Prevalence of new psychoactive substances addiction: a hospital-based cross-sectional study

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Abstract

Background: New psychoactive substances are a combined group of chemical substances developed in an attempt to circumvent control and restrictive measures for traditional drugs. Until 2017, the countries of Central Asia remained a gray spot on the maps of epidemiological new psychoactive substances reports. The largest share of new psychoactive substances on the Kazakhstani market became of a serious concern for both the law enforcement authorities and the public health services during the last five years.

Objectives: The aim of the study was to assess the proportion of hospitalizations in Kazakhstan related to new psychoactive substances addiction over a three-year period (2016-2018) and to describe the patterns of new psychoactive substances use in the sample of admitted patients.

Material and methods: This study was a retrospective, cross-sectional investigation using regional databases consisting of the 2018 cases of hospitalizations at 16 state regional mental treatment centers and 3 state narcological clinics across Kazakhstan. We analyzed 345 cases of NPS addiction.

Results: The proportion of admitted in 2018 new psychoactive substances patients amounted to 10.01% (9.1%; 11.1%), comprising an ascending trend since 2016. The highest prevalence of the new psychoactive substances addiction was registered in Nur-Sultan, Almaty cities, and North-Kazakhstan region. Cathinones prevailed over other NPS groups (71.9%) and were mostly used in parallel with traditional opioids. Synthetic cannabinoids (28.1%) were associated with herbal cannabis use in three quarters of cases; smoking absolutely prevailed as the main route of their administration.

Conclusion: This study suggests that new psychoactive substances addiction is a current clinical phenomenon, which should be reflected in the development and revision of the national drug treatment programs across Kazakhstan. The disparity of new psychoactive substances prevalence in the regions should be considered in the development of local anti-drug plans by the health care service and law enforcement authorities.

Key words: new psychoactive substances, prevalence, addiction, hospital, pattern

Received: 2020-01-20
Accepted: 2020-02-09
UDC: 618.1

J Clin Med Kaz 2020; 1(55):11-16

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ЖАҢА ПСИХОБЕЛСЕНДІ ЗАТТАРҒА ТӘУЕЛДІЛІКТІҢ ТАРАЛУЫ: ГОСПИТАЛЬДЫҚ КРОСС-СЕКЦИЯЛЫҚ ЗЕРТТЕУ

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Эпидемиология новых психоактивных веществ: госпитальное кросс-секционное исследование

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СЕКЦИОННОЕ ИССЛЕДОВАНИЕ

Р АСПРОСТРАНЕННОСТЬ ЗАВИСИМОСТИ ОТ НОВЫХ ПСИХОАКТИВНЫХ ВЕЩЕСТВ: ГОСПИТАЛЬНОЕ КРОСС-СЕКЦИОННОЕ ИССЛЕДОВАНИЕ

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Введение: Новые психоактивные вещества – это комбинированная группа химических субстанций, разработанных для попытки уклонения от контрольных и держащих мер, принятых в отношении традиционных наркотиков. До 2017 года страны Центральной Азии предstawляли собой серое пятно на эпидемиологических картах, иллюстрирующих проблему новых психоактивных веществ. Найбольшая доля новых психоактивных веществ, приходящаяся на нелегальные рынки Казахстана в регионе представляет собой предмет для озабоченности как для правоохранительных структур, так и для системы общественного здравоохранения.

Цель: Цель настоящего исследования состояла в оценке пропорций казахстанских госпитализаций по поводу зависимости от новых психоактивных веществ за трёхлетний период (2016-2018 годы) и в описании паттернов потребления новых психоактивных веществ в выборке проплеченных пациентов.

Материалы и методы: Наше исследование было ретроспективным, кросс-секционным с использованием статистических баз по госпитализациям в 16 регионах центрального Казахстана и в нарикологических клиниках. Всего проанализировано 345 случаев зависимых от новых психоактивных веществ.

