

Ulusal Zehir Danışma Merkezi'ne 2015-2018 Yılları Arasında Başvurulan İntihar Vakalarının İncelenmesi

The Examination of Suicide Cases with Antidepressant Use Applied to National Poisoning Counseling Center Between 2015-2018

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ÖZ

Amaç: Bu çalışmada; 2015-2018 yılları arasında Ulusal Zehir Danışma Merkezi (UZEM)'ne başvuru alan antidepresan ile zehirlenme vakaları incelenmiştir. Türkiye ve diğer ülkelerin zehirlenme raporları karşılaştırılmıştır. Kritik sayılara ulaşan intihar davranışı, antidepresan kullanımının artması perspektifinde incelenmiştir.

Gereç ve Yöntemler: 2015-2018 yılları arasında UZEM'e bildirilen antidepresan zehirlenmesi vakaları incelendi. İntihar ve kazara zehirlenme oranları, yıllık intihar oranları ve antidepresan kullanımı yıllara göre karşılaştırıldı. Literatür örnekleri ile karşılaştırılarak değerlendirildi.

Bulgular: Antidepresan ilaç zehirlenmesiyle UZEM'e başvuru alan vaka sayısı 2015 yılında 16 656 vaka (% 8,26), 2016 yılında 16 708 (% 7,66) vaka, 2017 yılında 16 218 (% 7.59) ve 2018 yılında 17 017 (% 7.83) vaka olarak kayda geçmiştir. Toplam zehirlenme vakası; 2015 yılında 201 646 iken, 2018 yılında bu sayı 217 331'e yükselmiştir. Türkiye İstatistik Kurumu (TÜİK)'nden alınan verilere göre zehirlenme ile intihar 4. sırada yer almaktadır. 2017 yılında antidepresan tüketimi 48 milyon kutuya ulaşmaktadır ve bu durum antidepresanların son zamanlarda daha ulaşılabilir olduğunu göstermektedir.

Sonuç: UZEM'e bildirilen tüm vakalar arasında antidepresan ilaçlarla zehirlenme vakaları yüksektir. Ek olarak, antidepresanlarla zehirlenmede yüksek intihar vakaları dikkat çekmektedir. Toksikovijilans açısından bu yüksek oranlar değerlendirildiğinde, antidepresan kullanımının intihar riskini artırıp artırmadığı araştırılması gereken bir konudur.

Anahtar kelimeler: İntihar, zehirlenme, toksikovijilans, antidepresanlar

ABSTRACT

Aim: In this study; antidepressant drug poisoning cases between 2015-2018 which applied to National Poisoning Counseling Center (NPCC) has examined. Turkey's and other countries' poisoning reports has compared. Suicidal behavior, which has reached such a crucial point, have examined in the perspective of increasing antidepressant use.

Material and Methods: Cases of antidepressant poisoning between 2015-2018 reported to NPCC were examined, suicidal and accidental poisoning rates were compared with suicide rates and antidepressant use by years. It was evaluated by comparison with the literature.

Results: Number of cases applied to NPCC due to antidepressant poisoning were 16 656 cases (8.26%) in 2015, 16 708 (7.66%) cases in 2016, 16 218 (7.59%) cases in 2017 and 17 017 (7.83%) cases in 2018. Total cases of poisonings are 201 646 at 2015 and it increased to 217 331 at 2018. Suicide rates with antidepressant poisoning were determined as 77.10% in 2016, 76.84% in 2017 and 77.20% in 2018. By the data from Turkish Statistical Institute (TURKSTAT) suicides by poisoning is rated as 4th place. In 2017 antidepressant consumption reached to 48 million and it shows that antidepressants are more acquirable recently.

Conclusion: Poisoning cases with antidepressant drugs are high among the all applications reported to NPCC. In addition, the high level of suicide cases in poisoning with antidepressants is remarkable. When high rates considered by toxicovigilance, it is an issue that has to be investigated if antidepressant use increase the suicide risk or not.

