

Original Article

Abuse liability of gabapentin in the Saudi population after the pregabalin restriction: A cross-sectional study

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المخلص

أهداف البحث: سوء استعمال الأدوية الوصفية موضوع مثير للخلاف والجدل في المملكة العربية السعودية، وذلك بسبب سهولة الحصول على الأدوية من صيدليات التجزئة. تهدف دراستنا إلى تقييم ما إذا كان السكان السعوديون، في جدة، قد استبدلوا تعاطي بريجابالين - أحد الأدوية التي تم تقييدها مؤخرًا لصيدليات المستشفيات فقط - إلى جابابنتين.

طرق البحث: أجريت دراسة وصفية، وتم جمع وتحليل البيانات خلال شهر واحد، من خلال استبانة تم بناؤها ذاتيا ووزعت عبر منصات التواصل الاجتماعي. وشملت بنود الدراسة ما يلي: (١) الخصائص الديمغرافية للمشاركين؛ (٢) تاريخ الإدمان (إن وجد)؛ (٣) الاستخدام غير الطبي لجابابنتين (عدد مرات الاستخدام، الاستخدام المتزامن مع أدوية أخرى والمحفظات)؛ و(٤) طريقة اكتشاف الاستخدام غير الدوائي للجابابنتين.

النتائج: تم جمع ٣٧٠ مشاركة وكان معظم المشاركين من الإناث ٢٨٩ (٧٨.١٪)، ومعظم أعمار المشاركين دون سن ٣٠ سنة وعددهم ٣٠٠ (٨١.١٪)، وكان لدى ٧٢ (١٩.٥٪) شخصا تاريخ إدمان على الأدوية الوصفية. وكانت أغلب الأدوية التي ورد ذكرها هي بريجابالين ١٧ (٤.٦٪). بالإضافة إلى عدد اللذين أساءوا استخدام جابابنتين ١٠ (٢.٧٪)، حيث أفاد نصفهم (٥) عن سوء استخدام بريجابالين في السابق. معظم مسيني استخدام جابابنتين قد سمعوا عن تأثيره واستخدامه من الأصدقاء ٨ (٨٠٪) وكان أكثر الأسباب المحفزة للاستخدام هي "قضاء وقت ممتع" ٦ (٦٠٪). وبالإضافة إلى أن نصف مستخدمي جابابنتين قد أجابوا بأنهم يتعاطون الدواء بشكل أسبوعي.

الاستنتاجات: سلطت هذه الدراسة الضوء على احتمالية انتقال المسيئي استخدام بريجابالين إلى الجابابنتين. ننصح بتكثيف حملات التوعية لتثقيف كل من المجتمع وصيدليات التجزئة والمجتمعية بشأن هذه المسألة.

الكلمات المفتاحية: تعاطي؛ إدمان؛ جابابنتين؛ بريجابالين؛ المملكة العربية السعودية

Abstract

Objective: Following the recently conducted local studies on the growing misuse of pregabalin, Pregabalin misuse has received national attention. These studies have led to the authorities restricting the availability of pregabalin to hospital pharmacies alone. While the recent epidemiological studies and case reports found gabapentin to be misused worldwide, it was previously presumed to be free of any abuse potential. This study assesses the likelihood of there being a diversion to Gabapentin abuse following the Pregabalin restriction in Jeddah, KSA.

Methods: A cross sectional observational study was conducted between November 2017 and December 2017 using a self-constructed online survey via Twitter and WhatsApp. The survey items included participants' demographics, additional history, Gabapentin for non-medical use (frequency, concurrent use with other drugs, and motivators), and how the participants knew about the Gabapentin misuse. The data was subjected to a descriptive analysis via the utilization of frequencies and percentages. The analysis was carried out by using SPSS V21.

Results: Data of the 370 respondents who took the surveys were collected. Most of the respondents were women (n = 289; 78.1%) and below the age of 30 years (n = 300;

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81.1%). A total of 72 respondents (19.5%) had a history of psychoactive drug abuse. Ten of the respondents reported Gabapentin misuse (2.7%). Half of the participants reported prior Pregabalin misuse, and were unemployed. Most of the misusers ($n = 8$; 80%) came to know about the psychotropic effects of Gabapentin from friends. The most common motives for using it were to 'have fun' and 'peer pressure' ($n = 6$; 60%). Half of the misusers used Gabapentin on a weekly basis.

Conclusion: The findings of our study suggest a potential diversion from Pregabalin to Gabapentin misuse. Regulations and periodic reviews of the psychoactive prescription medications available in the community pharmacies are essential.