Результаты: Пропорция госпитализированных с зависимостью от новых психоактивных веществ пациентов составила в 2018 году 10,01% (9,1; 11,1), демонстрируя восходящий тренд с 2016 года. Наиболее высокая распространенность госпитализаций с зависимостью от психоактивных веществ зарегистрирована в городах Нур-Султан и Алматы, Северо-Казахстанской области. Катиноны преобладали среди других групп НПВ (71,9%) и чаще использовались параллельно с традиционными опиоидами. Синтетические каннабиноиды (28,1%) ассоциировались с растительным каннабисом в трети случаев, курение в абсолютном числе превалировало как основной способ в 28,1% случаев. Катиноны чаще выявлялись среди других групп НПВ (71,9%), и чаще использовались параллельно с традиционными опиоидами. Синтетические каннабиноиды (28,1%) ассоциировались с растительным каннабисом в трети случаев, курение в абсолютном числе превалировало как основной способ в 28,1% случаев.

Заключение: Наше исследование показало, что зависимость от новых психоактивных веществ представляет современный клинический феномен, актуальный для лечебных программ по всему Казахстану. Региональные различия в распространенности новых психоактивных веществ должны быть учтены при разработке антинаркотических планов и программ правоохранительными органами и службой общественного здоровья в конкретных городах и областях Казахстана.

Ключевые слова: новые психоактивные вещества, распространенность, зависимость, стационар, паттерн

Introduction

New psychoactive substances (NPS) are a combined group of chemical substances that have been developed in an attempt to circumvent control and restrictive measures for traditional drugs. Initially, NPS were distributed as legal analogues of illegal narcotic stimulants and hallucinogens, gradually moving to the list of prohibited psychoactive substances in connection with the strengthening of legislative control around the world.

According to the United Nations Office on Drugs and Crime (UNODC) World Drug Report, 892 different substances have been newly reported in addition to the traditionally known narcotic drugs. The first official information became available in UNODC drug report on the regional market of synthetic narcotics in December 2017. According to this document, in Central Asian countries there has been a significant increase in the number of identified NPS: from 1 in 2013 to 49 in 2016 [1].

Understanding this new phenomenon in society for the development of appropriate decisions and measures emphasizes the relevance of the epidemiological studies of the NPS use prevalence among the population and the NPS market. Difficulties in the analysis of the prevalence of the NPS problems are caused by significance of NPS identification requirements for laboratories. Barriers in assessing the prevalence of NPS consumption are generated by the lack of standardized monitoring algorithms both among the general population and among vulnerable groups. The epidemiological information is currently being accumulated separately at the country level and within sporadic regional studies.

Until 2017, the countries of Central Asia remained a gray spot on the maps of international epidemiological NPS reports. The first official information became available in UNODC drug report on the regional market of synthetic narcotics in December 2017. According to this document, in Central Asian countries there has been a significant increase in the number of identified NPS: from 1 in 2013 to 49 in 2016 [2].

The largest share of NPS on the Kazakhstani market is of a serious concern for both the law enforcement authorities and the public health service. This fact is exacerbated by poor standard monitoring procedures addressing NPS prevalence and an absence of comprehensive assessment of their harms in the given country [3].

The only pilot study to assess the proportion of Kazakhstani NPS consumers among drug addiction patients was conducted in 2017, which showed a NPS prevalence of 1-2% throughout the country with wholly disproportionate distribution of the indicator among different regions. As an illustration, state drug addiction clinics in the western regions (Aktau and Atyrau) did not admit any NPS patients, whereas in the northern regions
patients demonstrated symptoms of NPS abuse [4]. The pilot results notwithstanding, the regular analysis of hospitalizations related to NPS abuse and NPS addiction is far cry from an implementation into the public health practice.

Both the discrepancy and shortage highlight the importance of the regular monitoring of NPS prevalence in the nation-wide sample of drug-addicted patients. The indicator, as one of the few available, helps implicitly estimate the number of NPS consumers in the country and forecast the extension of NPS demands in illegal local narcotic markets.

Addressing aforementioned challenges, this study investigated the proportion of hospitalizations related to NPS addiction including cases with psychotic complications in anamnesis. The study had two specific aims: firstly, to identify the regional structure of NPS-related hospitalizations in the context over a three-year period; and secondly, to describe the patterns of NPS use in the sample of admitted patients.

