

Potential for Tramadol Abuse by Patients Visiting Pharmacies in Northern Iran

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Abstract:

Background: It has been almost three decades since tramadol was introduced to the market as a centrally acting analgesic. It is claimed to have weak opioid properties and a low dependence potential in opioid-addicted patients. This study was designed to investigate the suspicion of potential tramadol abuse among patients visiting pharmacies in Babol, one of the major cities in northern Iran.

Methods: Under supervision by pharmacists, a questionnaire designed to monitor drug abuse was filled out for every patient who requested tramadol from Babol's pharmacies during 6 months (Aug. 2007 till Feb. 2008). The data obtained were used to derive descriptive statistics and to make a comparison with results from other countries.

Results: Of 162 patients (or someone on their behalf) who had sought tramadol from a pharmacy, 92 (56%) patients did not have a prescription. At least 103 (64%) patients reported criteria for addiction (ie, for feeling of psychological well being, unable to cease taking the drug, more than two weeks of tramadol use). In total, 145 (89%) patients were aged younger than 30 years, and 90 (55%) patients were aged younger than 18 years. More than 63% of patients reported a history of addiction or drug abuse. Most of the patients with no prescription (88%) had abuse/addiction criteria.

Conclusion: Patients who request tramadol from pharmacies in Babol seem to have a high potential for drug abuse, in particular those who do not have prescriptions. The high prevalence of people under 18 years of age seeking tramadol could be a worldwide trend. We recommend further governmental support for pharmacies to deal with tramadol abusers in northern Iran.

Keywords: tramadol, drug abuse, addiction, pharmacy, Iran

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Introduction

Tramadol is a centrally-acting analgesic with weak μ -opioid agonist properties, and is a weak inhibitor of norepinephrine and serotonin reuptake.¹ It has been marketed in an unregulated manner as a new generic prescription drug in Iran by The Office of Controlled Drugs and Substances during 1999–2007 in retail pharmacies. Recently, it has become one of the most widely dispensed analgesics in Iran's essential drugs list. Preclinical, clinical, and epidemiologic studies prior to 1994 suggested that tramadol has a low abuse potential^{2–6} which led the Drug Abuse Advisory Committee to recommend to the US Food and Drug Administration (FDA) that tramadol be approved as a nonscheduled analgesic.⁷ This decision was based not only on the anticipated low abuse potential, but also on the recognition that pain is often undertreated and that physicians are less likely to prescribe scheduled analgesics, especially for chronic pain. Two Phase IV studies, as well as a postmarketing surveillance study, have evaluated tramadol abuse in the US.^{8,9} Studies that have evaluated the psychological dependence and compulsive use of opioids, which are the defining features of dependence/addiction, have reported an abuse rate of 3%–16%, and defined the term “addiction” as an inability to cease use of the drug, compulsive use, continued use despite harm, and craving upon cessation of taking the drug.^{8,10} Behaviors indicating addiction include inability to take medications according to the schedule recommended by the prescribing doctor, taking multiple doses together, isolation from family and friends, inability to cease use of the drug, and use of analgesic medication (ie, tramadol) for effects other than analgesia, eg, sedation, anxiety, or intoxication.¹⁰ We used these criteria to design a questionnaire to evaluate the potential for drug abuse in a pharmacovigilance study on tramadol in northern Iran.

Methods

A multichoice questionnaire was designed to evaluate potential drug abuse as well as patient demographic information (see Table 1), and was completed by medical science students under direct supervision by pharmacists. All customers (with or without prescriptions) who requested tramadol from seven pharmacies in Babol city participated in this survey.

Patient information was obtained anonymously during a private consultation in the pharmacies after verbal consent. Tramadol addiction symptoms were deemed to be increased tramadol dosage or continuing its use without a physician's permission, inability to stop using the drug or to decrease the dose, or feeling “incomplete” upon its withdrawal.⁸ The completed questionnaire data were pooled and analyzed using SPSS software.