Keywords: Abuse; Addiction; Gabapentin; KSA; Pregabalin

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Introduction

Prescription drug abuse is a growing problem in KSA. This is due to a number of factors, such as ease of access to medications with euphoric or inhibitory effects via some community pharmacies (not requiring valid prescriptions prior to dispensing),¹ and the mis-conception and perception that prescription drugs are less harmful than the other illicit drugs.^{2,3}

The Ministry of Health (KSA) has passed many regulations and policies to regulate the dispensing pattern of prescription-only medications. They also moved controlled substances to the hospital pharmacies to facilitate a better protection and control of the dispensing pattern of drugs such as opioids and Pregabalin (recently).⁴

Pregabalin misuse received national attention following the recent studies conducted locally. This led to the authorities restricting the availability of Pregabalin to hospital pharmacies alone in order to ensure that there are stringent dispensing methods in place.⁵ Recent epidemiological studies and case reports have found a similar Gabapentinoid (Gabapentin) misuse across the world,^{6–9} while it was previously presumed to have no abuse potential.^{10,11}

Both Gabapentin as well as Pregabalin work by decreasing the central neuronal excitability via their GABA-mimetic action.¹² Pregabalin has been approved by the Food and Drug Administration (FDA) for numerous indications such as neuropathic pain associated with diabetic peripheral neuropathy, postherpetic neuralgia, spinal cord injury, fibromyalgia, and as an adjunctive therapy for adult patients with partial onset seizures.¹³ Gabapentin has been approved by the FDA for postherpetic neuralgia management and as an adjunctive therapy for the treatment of partial seizures.¹⁴

However, owing to Gabapentin's several off-label uses such as use for bipolar disorder, neuropathic pain, diabetic neuropathy, migraines, restless leg syndrome, and drug and alcohol withdrawal seizures, it has been widely prescribed by and dispensed commonly among physicians and pharmacists.¹⁵ In addition to its low cost, the rapid dose titration schedules and it being 'uncontrolled' make it easier for the public to acquire it and potentially misuse or abuse it.¹⁶

A study conducted in the United Kingdom reported an increase in the prescriptions of Gabapentin by 150% in just 5 years.¹⁷ The prevalence of Gabapentin misuse in the general population has been reported by a systematic review that included reports from the United States, the United Kingdom, Germany, Finland, India, South Africa, and France. The review found the prevalence in the general population to be 1%, with 40–65% misuse cases found among individuals with prescriptions and 15–22% cases found among opioid abusers.¹⁸

Some of the recent studies that aimed to shed light on the prevalence of Gabapentin misuse reported the effects to vary based on the varying doses, past experience of users, psychiatric history, and expectations. Misusers tend to use Gabapentin in doses of above 3600 mg at once, and usually in combination with other centrally acting substances such as opioids and alcohol.^{7,19–21} Furthermore, Gabapentin's use with opioids is associated with 60% increased odds of opioid related deaths and 4-fold increase of respiratory depression and/or altered mental status.^{22,23}

The aim of this study is therefore, to assess the likelihood of there being a diversion to Gabapentin abuse following the Pregabalin restriction in KSA.

Materials and Methods

A cross-sectional observational study was conducted. The study was conducted between 30 November 2017 and 5 December 2017, and the data were collected through a self-constructed online survey. An Arabic self-constructed online survey was validated by the experts in medication misuse. Following this, Google Forms® were distributed randomly via social media (Twitter, and WhatsApp). We chose the respective social media platforms as they are the most common used platforms in the country.²⁴ A brief description of the survey, including the inclusion criteria (age >16 years) and the aim of the study, was provided. In addition, the respondents were assured anonymity and guaranteed confidentiality. Their Consent was obtained through a question check made at the beginning of the survey and before the proceeding to answering the questionnaire items. The data were subjected to a descriptive analysis via the utilization of the frequencies and percentages. The analysis was carried out by using SPSS V21.

The survey items included: (1) demographics of the respondent (age, gender, education level, income level, and employment status); (2) addiction history (cigarettes, prescription and non-prescription medications); (3) Gabapentin for non-medical use (frequency, concurrent use with other

substances, misuse motivators); and (4) how they learned about the Gabapentin misuse.

Results

A total of 370 respondents completed the survey. Majority of the respondents were women ($n = 289$; 78.1%), were between the age of 21 and 25 years ($n = 170$; 45.9%), and had a bachelor or diploma degree ($n = 277$; 74.9%). Most of the respondents' monthly income ranged from 5000 to 12,000 SAR ($n = 165$; 44.6%). Over half of the respondents were employed ($n = 258$; 69.7%) (see Table 1).

Only 76 (20%) respondents were smokers, and 72 (19.5%) had a history of previous psychoactive drug use. Majority of respondents did not specify the drugs that were abused ($n = 42$; 58.3%). However, Pregabalin ($n = 17$), and Alprazolam ($n = 10$) were reported by 23.6% and 13.9% of the respondents, respectively. While the others reported tramadol ($n = 2$; 2.8%) to a small extent, only one mentioned the name of MDMA 3,4- (Methylenedioxyamphetamine) ecstasy (see Table 2).