Keywords: Suicide, poisoning, toxicovigilance, antidepressants

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INTRODUCTION

Increased use of antidepressants in the pursuit of increasing psychiatric disorders is remarkable recently. According to report published by the Psychopharmacology Association; International Marketing Service (IMS) data shows, in 2003 the antidepressant consumption in Turkey stated as 14 million 238 thousand boxes and in 2008 it increased 120% as a result of it reached to 31 million 302 thousand boxes. This rate was increased 260% with 36 million 881 thousand boxes consumed in 2012 (1). Caner et al. (2) stated at their study in 2018; in Turkey there are almost 400 thousand of boxes of antidepressant sell per month and it shows an upward trend monthly. Also, Organization for Economic Co-operation and Development (OECD) datas showed that after 2012, the consumption of antidepressants in Turkey has continuously increased on the basis of the defined daily dose (DDD) per 1000 people. The DDD ratio, which was 37 in 2012, reached to 43.5 in 2018 (3). Another study by Özeken (4) in 2018 shows that 48 million 226 thousand boxes of antidepressant sold and the most selling antidepressant is escitalopram with 9 million 669 thousand boxes. Even known as the safest antidepressants, in SSRIs prospectus there are phrases like; "If you are depressed and/or have anxiety disorders you can sometimes have thoughts of harming or killing yourself. These may be increased when first starting antidepressants, since these medicines all take time to work, usually about two weeks but sometimes longer. Patients under 18 have an increased risk of side-effects such as suicide attempt, suicidal thoughts and hostility (predominantly aggression, oppositional behaviour and anger) when they take this class of medicines."

First generation antidepressants (MAOIs and TCAs) are no longer preferred due to their fewer treatment effects, serious side effects, narrow therapeutic index and severe toxicity in overdose. Drugs that the most seen in cases of poisoning which applied to NPCC are; paracetamol (6.78%), combined upper respiratory system drugs (4.33%), amitriptyline (4.07%), sertraline(2.47%) and flurbiprofen (2.05%) in 2008 (5). Yakıştıran et al. (6) in the 2006 NPCC report as stated the most used antidepressants in poisoning cases are; amitriptyline (36.7%), sertraline (11.42%), citalopram (9.31%), opipramol (7.26%) and mirtazapine (6.37%). Another study in 2017, Yeşiler et al. (7) found that antidepressants (22.7%) were the most common cause of drug intoxications. They found specifically citalopram (SSRI) poisonings with a rate of 30%, followed by amitriptyline poisonings with a rate of 20% (7). A 2017 study by Sungur (8) at Eskişehir Osmangazi University Medical Faculty emergency department showed drug poisoning in 465 cases and just by single drug; 37 cases of SSRI

poisoning and 7 cases of TSA poisoning were seen. Safety and effectiveness of SSRIs against TCAs and MAOIs were remarked recently; therefore SSRIs started to prescribe more. If SSRI prescriptions increase, it'll become more accessible at every house and that's concerning for suicidal or accidental poisoning.

MATERIAL AND METHODS

Ethics committee approval was gained from the ethics committee of Uskudar University (Date: 26/11/2020, Decision No: 61351342/ 2020-523). The study was planned retrospectively. In this study, the literature on poisoning with antidepressants and suicide cases was conducted. Articles, journals, books and thesis from libraries such as YÖKTEZ, Elsevier, PubMed, Web of Science, Türkiye Klinikleri etc. were investigated. Correspondences for permissions were made with the Republic of Turkey Ministry of Health to obtain data from NPCC. Datas from NPCC interpreted together with the data obtained from TURKS-TAT, World Health Organization (WHO) and OECD and compared with the worldwide rates. The poison counseling center reports of various countries have been compiled and the most frequently applied; suicide methods, poisoning agents, suicide numbers were compared and the results were interpreted. With the datas from UZEM and other researches conducted in Turkey; the rate of antidepressant and suicide cases, accident and suicide rates in poisoning with antidepressants, the most common active ingredients, antidepressant use and suicide rates, the frequency of antidepressant use and the increase in sales were evaluated. Thus, both nationally and globally the increase in the use of antidepressants and suicides with antidepressants were evaluated in a general framework.

