Community Pharmacists Experience of Pregabalin Abuse and Misuse: A Quantitative Study from Jordan

Abstract

Pregabalin is an anticonvulsant that has an abuse potential. The aim of this study was to investigate abuse/misuse of pregabalin in Jordan from the perspective of community pharmacists. A cross-sectional survey using a structured questionnaire was delivered to a sample of community pharmacies. Self-reported method was used to fill the surveys. A total of 151/205 questionnaires were completed (response rate = 74.1%). A total of 132 respondents (87.4%) reported cases of pregabalin abuse in their pharmacies. Less than half of the respondents (n = 69; 45.7%) indicated that pregabalin requests were, in most of the cases, not accompanied by prescriptions. More than half of the sample (55.8%) noticed an increased pattern of pregabalin abuse/misuse during the last six months. The study underscored the need for regulatory efforts and pharmacovigilance to manage pregabalin abuse, along with a pharmacist and patient education at a community pharmacy level.

Keywords: Abuse, Communiy Pharmacy, Jordan, Pregabalin, Survey

Introduction

Abuse and misuse of prescription drugs are reported to be a global problem (Lessenger & Feinberg, 2008). Misuse of prescription drugs is defined by the National Institute on Drug Abuse (NIDA) as taking a medication in a manner or 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 (i.e., to get high). The latter definition is what is described sometimes in the literature as drug abuse (Hughes et al., 1999; Wazaify et al., 2006). While the updated definition of misuse of non prescription medicine (NPM) is to be used for a legitimate medical purpose, but in an incorrect manner either in terms of dose or duration (Wazaify et al., 2016). Abuse of NPM was defined as the use for a non-medical purpose, e.g. to achieve mind-altering effects or weight loss (Fingleton et al., 2016). NPMs misuse and abuse have increased lately, especially with the self-care revolution, the increasing number and access to medicines and the wide availability of online health information (Wright et al., 2015). By definition, any prescription or non-prescription drug can be misused, but only specific products can be abused ~~as follows.~~ (Fingelton et al., 2016). The most commonly reported prescription medications to be abused worldwide are stimulants such as methylphenidate and central nervous system (CNS) depressants such as sedatives (e.g. benzodiazepines, opioids, or pregabalin (Loftus & Wright, 2014; (NIDA, 2014).

Pregabalin is an analogue of the gamma-aminobutyric acid (GABA) mammalian neurotransmitter and its structurally related compound; gabapentin. They act as inhibitory modulators of neuronal excitability that reduce ectopic neuronal activation of hyperexcited neurons while normal activation remains unaffected (Papazisis & Tzachanis, 2014). Pregabalin is approved for the treatment of partial epilepsy; generalized anxiety disorder;

peripheral and central neuropathic pain and fibromyalgia with an accepted dosage range of 150 mg to 600 mg/day (Papazisis & Tzachanis, 2014). The reported euphoria that occurs as an adverse event in up to 10% of patients is the main cause that ~~would lead~~ contributes to abuse (Schwan et al., 2010).

A study conducted in Germany revealed that 12.1% of urine specimens that had been collected from addicts to heroin and other substances, tested positive for pregabalin without medical purpose for its use (Grosshans, et al., 2013). Another study conducted in the UK suggested that patients at high risk of addiction were prescribed higher than the recommended dose of pregabalin. Pregabalin and gabapentin were used alongside opiates to potentiate their effects. Also they can be used alone in higher than recommended doses to produce sedation and psychedelic effects. ~~So, the author~~ This study concluded that the quantities supplied should be limited because of the possibility of misuse (Loftus and Wright, 2014).

In Jordan, like other countries in the region, with the exception of controlled drugs (e.g. opioids and some benzodiazepines), almost any medicine can be bought from the community pharmacy without a prescription (Wazaify & Scott, 2017). The Jordan Food and Drug Administration (JFDA) is the legislative body that classifies medications into prescription and Over-The-Counter (OTC) drugs. However, in many cases, this legislation is not strictly enforced (Wazaify and Albsoul-Younes, 2005). ~~This a A~~vailability linked with the affordability and perception of safety of such products by the general public (Wazaify et al., 2008), may lead to the abuse of more and different kinds of ~~nonprescription~~

