

Non-medical use of Synthetic Opioids

Highlighting Tramadol

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Objectives

- Highlighting updates regarding Tramadol Dependence and Abuse on the regional and International level.
- Addressing Falsified Tramadol Trafficking.
- Discussing the need for International control of tramadol.

THE PROBLEM OF NON-MEDICAL USE OF TRAMADOL

Tramadol in high doses

- High doses of tramadol produce a signal of abuse potential, with increases on some prototypic measures such as “Liking” and increased Street Value ratings, but that this effect is seen only at supratherapeutic doses .

Source: Stoops et al , Pharmacodynamic Profile of Tramadol in Humans: Influence of Naltrexone Pretreatment, Psychopharmacology (Berl). 2012 Oct; 223(4): 427-438.

The global problem

United States of America

- According to the National Survey on Drug Use and Health (NSDUH) in 2012, 3.2 million people in the U.S. aged 12 or older used Tramadol for non-medical purposes in their lifetime.
- The Drug Abuse Warning Network (DAWN) reported that an estimated 16,251 emergency department visits were related to Tramadol non-medical use in 2010 and an estimated **20,000** related non-medical visits in 2011.
- The number of emergency department visits involving Tramadol abuse or misuse increased approximately 250% from 2005 to 2011

(Source: Drug Enforcement Administration, Office of Diversion Control, Tramadol, July 2014)

The global problem

Canada

- Canada has published a notice in part 1 of the Canada Gazette proposing a move of Tramadol to schedule 1 of the controlled substances in June, 2018.

Source: Boudreau, M. (2018, June 16) Notice to interested parties – Proposal to add Tramadol to Schedule I to the Controlled Drugs and Substances Act and the Schedule to the Narcotic Control Regulations. *Canada Gazette*. Part I, Vol 152, Number 24. Retrieved from <http://www.gazette.gc.ca/rp-pr/p1/2018/2018-6-16/html/notice-avis-eng.html>

The global problem

Northern Ireland

Studying Tramadol related deaths in Northern Ireland from 1996 to 2012 showed significant increase in the later years

- In 2001, tramadol deaths represented 9% of all drug misuse deaths rising to 40% in 2011. Tramadol related deaths were found in combination with other drugs/medicines (49%), alcohol (36%) or **alone (23%)**.

(Source: Randall C. and Crane J. 2014, Tramadol deaths in Northern Ireland: A review of cases from 1996 to 2012. Journal of Forensic and Legal Medicine.23, 32-36)

The global problem

Sweden

- Among 73 treatment-seeking adolescents and young adults at an outpatient facility for young substance users in Malmo, tramadol was the most prevalent opioid detected in hair analysis (31% of cases)

(Source: Olsson et al (2017) High rates of Tramadol use among treatment seeking adolescents in Malmo, Sweden: A study of Hair Analysis of Nonmedical Prescription Opioid Use. Journal of Addiction Vol 2017)

The global problem

Finland

- A report about the Abuse and fatal poisoning involving prescription Opioids showed that Tramadol overdose was one of the main causes of death regarding fatal opioid overdose.
- Tramadol and Codeine poisonings, as well as methadone and Buprenorphine poisonings, were mutually similar.

Source: Häkkinen M 2015 – ABUSE AND FATAL POISONINGS INVOLVING PRESCRIPTION OPIOIDS – Revelations from postmortem toxicology
<https://helda.helsinki.fi/bitstream/handle/10138/153825/abuseand.pdf?sequence=1>

The global problem

Iran

Potential for Tramadol abuse by patients visiting pharmacies in Northern Iran

- Study showed that more than half the individuals asking to buy Tramadol from pharmacies on Northern Iran did not have prescription and showed criteria of addiction (56%, 64% respectively). 55% of these individuals were below 18 years old.

(Source: Zabihi B. et al 2011 , Potential for Tramadol abuse by patients visiting pharmacies in Northern Iran, Substance Abuse: Research and Treatment, 2011:5 11–15)

The global problem

China

- A study conducted in Guangzhou city of China showed that tramadol has a high risk of producing dependence potential. A history of tramadol abuse with a long period and/or high doses maybe one of important risk factors for those with no prior drug abuse history.

