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A REVIEW ON THE EFFECT OF OPIOID AND OTHER ILLEGAL DRUGS ON FORENSIC STUDY

A REVIEW BY

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ABSTRACT:

Opioids are one of the most important drug classes in forensic toxicology and this study mainly focus on how the illicit use of opioids is increasing across the globe via illegal online sellers and their pharmacological actions mainly the side effects and how the consumption of overdose affects the daily activity of individuals including driving as well.

Manuscripts are categorized by study context and subject matter like: controlled experimental administration, illicit use, prescription use, retrospective forensic toxicology and polydrug consumption.

This study is carried out for the discussion and acknowledgement of chemistry, pharmacology, uses and effects of opioids along with their analysis and interpretation.

This study also focuses on how the excess use of opioid drugs makes impacts on dentistry, general health, mental health, financial constraints, behavioural changes and increased rate of mortality in individuals. This review will also provide the information about some commonly used drugs such as xylazine, naloxone, heroin, fentanyl, cocaine, methamphetamine, etc and also give the glimpse of their usage, their exposure to citizens, their overdosing limits, their cytotoxic or adverse effects on body, signs and symptoms and health risks treatment on their poisoning, antidotes and the effective strategies to reduce the risk of overdose.

INTRODUCTION:

Opiates are one of the most important classes in forensic toxicology due to their widespread medical and illicit use. While most of the naturally occurring and semi-synthetic derivatives share morphine like structure, synthetic opioids encompasses a wide variety of chemicals classification. Despite their structural differences, they all exhibit opioid receptor activity at various receptor sub-types. This study will mainly set its focus on how the World is becoming opioid epidemic, with an increased number of individuals taking psychoactive drugs while executing the task of everyday life. This review assesses the current literature regarding opioids as they relate to neurocognitive function. More recently the emergence of Novel Synthetic Opioids (NSO) have significantly complicated the landscape of opioid use and states that taking prescription

opioid for a longer periods of time or in higher dosages can increase the risk of overdose, addiction and death as well as insufficient training in pain management. A conditional logistic regression have been used to find temporal association and dispensing of drugs and the time of death. In year 2016, among synthetic opioid-involved overdose deaths, almost 80% involved another drug or alcohol, such as: another opioid, heroin, cocaine, prescription opioids, benzodiazepines, alcohol, psychostimulants, antidepressants etc.

Recent data indicates that the involvement of opioids in stimulant involved deaths is increased in decade. The CDC 2016 guidelines for prescribing opioids for chronic pain offers recommendation that may help to improve prescribing practices and ensure that all patients receive the safer, more effective pain treatment. Healthcare providers can also earn continuing the education through the interactive training series called applying the CDC guideline for the prescribing opioids.

KEYWORDS: opiates, forensic, toxicology, pharmaceuticals, interpretation, prescription, illicit, chemistry, pharmacology, tranquilizers, analysis, Novel Synthetic Opiates (NOS), mortality.

CONTENT:

Opioids are one of the most important drug classes in forensic toxicology due to their widespread medical and illicit use. While most of the naturally derived the term opioids refers to all natural semi-synthetic, synthetic derivatives. While most of the naturally occurring and semi synthetic derivatives share a morphine like structures, synthetic opioids encompass a wide variety of chemical classification. despite their structural differences, they all exhibit opioid receptor activity at various receptor subtypes. Most recently the emergence of novel synthetic opioids (NSOs) has significantly complicated the landscape of opioid use. The United States is in the midst of an opioid epidemic due to irresponsible prescribing practices, the availability of diverted pharmaceutical product, and illicitly manufactured drugs. Increases in opioid use disorder and fatal overdoses nationwide. have significantly impacted forensic toxicology. the pharmacology of opioids has been widely studied, but the effect of opioids on psychomotor function, driving and the motor vehicle collision remain less clear. Clinicians are facing the challenges of controlling patient pain while also reconciling conflicting messages from literature about how safe it is for their patient taking opioids to engage in potentially dangerous routine tasks. From 2010-2020 there were significant increase in overdose deaths involving synthetic opioids, heroin, and other illicit or prescription drugs. among synthetic opioid involved another drug or alcohol, such as another opioid, heroin, cocaine prescription opioid, benzodiazepines, alcohol, psychostimulants. in 2020 approximately 40% of deaths involving IMFs also involve stimulants. The overdose epidemic has grown increasingly complex by co-involvement of prescription and illicit drugs. For example, synthetic opioids (primarily IMFs) were involved in 23.7% of death involving prescription opioids 37.4% involving heroin, and 40.3% involving cocaine in 2016.