**Material and methods**

Our study was conducted at 16 state regional mental treatment centers and three narcological clinics (Pavlodar Branch Of Republican Scientific And Practical Center Of Mental Health, Nur-Sultan Drug Addiction And Psychotherapy Center, Karaganda Drug Addiction Dispensary), which admit patients with symptoms of chemical addiction for detoxification and rehabilitation. This was a retrospective, cross-sectional study using databases consisting of the 2018 cases of hospitalizations at the given clinics and treatment centers. Considering the regional heterogeneity in the functioning of databases, we developed a standard research form to extract particular data related only to patients with NPS addiction: sex, age, ethnicity, education, occupation, concurrent clinical diagnoses, primary and secondary drugs of abuse, duration and frequency of NPS abuse, ways of NPS administration, history of psychotic complications. Trained specialists completed the forms only for those cases that presented with NPS addiction or NPS abuse diagnosed in accordance with related criteria of the rubrics of the International Classification of Diseases the 10-th version (ICD-10) – “F11-19”. Treatment records were checked by 19 specialists to confirm the history of NPS use as the only inclusion criterion for the study and to exclude cases of the repeated hospitalization in the given year. After applying inclusion and exclusion criteria, we analyzed 345 cases of NPS addiction.

The primary endpoints of this study were the distribution of the main demographic variables and the regional proportion of subjects admitted to the state mental hospitals due to NPS problems. The secondary endpoints of this study included patterns of NPS use and anamnestic pathways toward NPS addiction.

**Statistical analysis**

Statistical analysis was based on descriptive and comparative statistical methods. Descriptive data were presented as frequency in absolute numbers (n) and percentages for categorical variables (%), as well as mean and standard deviation for numerical variables. Data comparisons were provided with the Mann-Whitney test (U) and the Wilcoxon test (W) for numerical variables, along with the Chi-Square test ($\chi^2$) for categorical variables. The level of significance was set at $p$ – value ($p$) $< 0.05$. Crude risk ratio was calculated with a 95% confidence interval (95% CI) to verify connection between social characteristics and treatment indicators. Graphical presentation was used to describe data in percentages and 95% CI. All analytical procedures were performed with the Statistical Package for the Social Sciences (Version 20.0, SPSS Inc., Chicago, IL, USA).

**Ethical considerations**

The protocol of the study was approved by the Independent Ethics Committee of National Medical University as part of the reviewing of the grant application “Epidemiological portrait of NPS in the Republic of Kazakhstan: investigational epidemiologic study (EPI-NPS-KZ)” (27.03.2019, No.4(81)).

**Results**

The study sample was mostly males: 285 patients with NPS addiction (82.6%). Age ranged between 15 and 60 years old. The main demographic characteristics by gender are summarized in Table 1. Compared to males, female patients were more often under 25 years old, of Russian ethnicity.
Formal clinical diagnoses related to the following ICD-10 rubrics: “F12” formulated in 78 cases (22.6%), “F15” in 191 cases (55.4%), “F19” in 71 cases (20.6%). We identified significant differences in the proportion of particular NPS addiction in the regard to gender. Synthetic cannabinoid addiction were diagnosed in 76 male patients (26.7%) versus two females (3.4%) - $\chi^2=15.7$, $p<0.001$. Formal diagnosis of “F12” correlated with younger age (under 25 years old) – RR=1.58 (1.07; 2.34), $p=0.03$. Polysubstance addiction “F19” prevailed in the older subgroup – RR=1.84 (1.04; 3.27), $p=0.04$.

Anamnestic self-reports on the use of particular NPS corresponded to the clinical diagnoses. Three quarters of the analyzed cases related to synthetic stimulant misuse – 248 (71.88 %) that demonstrated the aforementioned correlation with age and sex.

The chemical verification of NPS group was provided only for one in fourteen patients. Hence, ICD-10 diagnostic procedures were based exclusively on clinical implications and anamnestic information. Self-reported cases of NPS use were described in slang: “scrorost”, “krissy”, “pivik”, “meph”, “spicy”.

We calculated the proportion of NPS addiction in relation to the number of hospitalizations with abuse of any psychoactive substances except alcohol. In 2018 among all patients with substance use disorders, the NPS proportion amounted to 10.01% (95% CI: 9.1%; 11.1%). Comparing the national rate in the given period with those of 2016 and 2017, an ascending trend in the number of NPS hospitalization was observed: in 2016 – 3.91% (3.2%; 4.7%), in 2017 – 8.23 (7.3%; 9.2%). Figure 1 summarizes the regional distribution of NPS hospitalizations over three years.