RESULTS

The main causes of poisoning listed as; intentionally (suicide, to enjoy), accidentally, criminal (murder) and other causes. Suicide with the intoxication is the 4th most used suicide method in Turkey. The most common acute poisoning agents in Turkey according to datas from NPCC; medicines (analgesics, antidepressants, antihistamines, antihypertensives), pesticides and insecticides (organophosphate, carbamate insecticides), cleaning chemicals (bleach, detergent, naphthalene), toxic gases (carbon monoxide), other chemicals, plants and nutrients (fungi, delibal , plants), poisonous animal stings (scorpion, snake, spider) (9).

That Figure 1 shows rapid increase between 2005 and 2010. And after 2010 it shows upward trend by years. Datas between 2015 and 2018 has increased trend too even the last 2 years of data is not involved.

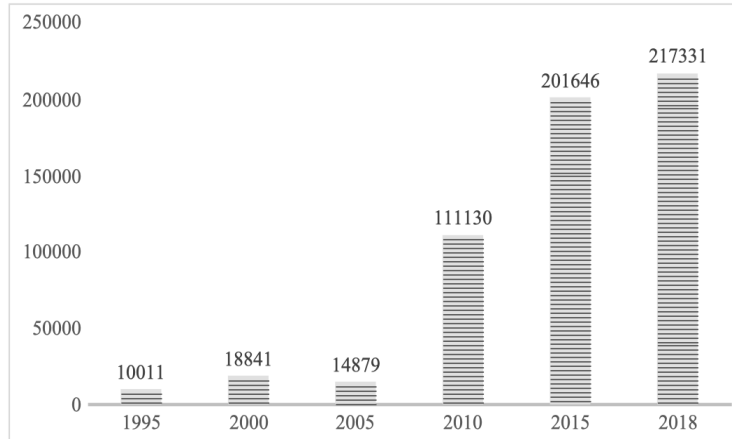


Figure 1. Total NPCC applications between 1995-2018 (5)

Table 1. Total cases and antidepressant poisoning cases between 2015-2018 which applied to NPCC

YEARS	TOTAL CASES	POISONING WITH ANTIDEPRESSANTS	%
2015	48.9±13.6	16 656	8.26%
2016	2.4±0.9	16 708	7.66%
2017	46/106	16 218	7.59%
2018	72/80	17 017	7.83%

Total poisoning cases which applied to NPCC determined as (Table 1); 201 646 cases at 2015, 218 120 cases at 2016, 213 676 cases at 2017 and 217 331 cases at 2018. From these cases; 16 656 cases (8.26%) in 2015, 16 708

cases in 2016, 16 218 cases in 2017 and 17 017 cases in 2018 applied as antidepressant poisoning. Even though it shows downward trends few years, it started to rise again at 2018.

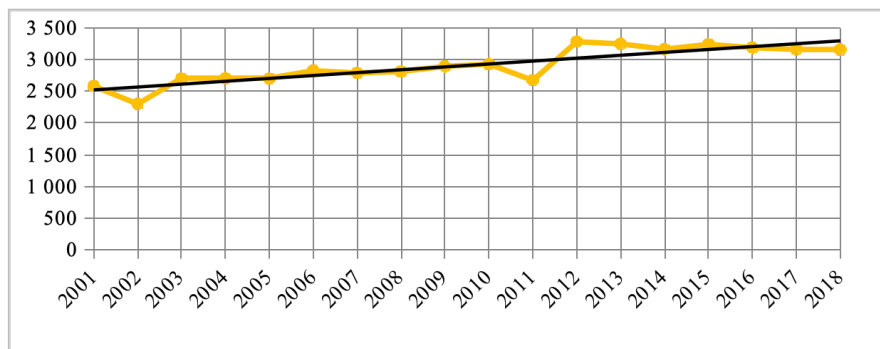


Figure 2. Total suicide cases numbers from TURKSTAT (10)

According to TURKSTAT data a linear upward trend have seen over the years (Figure 2). Increased suicide rates is expectable because of population rise but suicide rates shows greater speed than population increase which is concerning.