This study investigates severity of dependence upon heroin, cocaine and amphetamines in a group of 200 heroin users, 75% of whom were not in contact with any treatment agency for drug takers who were current users of more than one drug, heroin produced more severe dependence than either cocaine or amphetamine and many users of these stimulant drugs reported having experienced no problems of dependence. Severity of dependence was influenced by route of administration as well as type of drug. Severity of dependence was corelated with dose and duration of drug use; it was also associated with previous attendance at a drug treatment agency, through dependence problem were also common among heroin users who had never received treatment. Implications of these findings are discussed below.

Impact of opioid use on dentistry

The oral consequences of opioid drug use are commonly attributed to personal neglect of general health and financial constraints. These factors are compounded by the increasingly recognized range of physical effects by opioid drugs. The dental management of opioid drug dependents is further complicated by a variety of infections and behavioural modifications commonly associated with opioid use. Adequate strategies for the oral care of opioid users need to take cognisance of broad medical issues for these people along with an appropriate personal approach.

Recent data indicates that the involvement of opioids in stimulant-involved death is increasing. Nearly three-quarters (72.7%) of cocaine-involved overdose death also involved opioid in 2017. Previous data have indicated that synthetic opioids, in particular, appear to be driving increase in cocaine-involved overdose death. approximately one-third of psychostimulants-involved death also involved synthetic opioids in 2019.

A tranquilizer not approved for use in human called xylazine is increasingly being found in US illicit drug supply and linked to overdose death. Xylazine can be life threatening and is especially dangerous when combined with opioids like fentanyl.

The presence of xylazine in drugs tested in labs increased in every region of the United States from 2020-2021, with largest increase in the south. studies from specific areas found similar increases. One study from 10 US cities showed xylazine was involved in less than 1% of drug overdose death in 2015 and in nearly 7% in 2020.in samples from eight syringe service program in Maryland tested between 2021-2022, xylazine was found in almost 80% of drug samples that contained opioids. 10 in Philadelphia, Pennsylvania, xylazine was found in 31% of heroin and/or fentanyl overdose death in 2019.

In a recent study from CDC's State Unintentional Drug Overdose Reporting system (SUDORS), among 20 states and Washington D.C. the monthly percentage of death involving Illegally Made Fentanyl (IMF) with xylazine detected increased from 3% in January 2019 to 11% in June 2022.

Department of Health and Human Service (HHS) hosted an event which was aimed at leveraging technology and data driven solutions to help combat opioid epidemic. The authors of an interdisciplinary team from academia private sector and the US center of disease control and prevention also participated in event as a part of prevention track.

Various researchers and clinical scientists have proven that taking prescription opioids for a longer period of time or in higher dosages can increase the risk of opioid use disorder i.e. addiction, overdose, and death as well. It is important for patients and providers to discuss the risk opioids, consider alternative therapies and if prescribing opioids is appropriate, the provider should offer fewer prescriptions for fewer days and at also at lower dosages.

The overall opioid prescribing rate in United States peaked and levelled off from 2010-2012 and has been declining since 2012, but the amount of opioids in Morphine Milligram Equivalents (MME) prescribed per person is still around three times higher than it was in 1999. MME is away to calculate the total amount of opioids accounting for differences in opioid drugs type and strength. Research say that there was more than 19% reduction in annual prescribing rates from 2006 to 2017. The decline in opioid prescribing rates (>=90 MME) since 2008 suggest that healthcare providers have become more cautious in their opioid prescribing practices. In 2017,however, there were still almost 58 opioid prescription written for every 100 Americans.

More than 70% of Americans had at least one opioid prescription dispersed per patient. Per prescription the average daily amount was more than 45.3 (MME). The average number of days per prescription continues to increase, with an average of 18 days on 2017. There is a wide variability at the country level in the amount of opioids received per resident. Countries with higher prescribing have been shown to have these characteristics.

i)Generally smaller cities or larger towns. ii)
Higher percentage of white residents. iii)
Higher number of dentist and primary care physician per capita. iv)
More people who are insured or unemployed. v)
More residents who have diabetes, arthritis or any one disability.