When asked about Gabapentin, 17 of the 370 participants reported previous use (4.6%). Only 7 (41.2%) of the

Table 1: Respondent demographics (N = 370).

		N (%)
Gender	Female	289 (78.1)
	Male	81 (21.9)
Age (years)	16–20	100 (27)
	21–25	170 (45.9)
	26–30	30 (8.1)
	30 and above	70 (18.9)
Level of education	Middle school	3 (0.3)
	High school	69 (18.6)
	Bachelor or Diploma	277 (74.9)
	Higher education	21 (5.7)
Level of income (SAR)	Less than 5000 monthly	61 (16.5)
	5000–12,000	165 (44.6)
	12,000–16,000	66 (17.8)
	6000 and above	78 (21.1)
Employment	Employed	258 (69.7)
	Unemployed	112 (30.3)
Smoking	No	294 (79)
	Yes	76 (20)

Table 2: History of psychoactive drug abuse (N = 370).

		N (%)
History of psychoactive drug use	No	298 (80.5)
	Yes	72 (19.5)
	Unspecified ^a	42 (58.3)
	Pregabalin ^a	17 (23.6)
	Alprazolam ^a	10 (13.9)
	Tramadol ^a	2 (2.8)
	MDMA ^b	1 (1.4)

^a Percentages are derived from total number of respondents with history of substance abuse ($n = 72$).

^b MDMA = 3,4-Methylenedioxyamphetamine (also known as ecstasy).

Table 3: Habits and factors related to gabapentin misuse (N = 10).

		N (%)
Frequency	Sometimes (once a week)	5 (50%)
	Rarely (once a month or less)	3 (30%)
	No Answer	2 (20%)
Used in combination with	Nothing or not specified	8 (80%)
	Marijuana	1 (10%)
	Alcohol	1 (10%)
Motivators (purpose)	Experimenting	2 (20%)
	For fun and socializing	6 (60%)
	To get high/euphoria	1 (10%)
	No answer	1 (10%)
		1 (10%)
How did you hear about it	Friends	8 (80%)
	Social media	1 (10%)
	No Answers	1 (10%)
Pharmacists requested a prescription before dispensing	Yes	2 (20%)
	No	5 (50%)
	No Answer	3 (30%)

respondents with previous use had reported of using Gabapentin for medical purposes, while the other 10 (58.8) reported using Gabapentin for recreational purposes. (Figure 1). While five of them used it only on a weekly basis, most⁸ of them used it alone. One of the respondents reported of mixing it with alcohol and another with marijuana. Furthermore, half of these respondents had previously used pregabalin (Table 3). Moreover, while 8 had heard about the psychotropic effects of Gabapentin from friends, 6 of

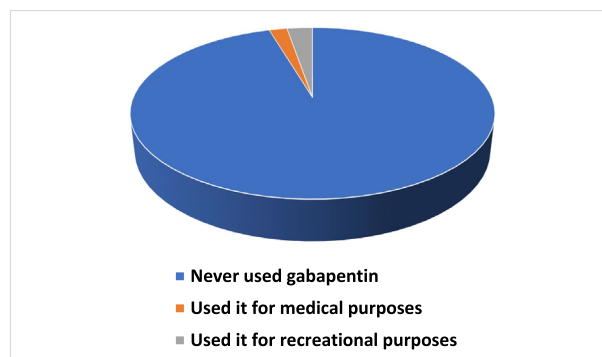


Figure 1: Gabapentin use for medical and non-medical purposes.

them chose 'to have fun and socialize' as the main motive for misuse. Of these 10 who reported Gabapentin abuse, only two of them had a prescription for it. Of the remaining 8, while 5 of them reported of acquiring it from the pharmacy without presenting a prescription to the pharmacist upon dispensing it, three of them did not answer the question.

Further sub-analysis of the 10 respondents misusing Gabapentin revealed that 6 of them were between the ages of 21 and 25 years, 7 were smokers, and 5 had a previous history of other substance-drug abuse. Moreover, 5 were unemployed, 8 of them had heard about the psychotropic effects of Gabapentin from friends, and 6 of them selected 'to have fun and socialize' as the main motive for misuse.

Discussion

Although KSA is known to have strong restrictions and strong Islamic traditions against alcohol and illicit drug use, people still use such substances despite them being socially and/or religiously unacceptable. Half (50%) of the respondents misusing Gabapentin had previously used Pregabalin, both of which are prescription drugs. The above finding may suggest a diversion from Pregabalin misuse to Gabapentin, a similar psycho-depressive agent.