As explained at Table 2, even at very different countries (economically, geographically etc.) antidepressants is seen at poisoning cases oftenly. Intentional poisoning has seen at higher rate in South Africa and lower rate in United Kingdom. At South Africa the most used agent is

insecticides because it's more accessible (13). Insecticides are more available at rural countries. Accessibility is the key point at suicidal poisoning cases. Compare to these countries, in Turkey; 217 331 poisoning case has seen at 2018. By NPCC datas 17 017 cases are antidepressant poisonings. And the most used agents are; paracetamol, nonsteroidal anti-inflammatory drugs (NSAIDs), amitriptyline and sertraline (6). As it seen analgesics are coming first at poisoning cases. Because analgesics, especially paracetamol and ibuprofen are the most commonly used drugs at every country.

Table 2. Other countries' National Poisoning Center Reports of 2018 (11–14)

2018	Total cases	Intentional poisoning (%)	The most used 4 agents
USA	2 099 751	19.10%	ibuprofen, cleaning substances, cosmetics, trazodone
United Kingdom	40 466	10.20%	paracetamol, ethanol, ibuprofen, sertraline
South Africa	11 420	29.70%	insecticides, cleaning substances, antidepressants, analgesics
Finland	37 443	13.30%	paracetamol, ibuprofen, quetiapine, levothyroxine

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Table 3. Percentage of poisoning causes by years

2018	Causes of Poisoning	Numbers of Cases	%	TOTAL
2016	Suicide	12 883	%77.10	16 708
	Accident	2 232	%13.35	
	Other	1 593	%9.53	
2017	Suicide	12 462	%76.84	16 218
	Accident	2 094	%12.91	
	Other	1 662	%10.24	
2018	Suicide	13 137	%77.20	17 017
	Accident	2 076	%12.20	
	Other	1 804	%10.60	

It has shown at Table 3 by datas from NPCC that suicidal poisoning cases are quite high among the total antidepressant poisonings. Suicidal antidepressant poisonings are between 76 and 77 percentage by 2016 to 2018. Antidepressants are one of the most used drugs for suicide in Turkey. It also shows high rate in other countries but different agents has seen at different countries. For example; while trazodone is the most used in intentional poisonings in USA, sertraline is the most seen in UK and quetiapine is the most seen in Finland (11,12,14). In Turkey, researches conducted before 2008 have shown that poisoning with amitriptyline is the most common, but recent studies have drawn attention to increased rates of poisoning with SSRIs. Datas from WHO shows, compared with other countries (Figure 3), Turkey's suicide rate is significantly lower. Although Finland is a country with a high level of welfare, the high suicide rates are remarkable. This can be ex-

plained by prolonged nights and winter months. And high rates of suicide is understandable as there is not enough psychiatric services in South Africa.

DISCUSSION

Datas from the NPCC and literature show that applications to poison counseling center in our country have increased over the years. The number of applications, which was 1 143 in 1993, increased to 217 331 in 2018 (16). The correlation between suicide rates and poisonings shows that suicide numbers increased from 11 384 in 1980-1990 to 28 086 in 2010-2018 (10). Increasing suicide rates coincide with the increased poisoning applications to NPCC. It seems that the number of applications expected to increase with the increasing population over the years is much higher than the population increase.