OTC-and prescription drugs (Albsoul-Younes et al., 2010). A study conducted in Jordan in 2014 highlighted the changes that may have happened ~~in~~ relating to this problem during the previous 10 years. The study showed the retraction of some products' suspected of abuse (e.g. misoprostol). ~~On the other hand,~~ New products have additionally appeared on the ~~new~~ list, such as the anticonvulsant, Lyrica® (Pregabalin) and ~~certain~~ specific ophthalmic drops with sympathetic, antihistamine or anticholinergics properties (e.g. cyclopentolate, Wazaify et al., 2016). This resulted in the ~~addition~~ inclusion of pregabalin containing products to a list of restricted drugs where use t~~hat~~ requires a medical prescription. but was not competent to be under scheduled controlled drugs (JFDA, 2014). In addition, it prohibited the supply of samples of drugs containing this substance or granting quantities of incentives on the quantities sold of medicines (Jordan Food and Drugs Administration, 2017a).

According to the Jordanian Drug and Pharmacy Practice Law (2013), opioids, opioid derivatives, or opioid containing preparations are controlled as Schedules 1–8 drugs. The pharmacist is required to keep a record of these special prescriptions and supply against them, for JFDA inspection. As such, a pharmacist will be subject to prosecution if found to be selling Schedules 1–8 products (Jordan Food and Drug Administration, 2017b). However, some prescription-only-medicines that are liable for abuse are not scheduled yet in many Middle Eastern countries (e.g. pregabalin ~~(~~At the time this study was conducted), performance enhancing hormones, some anticholinergic drugs).This aborts the chance to trace any violation and allows some pharmacists to sell such preparations without a prescription. (Wazaify & Scott, 2017).

Scheduling of pregabalin was documented in 2005 in the USA as schedule V of the Controlled Substances Act (CSA; Drug Enforcement Administration, Department of Justice, 2005). In Jordan, pregabalin has been scheduled to be controlled as schedule III controlled drug ~~on~~ since December 7th, 2017, (Jordan Food and Drug Administratiuon, 2017c). This study ~~came~~ was conducted prior to the scheduling of the drug in Jordan and aimed to investigate the experience of community pharmacists regarding the abuse and misuse of pregabalin products in their practice setting.

Materials and Methods

Study design, setting and subjects

This is a cross-sectional quantitative study that was conducted in Amman- Jordan between November 2016 and January 2017 to evaluate the experience of community pharmacists' regarding pregabalin products abuse and misuse. During the study period, 205 pharmacists and pharmacy assistants were approached in different community pharmacies (independent or chain) located in different regions in Amman, the capital of Jordan. They were asked to participate in this study by filling a prevalidated, prepiloted questionnairebelow). *Drop and Pick* technique was used in this part of the study to collect the data from pharmacies as explained below.

Study questionnaire and data collection

A previously validated and tested questionnaire was used in this study. The questionnaire was based originally on that used by Hughes et al. (1999). However, in order to be able to use it in Jordan the questionnaire was translated to Arabic and then back-translated to English in order to assure validity. Every effort was made during the review of literature

~~review~~ to ensure content validity. Moreover, various drafts of the questionnaire were evaluated individually by three senior academics who were PhD holders (Pharmacy Practice, Public Health Policy and a Statistician) in order to ensure face validity. The final version of the questionnaire was then distributed using drop and pick technique. Self-reported method was used to fill out the questionnaire. In this approach, the ~~study researcher~~ first author (A.A) went to different community pharmacies and handed the questionnaire personally to all pharmacists available in the shift. The completed surveys were picked up at a later time. The questionnaire was anonymous and consisted of two sections:

Section One

Limited demographic details were collected, so as to protect pharmacists' anonymity. Participants were requested to state only the name of their area where their pharmacy was located and to allocate it as being on a main road, a side street, or in a mall. Finally, pharmacists were asked to state their gender and years of experience in the profession.