Healthcare providers report concerns about opioid-related risk of addiction and overdose for their patients, as well as insufficient training in pain management. The 2016 CDC Guideline for prescribing opioids for chronic pain offers recommendation that that may help to improve prescribing practices and ensure patients receive safer, more effective pain treatment. Healthcare providers can also earn continuing education through this interactive training series called applying the CDC Guideline for Prescribing opioids.

Here is some important general information about some of the drugs that are mainly used by population on the large scale and which help the people to get them better about their use and also the risk factors.

Cocaine was involved in nearly in 23% of overdose death in 2021. It is a schedule II drug.

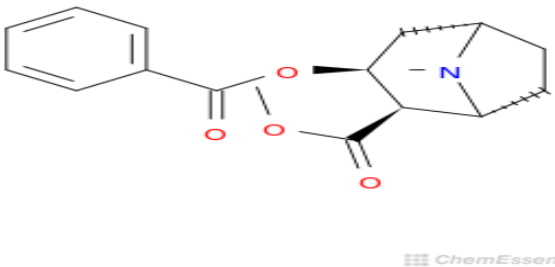
Cocaine: Biological source: *Erythroxylon coca*

1)Molecular formula: C17H21NO
2) IUPAC ID: methyl(1R,2R,3S,5S)-3-(benzoyloxy)-8-methyl-8-azabicyclo[3.2.1] octane-2-carboxylate.
3) Metabolites: Norcocaine, benzoylecgonine, cocaethylene.
4) Pharmacology :
i) Administration :- oral, intravenous, intranasal.
ii) Absorption :- great throughout body.
iii) Distribution :- 4.2L/kg after oral administration.
iv) Metabolism :- liver.
v) Bioavailability :- 90% when smoked and 80% after intranasal use; plasma half life is 1 hour.
vi) Excretion:- through renal clearance-116.2 ml/kg
5) Uses: local anaesthetic and vasoconstrictor.
6) Contraindication : allergy, hypersensitivity, hypertension or cardiovascular disease.
7) Other names: coke, blow, snow, crack, etc.
8)Mechanism of action: Blocks sodium channel and interference with action potential. The standard explanation is that cocaine blocks the norepinephrine reuptake transporter in peripheral sympathetic nerve terminals, thereby increasing the norepinephrine concentration in the synaptic cleft.
For example-Dopamine-inhibition of dopamine in pre-synaptic axon terminals increase dopamine receptor activation in post synaptic neurons, which causes the euphoric felling and arousal. 9) Side effects: bloody nose, trouble breathing, abnormal heart rhythms, chest pain, dilated pupils, inability to get or keep an erection, insomnia, restlessness, anxiety, paranoia, tremors, dizziness, muscle spasm, abdominal pain, stiffness in the back or spine, nausea, diarrhoea, extremely low blood pressure. In rare cases cocaine may lead to sudden death after its first use. This is often due to cardiac arrest or seizures.

Here are some severe side effects after a long term use of cocaine:

a) Lost of sense of smell: heavy and prolonged use can damage the odour receptor in the nose.
b) reduced cognitive abilities: this include memory loss, lower attention spam, or decreased decision making ability.
c) Inflammation of nose tissues: prolong inflammation can lead to collapse of the nose and nasal cavity, as well as holes in the roof of the mouth.
d) Lung damage : this can include scar tissue formation, internal bleeding, new or worsening symptoms of asthma, or emphysema.
e) Increased risk of nervous system damage: risk of affecting the CNS, such as Parkinson's may increase.

10)Structural formula of cocaine:



- Powerful CNS stimulant.
- Illegal drug.
- Highly addictive.
- Can be snorted, smoked, or dissolved and injected into a vein.
- For cocaine, injection and smoking were associated with equivalent dependence ratings and both of these routes were associated with more severe dependence than cocaine used intranasally.
- Local anaesthetic and vasoconstrictor properties make its useful for topical application.

Over 5 million Americans reported current cocaine use in 2020, which is almost 2% of the population. Cocaine involved overdose death rates in the united states decreased from 2004 to 2012 nut began increasing again in 2012. Non-hispanic black people experienced the highest death rate for overdoses involving cocaine overdose death rate increased by nearly 22%, with more than 24000, Americans dying in 2021 from an overdose involving cocaine.

This same study have found that Symptoms of cocaine-related heart problems.