Results

The answers to the questionnaire are summarized in the table. Briefly, of 162 customers seeking tramadol from Babol pharmacies, 94 (58%) did not have a prescription. Most of the customers (69%) had taken tramadol for more than two weeks during the previous year, and 68% have used tramadol within the previous month (see Table 1). More than 65% of customers who sought tramadol reported an addiction history at least to a single drug and more than 57% had at least one sign of addiction to tramadol. More than 55% of the customers seeking tramadol were under 18 years of age, and 89% were aged younger than 30 years (see Fig. 1). More than 71% had been able to get access to tramadol without a prescription in the past. More than 71% had taken at least two courses of tramadol (each for more than one week's duration) during the previous year (see Table 1).

Discussion

The results of this study show that the majority of people seeking tramadol from Babol's pharmacies are adolescents/young adults taking tramadol orally and with criteria for drug addiction.

Although there are some animal studies showing that tramadol might aggravate the side effects of opioid addiction,¹¹ there is a lack of evidence to confirm the effects of tramadol dependency when it is used alone in healthy volunteers. However, clinical and pharmacovigilance reports have indicated a potential for tramadol abuse by opioid-addicted individuals.^{4,6,9,12}

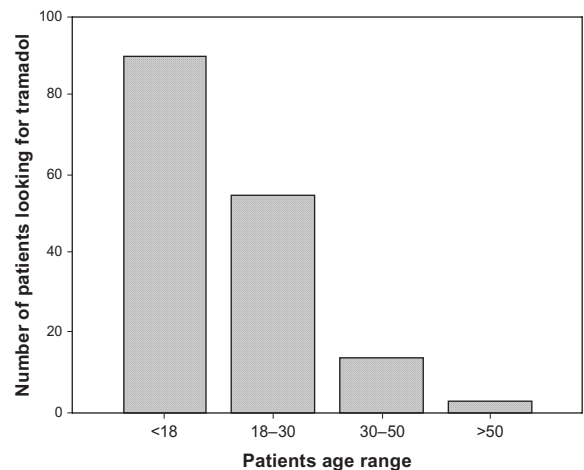
Dispensing of prescription only drugs by pharmacies without a valid prescription is illegal in Iran, so patients' access to prescribed drugs without a prescription is assumed to be negligible. However, in some circumstances, some exceptions might be

**Table 1.** Patients' (or customers on their behalf) cumulative answers to the questionnaire (percentage).

Do you have a prescription?
No: 94 (58%) Yes: 68 (42%)
Who do you want tramadol for?
Yourself: 68 (42%) Someone else: 43 (27%) Both: 51 (31%)
What age group are you in?
<18 years: 90 (55%) 18–30 years: 55 (34%)
30–50 years: 14 (9%) >50 years: <3 (2%)
Have you used tramadol before?
Yes: 115 (71%) No: 47 (29%)
How many times during last year have you used tramadol continuously for more than one week?
0 time = 7 (4%) 1 course = 43 (27%) 2 courses = 67 (41%)
3 courses = 11 (7%) 4 courses and more = 34 (21%)
Have you ever been given tramadol without a prescription?
Yes: 115 (71%) No: 47 (29%)
When did you last time use tramadol (how many months ago)?
Less than a month and always users = 20 (12%),
1 month = 82 (51%), 2 months = 27 (17%), 3 months and before = 33 (20%)
What kind of tramadol preparation do you require?
Injection: 40 (25%) Tablet:* 121 (75%)
What are you using tramadol for?
Chronic pain** 32 (19%), acute pain*** 48 (30%), psychological well being 82 (51%)
Do you have or ever had any kind of addiction to opioids or any other drugs?
Yes: 105 (65%) No: 56 (35%)
Have you ever needed to increase your tramadol dose without checking with your physician?
Yes: 68 (42%) No: 94 (58%)
Have you ever felt that you could not stop or decrease your use of tramadol?
Yes: 92 (57%) No: 70 (43%)
Have you ever felt "incomplete" when stopping tramadol use?
Yes: 69 (43%) No: 93 (57%)

Notes: *Including different trade names (eg, Biomadol®); **pain lasting more than two weeks, including cancer and chronic inflammatory disease; ***pain resulting from acute injuries (eg, trauma, headache, renal colic pain) lasting only for a few days.

considered appropriate. Pharmacy staff might dispense the minimum amount of a prescription medicine for customers who are known to be on a specific prescribed medication, and ask them to provide their prescription on their next visit to the pharmacy. A small minority of patients might be too socially insecure or financially poor to renew their prescription (pharmacists can do nothing more than dispense the minimum amount of medicine, and usually at no cost to the customer).