Section Two

Section two included the following points:

- Pharmacists' awareness regarding pregabalin liability for abuse and main side effects
- Pharmacists' experiences with customers suspected of abusing the drug and what the signs that led the pharmacists and the researchers to suspect them, for example (the pattern and repeated requests, pharmacists' familiarity with patients and the quantity requested).
- Reporting of any pregabalin drug they had suspected in the past six months of being abused, and if they noticed the request trends were changing. The main pregabalian

products available in the Jordanian market at the time of study were: Lyrica®, Zega®, Galica®, Regab® , Epigab® and Neogaba®

- Description of suspected cases of abuse in their own pharmacies (if any), and a profile of the typical abuser of each product identified.
- Maximum number of packs that they had been requested to sell and which they suspected of being abused, and whether the patients who purchased (or attempted to purchase) these products were regular or new customers.
- Information on any strategies the pharmacists had in place to limit suspected abusers' access to the products.

Statistical analysis

The data of the completed questionnaire were coded and entered into SPSS software-version 22 for analysis. Descriptive analysis was conducted and frequency distributions were collected for responses to all questions. Chi square and Fisher exact tests were used to detect significant relationship between variables. A p-value less than 0.05 was considered significant throughout the analysis.

Results

Demographic details of participating community pharmacy staff and pharmacies

A total of 152 out of the 205 distributed questionnaires (response rate= 74.1%) were returned. Questionnaires were filled by community pharmacists and pharmacy assistants at different independent and chain pharmacies in Amman (N=90). One questionnaire was

excluded due to missing data, which ended up with a total of 151 questionnaires to be analyzed.

The majority of respondent pharmacists (n=95, 62.9%) were between 20 and 30 years of age and had a Bachelor of Pharmacy or Pharm. D degrees (n = 132; 87.4%). More than half of participating pharmacists were female (n = 89, 58.9%) and almost one-third of the pharmacists had up to one year of experience (n = 49, 32.5%). The majority of participating staff (n = 98, 64.9%) reported that they would not receive bonus if they had not achieved a target sale of products. Also, the majority of participating pharmacies were independent (n = 64, 71.1%), and located on a main road (n = 62, 68.9%). More than third of participating pharmacists (n=53, 35.1%) reported having incentive offers on pregabalin sales from medication stores. A summary of participating pharmacies and staff is provided in **Table 1.**

Insert Table 1 about here

Pregabalin products suspected of abuse and misuse

The majority of respondents (n= 132, 87.4%) suspected pregabalin product abuse/misuse in community pharmacies. Almost half of respondents indicated that pregabalin requests they had received were not accompanied by a prescription in most of the cases (n = 69, 45.7%). Most of the participated pharmacists (n=203/364, 55.8%) noticed an increased pattern of abuse/misuse with time as described in **Figure 1.**

Insert Figure 1 about here

Among pregabalin products, Lyrica® was the most frequently reported to be suspected of abuse (n=100 , 25.4%). It was reported to be mostly abused by male customers whose age ranged between 26-50 years, followed by Galica® and Zega® (n=84, 21.4%), and (n=81, 20.6%) respectively. Regarding most commonly abused strengths, 75 mg was reported to be the most frequently requested strength in community pharmacies (n=181, 46.05%). This was mainly by males whose age ranged between 26-50 years, followed by 150 mg (n=144, 36.6%). Table ~~3~~ 2 details the most frequently reported pregabalin products to be suspected of abuse/misuse by community pharmacists in Jordan.

Insert Table 2 about here

Pharmacists' methods to limit customers' access to pregabalin products

Pharmacists employed several methods to limit customers' access to products they had suspected of being abused. The two most commonly used methods, as stated by pharmacists, were insisting to have a valid prescription to dispense the product (n = 81; 54.4%) and refusing the sale and/or of stating that the product was not available (n = 70; 47%). Only 7 (4.7%) pharmacists reported that they had not acted on the problem and they had simply sold the requested products. These pharmacists ~~all~~ were all younger than 40 years of age (p = 0.636). Pharmacists with 1–5 or 6–10 years of experience had no statistically significant difference in refusing to sell the product and/or insisting to have a prescription to dispense the product (35.8% and 24.7%, respectively; p = 0.386) compared to those with less experience (16%). Also, there was no statistically significant difference in sale refusal/or insisting to have a prescription between pharmacists and pharmacy

assistants (88.9% vs. 11.1%; p = 0.692) or between pharmacy staff working in independent and chain pharmacies (61.7% vs. 38.3%; p = 0.803). More staff working in independent pharmacies (71.4%) than those working in chain pharmacies (28.6%) reported that they simply sold the requested pregabalin products just like any other product. Yet, this diffference was not statistically significant (p>0.05). Methods used to limit access to pregabalin were also not associated with gender of the pharmacists (p > 0.05). Details of the reported methods used by pharmacy staff to deal with suspected pregabalin abuse are summarized in **Table 3.**