(Source: Zhang and Liu 2013 - The Investigation of Tramadol Dependence with No History of Substance Abuse: A Cross-Sectional Survey of Spontaneously Reported Cases in Guangzhou City, China - BioMed Research International Volume 2013, Article ID 283425, 6 pages)

The situation in Egypt

Egypt

Results of National surveys

Prevalence of Tramadol Dependence among adults

- According to the updates of the ***National survey in Egypt***, the prevalence of Tramadol Dependence in 2015 among participants was 2.4% making Tramadol the second more prevalent substance of Dependence among Egyptians after Cannabis (Cannabis dependence prevalence 2.5%) with a slightly lower percentage.
- Moreover, the study shows that Tramadol is the most prevalent opioid that causes dependence with a significantly higher ratio than Heroin (*Heroin Dependence Prevalence 0.3%*).

(Source: National Drug Survey in Egypt , 2015 update)

Other African countries

The African problem

Nigeria

- Retrospective cross sectional study in which the clients' medical records for the stipulated period were retrieved from the Health Information Management Department of the Hospital. All relevant information which included; sociodemographic, clinical and drug-related information as well as the ICD-10 diagnoses of the clients were extracted
- Results show:
 - The prevalence of Tramadol abuse is 54.4% .
 - 91.5 % of the subjects obtained the drugs without a prescription.
 - 60.5 % met ICD-10 Diagnostic criteria of dependence

(Source: Ibrahim et al 2017 – Tramadol Abuse Among Patients Attending An Addiction Clinic in North-Eastern Nigeria: Outcome of a Four Year Retrospective Study. Advances in Psychology and Neuroscience. Special Issue: Substance Abuse: Perspectives, Trends, Issues and the Way Forward . Vol. 2, No. 2-1)

The African problem

Ghana

- Investigations show it is being used to provide manual workers with increased energy, staying alert for hours, especially for commercial vehicle drivers .
- Since 2017, over 500,000 capsules of Tramadol have been seized in Ghana.

Source: Okertchiri, JA(May 5, 2018) Ghana's Fight Against Tramadol Abuse. *Daily Guide*

Retrieved from: <http://dailyguideafrica.com/ghanas-fight-against-tramadol-abuse/>

The problem of illicit trafficking and falsified tramadol

National Egyptian Seizures

2010	132,799,052 tablets
2011	104,971,131 tablets
2012	435,622,885 tablets
2013	153,614,764 tablets
2014	156,775,468 tablets
2015	90,591,207 tablets
2016	217,057,333 tablets
2017	231,723,261 tablets

Total number = 1,523,155,101 tablets

Case Report

The Egyptian authorities seized 25,124,000 Tamol tablets 225 mg in the port of East Tafia in Port Said and 50,000,000 Tamol tablets 225mg in Misurata port in cooperation with Libyan authorities and Drug Enforcement Administration. They also seized 9808 tablets with defendants of the same case

(Total:75,133,808 Tablet).

(Money Laundering:

50,000,000 \$)





Falsified Tramadol

- National Council for Drug control in Egypt analyzed some of seized Tramadol tablets searching for the definite constituents. Three types were subjected for analysis.
- These drugs are: Tee Doll 225, Tramadol- 225 mg (Apple) & Super Tramadol- X 200 tablets (Strawberry).

- **1- Tee Doll 225**

- Each film coated tablet contains Tramadol hydrochloride BP 225 mg
- Approved colors used
- For export only
- Dosage: As directed by the physician
- Store in a cool, dry place. Protect from light.



Illicit Manufacture of Tramadol

- **2- Super Tramadol X 200 (Strawberry):**

Description: Red color tablets

- Analysis showed Tramadol and a Red coat Dye.
- Dye: Copper 3:6 Octachlorophthalocyanine
- (this dye not approved by FDA as food/drug additive, it is approved as a paint).



Illicit Manufacture of Tramadol

3- Tramadol- 225 mg (apple)

- Each film coated tablet contains Tramadol hydrochloride BP 225 mg
- Red Oxide of Iron and Titanium dioxide
- Dosage: As directed by the physician
- Store in a cool and dry dark place.