1. Cocaine can cause immediate heart related symptoms which include increased heart rate, sweating, palpitation, chest pain.
2. A Cardiovascular Magnetic Resonance (CMR) test can detect the damage. CMR performed in people who have used cocaine show excess fluid in the heart, muscle stiffening and thickening and changes to the motion of the heart walls.
3. An electrocardiogram (ECG) can also detect silent damage in the heart of people who have used cocaine ECG study in cocaine users found that the average resting heart rate is significantly lower in people who have used cocaine in comparison with people who have not used the drug.
4. It is also found that an ECG shows cocaine users have more severe bradycardia, or abnormally slow pumping and the severity of the condition worsens when person uses cocaine for a longer period of time.

Treatment of cocaine -related heart problems.

1. Most treatments for the cocaine related heart problems or cardiovascular issues are the same as what's use in people who haven't used the drug. However cocain use does complicate some cardiovascular therapies.
2. For example people who have used cocaine can not take beta-blockers. This type of critical medication works to lower blood pressure by blocking the effect of the hormone adrenaline. Blocking adrenaline slows the heart rate and allows the heart to pump less forcefully.
3. In individuals who have used cocaine, beta blockers may actually lead to greater blood vessel constriction, which can increase blood pressure even more.
4. Some physicians are also reluctant to use a stent in heart if a person have heat attack because it can increase risk of blood clotting. At the same time doctor may be unable to use clot0busting medication if a clot does actually form.

Cocaine damages more than just your heart. Other health issues of the drug causes may include:

Loss of smell from damage to the lining of the nose.

- Damage of gastrointestinal system from reduced blood flow.
- Higher risk of contracting infections such as hepatitis C and HIV.
- Unwanted and unhealthy weight loss
- Nausea
- Abdominal pain
- Respiratory diseases
- Weakened immune system
- Gangrene of the bowels

- Cough
- Asthma
- Irritability
- Jitters
- Temporary feeling of intense happiness or pleasure
- Headaches
- Mood swings
- Severe paranoia
- Auditory hallucinations
- Panic
- Illusions
- Anxiety
- Depression
- Impaired judgement
- Aggression
- Repetitive and abnormal behaviours
- Seizures
- Stroke
- Death

Symptoms of cocaine addiction include:

- A tolerance for the drug, requiring large amount to get high.
- An inability to stop or reduce usage.
- Withdrawal symptoms when usage stops.
- A desire to keep using even when health complication arise.
- A negative impact on quality of life, relationship, and employment.
- Spending excessive time and money looking for cocaine.
- Psychosis and hallucinations.
- Disappearing for binge session.

Getting the help for cocaine use- Regular cocaine use increases risk of heart attack and stroke. That's because cocaine can cause damage the heart almost immediately after beginning the use, and the damage builds the longer the drug being used.

Quitting cocaine doesn't immediately reduce the risk for cardiovascular health problems, since much of the damage can be permanent. However, quitting cocaine can prevent further damage, which reduces risk for heart related health issues, such as, heart attack.

What happens if you use cocaine while being pregnant?

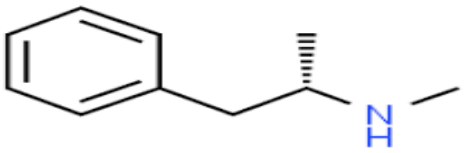
- Using cocaine while being pregnant is dangerous for both the mother and the fetus.
- The substances in cocaine can pass the placenta that surround the fetus and affects its developing heart nutrition source and nervous system.
- Hence there are chances of miscarriage, premature birth, cardiac and neurological defects in fetus.
- And impact on the brain's dopamine level can also remain In the mother after giving birth.
- Some postpartum symptoms include-
    - postpartum depression
    - anxiety
    - withdrawal symptoms like- nausea, diarrhoea, dizziness, irritability, intensive cravings etc.

Treatment – Cocaine is a highly addictive drug. Repeated use can lead to the dependence of the drug, which may make withdrawals more difficult. Have a talk with a physician about finding help to quit the drug. Physician may refer to a substance abuse counsellor or a rehabilitation facility. These organization can help to overcome withdrawals and learn to cope without the drug for a frequent cocaine user or even if the use is occasional, seeking for a professional help may be beneficial.

Millions of adults reported using Methamphetamine.