Insert Table 3 about here

The largest amount of commonly abused pregabalin products requested simultaneously by a customer ranged between 1 and 50 packs (mean = 3.24± 5.3). In 81.9% (n = 91) of suspected customer requests, the pharmacist refused to sell the product, either by claiming that the product was not available (n = 42; 37.8%) or by insisting on having a prescription to receive the product (n = 49; 44.1%). Only 15 pharmacists (13.5%) reported selling the exact requested amount and five (4.5%) reported selling a smaller amount than that requested.

Pharmacy staff perspective regarding pregabalin requests

The majority of pharmacists (n=120, 81.6%) reported that most of the customers requesting these products were new customers to their pharmacy compared to 18.4% reported most requests by regular customers (n=27). During the study, more than half (n=78, 52.7%) of

the responding pharmacy staff noticed a difference in requesting pregabalin after the announcement to restrict amount of sale by Jordan Food and Drug Administration (JFDA) in 2014. On the other hand, a little less proportion (n= 70; 47.3%) noticed that there had been no difference in drug requests.

Discussion

This study highlighted community pharmacists' experiences regarding the suspected abuse/misuse of pregabalin in their practice setting. To the best of authors' knowledge, this is the first study in the literature to explore the problem of pregabalin abuse/misuse from community pharmacists' perspective. A previous study conducted in Jordan investigated the abuse/misuse of all drugs sold with or without a prescription in community pharmacies highlighted the emergence of new drugs on the list of suspected drugs of abuse such as: ophthalmic drops and pregabalin (Wazaify et al., 2016). This may be due to the re-scheduling of some of the most common drugs of abuse in 2013 (e.g. Alprazolam) from *'prescription-only-status'* to become controlled as schedule III drugs (Jordan Food and Drug Administration, 2014). In other words, the restriction on commonly abused drugs, has possibly led to some people looking for a legal and available alternative (Wazaify and Scott, 2017). ~~The fact that~~ We speculate that this has resulted in more reported cases of abuse of pregabalin products in community pharmacies.

At the time this study was conducted, pregabalin was classified as a prescription only medicine that did require a prescription to be dispensed. However, the Pharmacy and Drug law does not require pharmacists to keep records of these prescriptions (Jordanian Food

and Drugs Administration, 2017d; unlike the scheduled products described above), thus making it difficult for regulators to trace violations and facilitating the pharmacists to illicitly sell such preparations without a prescription (Wazaify & Scott, 2017). This practice (i.e. selling prescription-only products without a prescription) has also been noted in other Arab countries like Egypt (Jousilahti et al., 1997), Kuwait (Matowe et al., 2003), and Palestine (Sweileh et al., 2004).

It is only after a series of studies that looked into this problem (Schwan et al., 2010; Millar et al., 2013; Al-Husseini et al., 2017a) from different angles, that pregabalin has been controlled in Jordan to be schedule III drug. (JFDA, 2017c). Since community pharmacists are the most acccessible health care professionals and the first defence line against abuse of prescription and non-prescription products (Dole & Tommasello, 2002), it is believed that the scheduling the drug and the consequent tightening of inspection on its sale in community pharmacies would limit this problem. ~~Another point worth mentioning,~~ We equally recognise howver that the restriction and scheduling of prescription drugs may limit acccess of genuine patients who need the drug for different ligitimate indications (e.g. neuropathy). The effect of such scheduling will only be revealed through further research in the coming few years that follow the scheduling.

