *J Am Osteopath Assoc* 2010; 110: 605-607.
13. Treede RD. Entstehung der Schmerzchronifizierung. In: Baron R, Koppert W, Strumpf M, Willweber-Strumpf A, editors. *Praktische Schmerztherapie*. Heidelberg: Springer. 2011: 3-13.
14. Deborah H, O'Brien C, Auriacombe M, Borges G, Bucholz K et al. DSM-5 criteria for substance use disorders: Recommendations and rationale. *Am. J. Psychiatry*. 2013; 170: 834-851.
15. Smith RV, Havens JR, Walsh SL. Gabapentin misuse, abuse and diversion: a systematic review. *Addiction*. 2016; 111: 1160-1174.
16. Chiappini S, Schifano F. A decade of gabapentinoid misuse: an analysis of the European Medicines Agency's 'Suspected Adverse Drug Reactions' database. *CNS Drugs*. 2016; 30: 647-654.
17. Grosshans M, Lemenager T, Vollmert C, Kaemmerer N, Schreiner R et al. Pregabalin abuse among opiate addicted patients, *Eur J Clin Pharmacol*. 2013; 69: 2021-1025.
18. Boden R, Wettermark B, Brandt L, Kieler H. Factors associated with pregabalin dispensing at higher than the approved maximum dose. *Eur J Clin Pharmacol*. 2014; 70: 197-204.
19. Papazisis G, Garyfallos G, Sardeli C, Kouvelas D. Pregabalin abuse after past substance-seeking behavior. *Int J Clin Pharmacol Ther*. 2013; 51: 441-442.
20. Gahr M, Freudenmann R W, Kölle M A, Schönfeldt-Lecuo-na C. Pregabalin and addiction: Lessons from published cases. *Journal of Substance Use*. 2014; 19: 448-449.
21. Al-Husseini A, Wazaify M, Van Hout MC. Pregabalin misuse and abuse in Jordan: A qualitative study of user experiences. *International Journal of Mental Health and Addiction*. 2017; 16: 642-654.