Methamphetamine: Biological source- *Ephedra sinica*

1) Molecular formula: C10H15N
2) IUPAC ID: (2S)-N-methyl-1-phenylpropan-2-amine
3) metabolites: 4-hydroxymethamphetamine and amphetamine
4) Pharmacology:
i) Administration :- orally ingested, snorted, smoked, injected.
ii) Absorption :- rapidly absorbed from GIT.
iii) Distribution :- through most organs especially lungs and intermediate part of brain.
iv) Metabolism :- Liver.
vi) Bioavailability :- 67% when smoked; plasma half life is 15 hours.
vi) Excretion :- through kidney.
5) Uses :- uses to treat Attention Deficit Hyperactivity Disorder (ADHD), used to treat obesity.
6) Contraindication :- glaucoma, overactive thyroid, severe agitation, moderate to severe high blood pressure, heart disease or coronary artery disease, or a history of drug abuse.
7) Other names: Ice, meth, speed, crystal.
8) Mechanism of action:- A potent full agonist of Trace Amine-Associated Receptor 1 (TAAR1), a G-Protein Couple Receptor (GPCR) that regulates brain catecholamine system. Methamphetamine is a CNS stimulant which after entering into the brain triggers a cascading release of norepinephrine, dopamine and serotonin which further affects the responses for regulating heart rate, body temperature, blood pressure, appetite, attention, mood, and responses related with alertness and alarm conditions. To a lesser extent methamphetamine acts as a dopaminergic and adrenergic reuptake inhibitor and high concentration as a monoamine oxidase inhibitor (MAOI). 9) Side effects:- people who use for long term can experience a range of negative health outcomes, including damage to the heart and brain, anxiety, confusion, insomnia, mood disturbance and violent behaviour.
10) Structural formula of Methamphetamine:-



- CNS stimulant
- Highly addictive
- Man made drug that can be snorted, smoked, injected or orally ingested.
- For amphetamine, there were no difference in severity of dependence rating for injection, intranasal or oral use.
- 53% met diagnostic criteria for methamphetamine use disorder.3% reported injecting methamphetamine in past year.

- Co-occurring substances use and mental illness were common.

Psychostimulants: Psychostimulants with abuse potential include both illicit drugs, such as methamphetamine and ecstasy, as well as prescription stimulants. Prescription stimulant, which are drugs used to treat conditions such as attention deficit hyperactivity disorders (ADHD) or depression, can also be misused. Approximately 5 million people in America misused the prescription stimulants in 2020.

Rates of overdose death from psychostimulants have been increasing since 2010. Nearly 33000 Americans died from an overdose involving psychostimulants with abuse potential in 2021, which was a 37% increase from previous year. Over 30% of all drug overdose death in 2021 involved psychostimulants.

Psychostimulant involved overdose death rates were consistently highest for AI persons compared to other racial and ethnic group from 2004.