**Table 2**

| Characteristics | Synthetic cannabinoids (n=109), mean± st. dev. | Synthetic cathinones, (n=257) mean± st. dev. | W, p-value |
|-----------------|-----------------------------------------------|---------------------------------------------|------------|
| Age First episode of use | 23.27±7.43 | 26.8±4.67 | 1.8, 0.07 |
| Onset of the dependency syndrome | 23.9±7.56 | 27.2±6.56 | 2.1, 0.03 |
| Daily dose | 1.0±0.94 | 0.77±0.69 | 0.7, 0.48 |
| Daily frequency of NPS use | 3.49±2.47 | 3.35±2.87 | 0.59, 0.56 |
| Weekly rhythm of NPS use | 4.62±2.27 | 5.47±2.23 | 1.08, 0.28 |

One in five admissions in the study was caused by psychotic symptoms: for synthetic cathinones, the rate was significantly higher (24.7%, n=61) compared with other NPS (5.6%, n=4). A half of those with current psychoses experienced up to two delusional and hallucinatory episodes in anamnesis.

**Discussion**

A vast majority of current publications focus their attention on acute effects of NPS intoxication and report more than 150 side effects caused by hundreds of toxic substances [5]. In addition, media reports shed lights on the most drastic cases of NPS abuse complications such as cardiac arrests, psychotic outbreaks, epileptic seizures and aggressive behavior...
In this regard, law enforcement authorities develop a broad range of controlling measures to alleviate NPS situation. As a result, experts register regular changes within illegal markets and continuous transformation of NPS user profiles. Initially supposed to substitute illegal narcotics, NPS have become associated with severe addiction symptoms and disruptive social negligence exceeding those of traditional drugs.

Patients with the NPS abuse and the NPS addiction constitute a vulnerable group underrepresented in medical programs and rehabilitation facilities all over the world. Meanwhile, serious side effects associated with NPS use warrant the broader utilization of evidence-based medical and psychosocial interventions for this group of population. Poor treatment compliance and low therapeutic retention limit the NPS patient capacities for complete remission and successful social adaptation [7].

The high-risk NPS use is widely regarded by a number of international boards as a modern phenomenon that absolutely needs to be subjected to thorough examination and scrutiny. According EMCDDA, the term high-risk NPS use covers the following conditions: combination of NPS and traditional drugs, injection of NPS, presence of socially marginalized background and concurrent mental health problems [8].

For the first time in Central Asia, according to available information, our study investigated the patterns of the high-risk NPS use in a hospital-based sample. We revealed that in 42.03% (n=145) of cases NPS addiction was accompanied by traditional drug abuse. Patients reported the combination of synthetic cathinones with traditional opioids in a fifth of the cases (20.87%), of synthetic cannabinoids in a third of the cases (28.1%). One-third part of stimulant users reported parenteral routes of drug administration including slamming, referred to in Russian as “marafony”.

In the present study we found that the prevalence of NPS addiction in drug using patients fluctuated among different regions, nationally comprising 10.01% (95% CI: 9.1%; 11.1%) of all substance use disorders except alcohol. The ascending three-year trend implicitly indicates the serious social and legal implications of the NPS emergence to consider and examine. The present results highlight the significance of this issue for public health, indicating the regions where NPS problems pose serious concern. We explain it as a result of the drastic penetration of new synthetic narcotics into the local markets from neighboring Russia and China. This assumption corresponds with the stable exponential growth of NPS hospitalizations in Pavlodar, North-Kazakhstan regions and Almaty city. Various social, legal and economic factors may contribute to the recent peak of NPS admissions in Nur-Sultan (Astana) city, such as tight restriction and consequential shortage of traditional narcotics on the illegal markets, larger young population, the role of state hub. Recently, an increasing number of epidemiological studies have shown that the NPS prevalence correlates with the effectiveness of legal prohibition systems. According to the world statistical data, the NPS prevalence in psychiatric or drug addiction clinics ranges between 10 and 30% related to the severity of NPS restriction [9].

In Kazakhstan, the legal system of NPS scheduling has developed over the nine-year period resulting in the prohibition of more than 100 harmful substances. In parallel, the government has established a procedure for the rapid banning of any other newly emerged drugs from the July of 2019 [10]. In light of these facts, we expect a substantial change in the 2019 NPS prevalence that justifies our interest in further investigation.