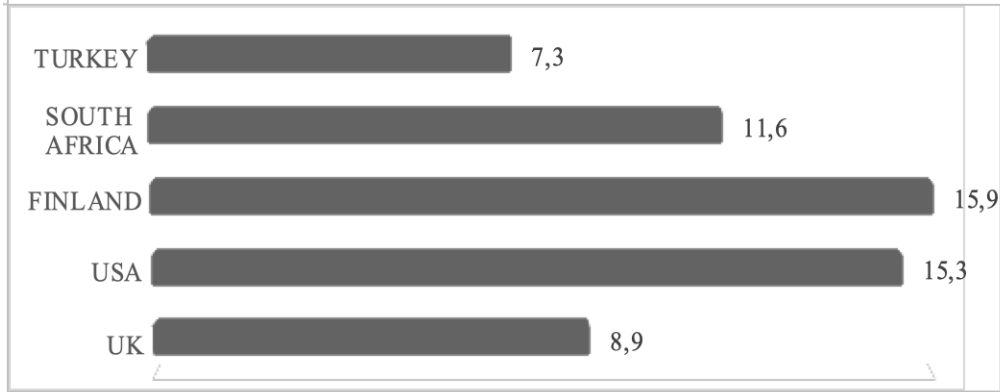


Figure 3. Suicide rates per 100,000 people (15)

Over the years, the population has increased 1.44 times, while applications have increased 190 times. The changing society, economy, media, health sector, technology and social environments over the years are effective in this increase. That drastic difference have emerged due to many different reasons such as; the newly released drug formulations as the development of the health sector, the increase in the availability of drugs, the increase in the number of drug boxes sold, increased suicide rates and increasing number of prescriptions. Also the rate of drug poisoning cases is quite high among all poisonings. Approximately 50% of poisonings are drug poisoning. In NPCC studies, analgesics (paracetamol and NSAIDs) are listed as first place and antidepressants take second place at poisoning cases (17). Datas from NPCC shows that ratio of suicidal poisoning cases with antidepressants are nearly 77% for three years. And accidental poisoning cases of antidepressants are between 12%-13%. The rate of suicidal antidepressant poisonings in total applications reported to NPCC in 2018 is 7.83% (17 017 people). In the results compiled from the studies; for children aged 0-6 years the accidental poisoning rates appear to be between 58%-65% (18). It was determined by the data obtained from TURKSTAT that suicides are concentrated between the ages of 15 and 35. Suicide rates in adults can be explained by the increase of prescribed antidepressant drugs in recent years and low cost of most antidepressants. Although the most poisonings are with non-prescription analgesics, the preference of antidepressants cannot be overlooked. Compared with other countries (USA, UK, South Africa and Finland) suicide rates in Turkey remains lower. Varnik et al. (19) conducted in his study that the most common method of suicide in Europe was the hanging (49.5%) and the second was poisoning with drugs (12.7%). Across Europe, more women than men have been reported to commit suicide by drugs. Also in Turkey, it is noteworthy that most of the suicide attempts with antidepressants are women.

In Turkey, USA, UK and Finland; drug related poisonings (analgesics and antidepressants) are higher compared to South Africa. Because in rural countries, it's easier to access pesticides rather than drugs. Furthermore, in Turkey's rural areas it is clear that suicide with pesticides is more frequent. Kaya et al. (20) in the study he conducted in Diyarbakır covering the years 2003 and 2005; 54 of 55 intoxication cases were taken to the intensive care unit with suicidal poisoning, and it was reported that 26 of these cases were poisoned with insecticide and 20 with antidepressants.

CONCLUSION

In Turkey, prescribing of TSAs and MAOIs has decreased over the years due to low therapeutic index and severe toxicity in overdose. Therefore, prescribed SSRI drugs has increased. At the applications to emergency services of hospitals, it is seen that the suicide cases with SSRIs have increased. The most common SSRIs that encountered in cases are; sertraline, citalopram and escitalopram. According to IMS datas Escitalopram is the most sold antidepressant drug (9 million 669 thousand boxes) in Turkey (4). It is noteworthy that the rate of suicide attempts is significantly higher in antidepressant related poisonings, which have a significant ratio among all therapeutic drug-related poisonings. This rate is important for toxicovigilance and it is thought that the epidemiological evaluation of these cases will contribute to the subject.

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Final Approval and Accountability- S.M.B .; Supervision- N.S.K.C.

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