Falsified Tramadol

In 2018, analysis done for some of the seized tablets by the the **Forensic Medicine Sector of Ministry of Justice of Egypt** some of the Seized Tablets revealed the presence of wide range of impurities rather than Tramadol HCl including CaSO₄ (Gypsum), , Sodium and Calcium Bicarbonate, Starch and Lidocaine

The African problem

- According to information obtained by UNODC, the non-medical use of tramadol, particularly in northern Mali and Niger, is evolving into a health crisis at an alarming rate.
- This mirrors the trend on the wider Middle East region where the misuse of tramadol has also become a major aspect of the wider drug problem over the past years, as it is increasingly unsupervised, and falls far above the recommended dosages when it is prescribed to patients (50mg per tablet). In the region, the dosage frequently reaches 200 or 250mg, which poses a significant health risk and can generate a strong dependence.

The African problem

- According to a UNODC report, tramadol seizures have increased from 300 kg in 2013 to over 3 tons in Sub-Saharan Africa in 2017.
- Information from the UNODC also indicates that Tramadol is smuggled through the Gulf of Guinea by transnational organized crime networks to areas of Sahel partially controlled by organized crime groups and terrorist organizations.
- Tramadol is regularly found with suspects arrested for terrorism in Sahel or with those who have committed suicidal attacks.

Source: United Nations Office on Drugs and Crime (2017, December 11) *Sahel and Beyond: UNODC sounds the alarm on the increase in trafficking and consumption of tramadol and its security and health implications.* [Press release] Retrieved from <http://www.unodc.org/westandcentralafrica/en/2017-12-11-unodc-warns-tramadol-us.html>

In text: (United Nations Office on Drugs and Crime, 2017)

The African problem

- Tramadol seizures:
- September 2017, over 3,000,000 tablets seized in Niger packed in boxes *bearing UN logo* being transported from Nigeria to Northern Mali.
- August 2017, Cameroonian customs on the border with Nigeria seized 600,000 tablets intended for Boko Haram.

Source: United Nations Office on Drugs and Crime (2017, December 11) *Sahel and Beyond: UNODC sounds the alarm on the increase in trafficking and consumption of tramadol and its security and health implications*. [Press release] Retrieved from

<http://www.unodc.org/westandcentralafrica/en/2017-12-11-unodc-warns-tramadol-us.html>

In text: (United Nations Office on Drugs and Crime, 2017)

- UNODC meeting regarding Opioid Crisis in West Africa in Abuja August 2018 -. It was declared that “Non-medical use and trafficking of tramadol is becoming the main drug threat in West Africa”.
- In addition in UNODC , Togo, Nigeria, Niger, Ghana, Benin and Côte d'Ivoire were the participating countries.

Source: United Nations Office on Drugs and Crime (2018, August 27) **UNODC organizes workshop to address opioid problem in West Africa**. Retrieved from

<https://www.unodc.org/westandcentralafrica/en/2018-27-08-ecowas-workshop-tramadol-abuja.html>

The International illicit trade

- In the past year, U.S. law enforcement officials estimate that 1 billion tramadol tablets have been seized by the United States and its international partners in counter- narcotics, and actual exports could be exponentially greater.
- Southeast Asian countries, which also do not regulate tramadol, are frequently used as transit countries, with tramadol repackaged in creative ways.
- Often, the tramadol is not seized until it reaches the Middle East

U.S. Department of State, International Narcotics Control Strategy Report 2018.

International Control

- The negative consequences of Tramadol abuse necessitate that its control be expanded beyond a national control mechanism to be included under **international control**.
- While International control should not hinder the accessibility to Tramadol for medical use, but rather prevent illicitly manufactured production, thus, it can be proposed that **Tramadol should be scheduled under international control allowing prior notification of its movement and trade**.

- The fourth schedule of 1971 Convention of Psychotropic Substances states that these Substances are presenting a risk of abuse, posing a minor threat to public health with a high therapeutic value.
- International Control **SHOULD NOT** prevent the proper access to Tramadol to patients who need it yet on the contrary may help in reducing the availability of Falsified Tramadol and guarantee safer access to Tramadol.

Thank You