Our finding revealed some distinctions in social profile of the NPS patients, compared to analogous studies with hospital-based samples. The sample of Kazakhstani NPS patients is distinct in that younger, has a higher rate of male unemployment. This may indicate the extreme vulnerability of the nation youth population that has become more exposed to the NPS emergency. Universal gender barriers in all drug treatment systems may explain the low proportion of women in hospital samples that was also observed in our study. The rate of psychotic complications in our sample corresponds with the international level of 30% and reflects the need for more robust emergency care addressing NPS poisoning and intoxication. The observed NPS use patterns indicated the high frequency of daily narcotization episodes along with variable NPS dosages in our patients that agree with the findings reported by Stanley and Subeliani [11, 12]. The short period between the first episode of NPS use and addiction onset demonstrated the rapid development of the NPS dependency syndrome and is consistent with previous literature data on destructive nature of synthetic drugs [13, 14].

Undertaking subgroup comparisons, we revealed that synthetic cannabinoids and cathinones differed with respect to ways of drug administration. Synthetic cannabinoids were smoked in cigarettes mixed with plants (peppermint and chamomile) or vaporized through bongs (in slang bombaster). Similar to the data of other studies (Stanley, Karila) [11, 15], most of our patients reported various ways of synthetic cathinone administration, including the high-risk parenteral (n=79, 30.73%). Thus, all the identified cases of HIV (n=30, 8.69%) and viral hepatitis (n=61, 17.68%) were related to stimulant drug use.

Analyzing polydrug use, we identified two main patterns of switching from traditional drugs to NPS. Primary opioid addiction was substantially associated with synthetic cathinone abuse; synthetic cannabinoids were more popular among natural cannabis users. The distinct pathways may be related to the observation of two different patient cohorts: older high-risk opioid users and younger low-risk marijuana users. Our findings complements international reports on different patterns of NPS use in diverse social groups: Kaptienny-Foveny underlines the role of synthetic cathinones as substitutes in the event of opioid shortage [16], several surveys in thousands young adults confirm the higher popularity of synthetic cannabinoids [17, 18].

The revealed low rate of laboratory-identified NPS cases is a matter of considerable concern. Less reliable self-reports of patient and non-speified immunoassay tests are the only confirmation of NPS additions for the state clinics. Meanwhile, a range of sources underlines the importance of advanced mass-spectral laboratories in the provision of toxicological information on the most complicated clinical NPS cases for the public health service [19, 20]. In our study, shortage of exact chemical data may limit accuracy of the NPS prevalence calculation and preciseness of subgroup analysis on the use patterns.

The present study involved several other limitations that should be considered. First, our data collection was conducted retrospectively, relying only on medical records retrieved from heterogeneous databases. Thus, the obtained information would be expected to be less factual than that of prospective studies, especially considering some present findings related to NPS additions pathways. Local discrepancies of rehabilitation programs limited our interpretations regarding the real reasons behind the revealed regional disparity of medical service utilization in the given sample. Namely, Nur-Sultan along with Pavlodar and Karaganda regions are provided with highly developed rehabilitation centers that could attract more patients.
to the clinics, contributing to higher admissions including those with NPS addictions in the regions. Moreover, our design did not allow the comparison of social profiles of NPS and traditional drugs users to assess the likelihood of NPS use among different groups of chemical addicts. Finally, the prevalence of NPS addiction and NPS use patterns were assessed in the hospital-based sample, whereas unregistered NPS users remain unrepresented within the study scope. This fact limits the extent of the extrapolation of our results and underlines the necessity for future studies addressing NPS epidemiology in various social groups.

**Conclusion**

Results of our study suggest that NPS addiction is a current clinical phenomenon relevant to the national drug treatment programs across Kazakhstan. The ascending 3-year trend of NPS hospitalizations indicates the essential role of progressive treatment component 2 was implemented by ResAd, s.r.o. (LLC), Prague, Czech Republic.

*Disclosures:* There is no conflict of interest for all authors.

*Sponsor of the study:* European Union, the CADAP 6 programme (DCI-ASIE/2015/356-893), component 2 – NFP. The component 2 was implemented by ResAd, s.r.o. (LLC), Prague, Czech Republic.

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**How to cite this article:** Mariya Prilutskaya, Oleg Yussepow, Nikolay Negay, Kuanysh Altynbekov, Makpal Tokayeva. Prevalence of new psychoactive substances addiction: a hospital-based cross-sectional study. *J Clin Med Kaz.* 2020; 1(55):11-16