More than half of the pharmacists in our sample, confirmed that they had received suspicious requests for pregabalin products, during the past six months, most of which was the brand name Lyrica® and with a strength of 75 mg. In contrast to the observational part of the study, *(Al-Husseini et al., 2018) the generic name Zega® and the concentration 150

277 mg were the most pregabalin products requested by self-medication method (Al-Husseini
278 et al, 2017b). This may be due to the fact that pharmacists in general believe that the
279 original brands are of higher quality and ~~to be~~ are more effective than the generic products
280 (Grover et al., 2011). Moreover, the original brand name is sometimes used as a substitute
281 for the less common generic name among people (e.g. Panadol vs. Paracetamol). Male
282 gender was the most commonly suspected of pregabalin abuse, in this study. This is similar
283 to different studies in the literature considering male sex as a risk factor to addictive
284 behaviour (Gahr et al., 2013; Gahr et al., 2014).
285
286 Another point worth mentioning is that some pharmacists reported that one of the main
287 reasons of increased pregabalin abuse recently was the incentive offers from medication
288 stores. This was believed to put pressure on the responsible pharmacist to buy and sell large
289 quantities of the drug to get such incentives. So it led the JFDA in 2017 to release an
290 announcement not to grant quantities of incentives on the quantities sold of medicines
291 containing pregabalin (Jordanian Food and Drugs Administration, 2017b).
292
293 Being classified as a prescription only medicine does not allow the pharmacist to dispense
294 the drug by him/herself without a prescription written by a physician, this is where the
295 professional and ethical judgement of the pharmacist is important. Where pharmacists need
296 to differentiate between being "*ethical*" and being "*legal*" as both terms, although relevant,
297 are definitely not interchangeable. Some pharmacists may respond and sell the requested
298 large amounts of products because they perceive this as being 'legal' since this drug is not
299 “scheduled”. Moreover, 13.1 % of final year pharmacy students either disagreed/strongly

disagreed or were unsure that it was unethical to sell controlled drugs to suspected misusers/abusers (Jaber et al., 2015). Thus, it is suggested that more focus should be stressed on the teaching and practice of ethics to pharmacy graduates (Wazaify et al., 2010).

The methods employed by Jordanian pharmacists to limit the supply of pregabalin products liable for abuse did not differ from those reported by pharmacists in other countries (Ball & Wild, 1989; Paxton & Chapple, 1996; Hughes et al., 1999). Traditional methods used by pharmacists have included refusal of sale of such products or keeping them out of sight and/or requesting a medical prescription (Paxton and Chapple, 1996; Hughes et al., 1999; Albsoul-Younes et al., 2010; Wazaify et al., 2016). These methods are of limited value as patients may seek a supply from another pharmacies or what is known as "*pharmacy-hopping*" (Van Hout, 2014). This problem could be minimized if pharmacists networked more frequently with one another where a suspected abuser would be reported to other pharmacies of the locality. A better and more comprehensive system is connecting all pharmacies electronically on a national level to report about drugs of potential abuse (Manchikanti et al., 2005). Moreover, an interventional harm minimization model to identify and refer those at risk of prescription or nonprescription drug abuse could be implemenetd in community pharmacies (Wazaify et al., 2006). Such model requires training of community pharmacists and more collaborative work with physicians and community addiction teams.

Limitations of the Study

This part of the study had been limited by the following: 1) the author's delivered the questionnaires to respondents by hand. Although the success of this strategy was reflected in the high response rate (74.1%), it also could have affected the anonymity of the questionnaire and subsequently whether the pharmacy staff felt comfortable to freely report their experience. We recommend that future studies use social media or specialized internet pharmacists for these kinds of studies; 2) the data in this study were based on pharmacists' and pharmacy assistants' perceptions of day-to-day events, which was highly subjective and represented only a single point of view. A direct observational pharmacy-based study (which was already conducted, Alhusseini et al., 2017) was considered more dependable in this regard; 3) the questionnaire was filled by pharmacy personnel in community pharmacies in Amman, the capital of Jordan, which is not representative of the whole Jordan. It is recommended that future studies involve a larger number of community pharmacies in different regions all over Jordan.

Conclusion

The majority of participating pharmacists had reported that pregabalin had the potential to be abused, with most of suspected pregabalin abusers ~~were~~ male aged between 26 to 50 years old and from moderate socioeconomic class. In addition, most of the pregabalin requests were not accompanied by a prescription and were noticed to be increased during the past six months. All these findings call the attention for implementation of effective community pharmacy based interventions to raise patient, neurologists and pharmacists awareness regarding pregabalin potential for abuse and ultimately restrict prescribing and or dispensing on this product to only those in medical need.

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