**Figure 1.** Age demographics of patients seeking tramadol from pharmacies in Babol, Iran.

A very small number of patients might have illegal access to their desired medicine through pharmacy employees without the pharmacist's knowledge.

Desperate opioid-addicted individuals should certainly seek opportunities to alleviate their drug cravings, but pharmacists in Iran have been trained to refer these patients to opioid detoxification clinics organized to support and treat addicts, and no prescription only drug should be dispensed without a valid prescription.

In Iran, physicians have used tramadol in the past for treating opiate dependency, even though this is not an FDA-approved indication but, because of its limited efficacy and troublesome adverse effects, this practice has waned. After all, taking tramadol without a prescription is considered to be drug abuse even if the drug is being taken for opiate addiction withdrawal syndrome.

Both rational and irrational use of tramadol has steadily increased during last two decades worldwide since it appeared in retail pharmacies as a nonscheduled analgesic in 1995.^{9,13} Tramadol was introduced to the market in Iran in 1997 as a centrally acting medicine with mild opioid properties.¹⁴ Despite early warnings about its potential for abuse by opioid-addicted individuals, access to the medication through Iran's retail pharmacies has been easy, and the concern has now been raised that tramadol is becoming a common medication of abuse, especially among youngsters.¹⁵

Opioids have been among the highest-ranked substances of abuse in Iran for centuries.¹⁶ Our finding



that young individuals are now abusing tramadol is consistent with previously reported tramadol intoxication rates among Iranian youngsters,^{14,15,17} and highlights further its potential risk for abuse among teenagers. A different age pattern for abuse of prescription drugs in the US has been reported in some studies,^{18,19} and the relatively young age profile of patients who are probably addicted to opioids in our study is of concern, because abuse of tramadol young in life might aggravate further the current prevalence of drug abuse in adults, and could lead to a socioeconomic issue in the future.

Because this study was performed in direct consultation with customers or their relatives using questionnaires designed to obtain information on personal medication history, there is the possibility of subjective bias and/or patients recall error.

Considering the high percentage of patients reporting previous access to tramadol without a prescription (more than 70%, see Table 1) who were mostly seeking tramadol for themselves and had shown at least one criterion for addiction to tramadol, it is likely that patients who request tramadol without a prescription are addicted to this drug or other opioids, and hence are highly vulnerable to tramadol abuse. In the last 15 years, the Iranian Ministry of Health and Medical Education has increased the number of retail pharmacies across the country, which has improved public access to most medicines. According to the regulations of the Ministry of Health and Medical Education, tramadol is a prescription only medicine, but addicted individuals are still able to obtain this drug without a prescription. Unfortunately, the prevalence of opioid addiction in Iran is relatively high, with the informal estimate that approximately 8% of the population is addicted to opioids. This is probably the main issue affecting poor control of dispensing of prescription only analgesics, including tramadol, in retail pharmacies in Iran.¹⁶

The validity of most of the questions contained in our questionnaire has already been tested in other populations,^{9,20} but its validity for a northern Iranian population has not as yet been clearly demonstrated. Nevertheless, the results obtained could be assumed to be valid, because patients tend to underestimate their drug abuse.

Conclusion

Tramadol is likely to be being abused by a proportion of customers seeking this drug from Babol's pharmacies, especially those who do not have a prescription. This might be because of the high number of opioid addicts in Iran. The young age profile of the patients identified as being addicted to tramadol might be related to the worldwide decrease in the prevalent age of individuals with opioid addiction. Our findings, as well as those of other studies reported in recent years, showing an increase in tramadol intoxication and morbidity, indicate a need for governmental support for pharmacies to deal with tramadol abuse, not only in northern Iran, but also in the rest of the country. In addition to public education, the recent efforts of the Iranian Ministry of Health and Medical Education in developing opiate detoxification centers across the country should be supported further by other governmental and international organizations to enable them to provide better and more widespread services to opiate-addicted patients. This could be helpful in decreasing the potential for tramadol abuse, especially among young people, if synchronized with ongoing public education.

Disclosure

This manuscript has been read and approved by all authors. This paper is unique and is not under consideration by any other publication and has not been published elsewhere. The authors and peer reviewers of this paper report no conflicts of interest. The authors confirm that they have permission to reproduce any copyrighted material.

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