As shown in our study, 50% ($n = 5$) of the Gabapentin misusers reported of obtaining the drug without being asked for a prescription by the pharmacist; however, we did not ask if they had acquired it from the street or from friends. In a recent survey of the community pharmacists in KSA pertaining to drug misuse and abuse, 36.4% of the pharmacists believed that the dispensing of controlled medications without prescription is essential for the pharmacy income. Almost 39% of them stated that they dealt with assumed drug misusers in the same manner as they dealt with other individuals. The above data is quite shocking considering that 84% of them had received training and education in drug misuse.²⁵

This calls for a more stringent dispensing policy, and the pharmacists need to be updated on the latest developments pertaining to drug misuse. The dispensing policies and awareness campaigns are still not stringent enough. One of the most important points to emphasize is the easy accessibility of prescription drugs through legitimate pharmacies without any boundaries.

Of the Gabapentin misusers, while 6 reported 'to have fun' to be their motivator for such misuse, 2 reported that they were just experimenting. Eight heard about such misuse from friends. Alosaimi et al. 2016 (titled 'Patients reasons for obtaining psychotropic medications without a prescription at retail pharmacies in Central KSA') have described the reasons for patients purchasing the psychotropic medications used to treat depression and anxiety without a prescription. The reasons provided by them primarily reflected the patients' beliefs that (1) there are minor risks in doing so, (2) the cost of physician visit is high, and (3) their physicians cannot be trusted or can provide adequate time.²⁶ As per an online survey conducted in the United Kingdom of the general population, those who misused Gabapentin or

Pregabalin procured it primarily from healthcare providers, family, and other acquaintances.²⁷

Healthcare providers should be aware of its misuse potential. Physicians and pharmacists should be educated on the ways of patients' deceptions.^{28,29} The lack of access to mental health or pain treatment facilities could also be the reason for obtaining these medications without a prescription. Extensive awareness campaigns should be held to tackle this issue. The regulatory guidelines to detect, minimize, and manage early signs of addiction should be further developed and implemented.³⁰ To have pharmacists consistently and actively conduct patient interviews prior to the handing of potentially misused medications, and following the regulations on demanding a valid prescription prior to dispensing are ways through which such danger to the public can be curbed.

This study has several limitations. They are as follows: (1) use of non-validated survey, (2) biased cohort selection, (3) small sample size, (4) short duration of the study, (5) cannot be extrapolated since most of the respondents were women <30 years of age and within Jeddah, KSA, and (6) only included those people who were active on social media and had access to technology.

Conclusion

Despite the limitations of this study highlighted in the discussion, we believe that this is one of the few studies that addresses the issue of Gabapentin abuse in KSA. Moreover, our findings suggest that there may be a potential for diversion from Pregabalin to Gabapentin misuse. Since Gabapentin was reported to have been used for non-medical purposes by only 13.9% ($n = 10$) of the respondents, half of these respondents have reported previous abuse of Pregabalin.

Of these 10 respondents, only 2 reported of presenting a valid prescription for acquiring it. Five of the 10 respondents reported of acquiring it directly from the pharmacy, without presenting a valid prescription for it. This is of serious concern as Pregabalin was also notably abused in the country, leading to the authorities allowing only hospital pharmacies to sell it. There is a great need for the enforcement of strict regulations along with periodic reviews of the psychoactive prescription medications dispensed at community pharmacies, particularly of those that are similar to the controlled substances such as Gabapentin.

Recommendations

We have multiple recommendations on how the Gabapentin potential for abuse following the Pregabalin restrictions can be accurately understood. First, conduct a randomized survey that includes a larger sample size, taking into consideration schools, universities, and rehab centres, and is spread over a longer period. Second, have a more evenly distributed and diverse respondent population with regard to gender and age. Third, perform an adequately

powered research that tracks Gabapentin filled prescriptions, and compares it to the Gabapentin dispensing rate of the community pharmacies across the country. Lastly, implement awareness campaigns led by the authorities to educate the public and community pharmacists periodically on prescription drug misuse and abuse.

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Conflict of interest

The authors have no conflict of interest to declare.

Ethical approval

This study was approved by the research ethics committee in King Abdulaziz University, faculty of pharmacy, on 30.11.2017 (Reference No: 1081439).

Authors' contribution

AAA, RAB, EAA, AFB designed the study and the methodology, collected the data, and wrote the manuscript. All the members contributed in various degrees to the analysis. AFB is the supervisor of AAA, RAB, and EAA, who were the PharmD students at the faculty of pharmacy, King Abdulaziz university, at the time of data collection and analysis. SOA reviewed the manuscript fully. All the authors have critically reviewed and approved the final draft, and are responsible for the content and similarity index of the manuscript.

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