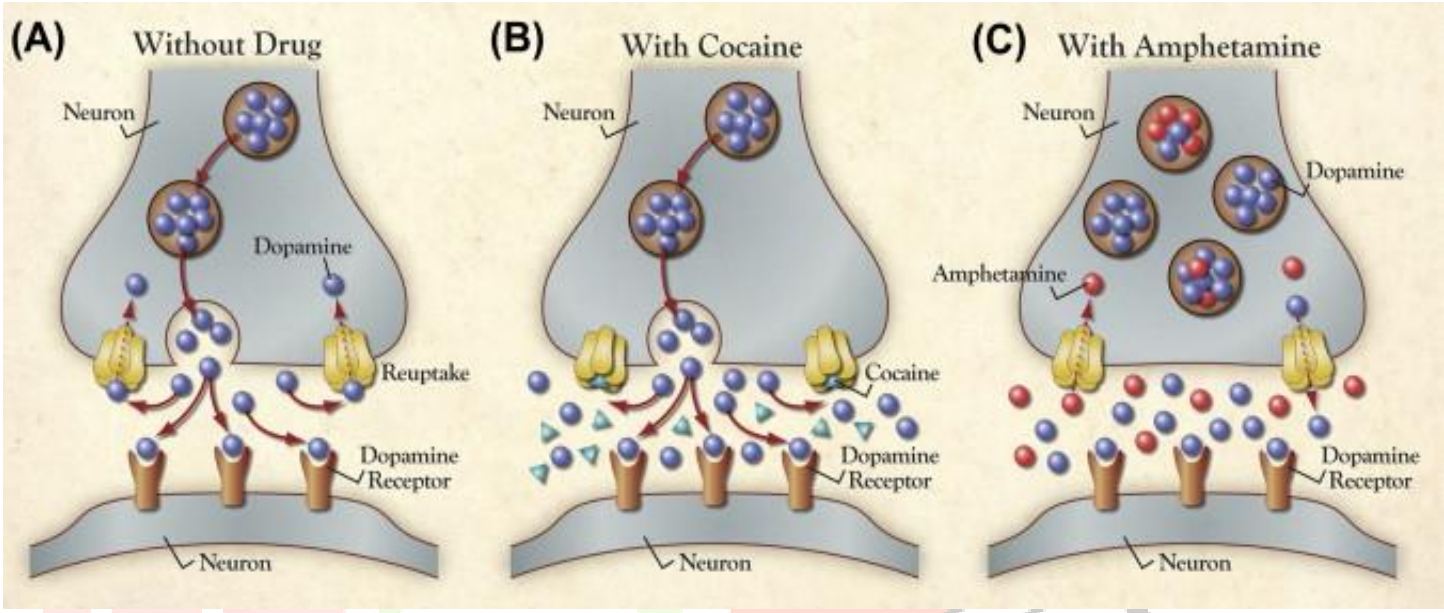


Fig. synaptic diagrams with and without psychostimulants

Cocaine increases the quantity of dopamine present in the synapse by blocking neurotransmitter reuptake. Amphetamine increases the quantity of dopamine present in the synapse by increasing neurotransmitter release. (A) Normal release and reuptake of dopamine from the presynaptic terminal. (B) Blockade of reuptake by cocaine increases dopamine in the synaptic cleft. (C) Increased dopamine release is produced by amphetamine, in which amphetamine reverses the action of the dopamine transporter.

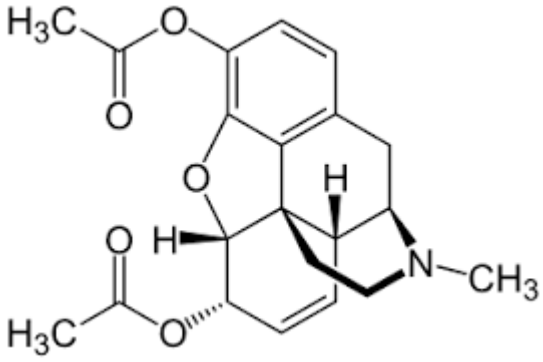
In addition to risking becoming addicted to methamphetamine people using it for long term may experience a range of negative health outcomes including damage to heart and brain. Identifying characteristics associated with past year methamphetamine use provides insight into population to prioritize for prevention and response efforts. Adult with limited income, those on Medicaid, people who are uninsured, those with lower education status, males, middle aged adults, and people who live in rural areas are at increased risk for methamphetamine use.

Treatment for methamphetamine use has been on rise- methamphetamine use amongst people who were admitted to drug related treatment has been increased.

-Tranquilizer called xylazine is increasingly being found in illegal drug supply and linked overdose death. Xylazine – which is not approved for use in people can be life threatening and is especially dangerous when combined with opioids like fentanyl.

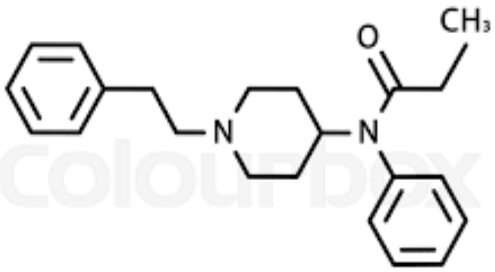
-Due to its impact on opioid crisis, fentanyl is adulterated with xylazine has been declared an emerging threat by white house's office of national drug control policy. On July 11 2023, the white house released a national response plan to address the emerging threat to fentanyl mixed with xylazine.

-The presence of xylazine in drugs tested in labs increase by almost 80% over the decade especially in heroin and fentanyl.



heroin

- Heroin produced more dependence than either cocaine or amphetamine.
- Heroin taken by injection was associated with more sever dependence than smoked heroin.



Fentanyl
$C_{22}H_{28}N_2O$

In recent studies from CDC's States Unintentional Drug Overdose Reporting System (SUDORS) among 20 states deaths involving Illegally Made Fentanyl (IMF) with xylazine detected increased from 3% in January 2019 to 11% in June 2022 as the sale of opioids by licit online sellers is has increased in these recent years. To obtain a summary of the content to isolate those clusters associated with illegal online marketing and sale using a Biterm Topic Model (BTM). After isolating relevant hyperlinks associated were then reviewed to assess the characteristics of illegal online sellers. This was retrospective, register-based observational study that utilizes data from the national board of forensic medicine, the prescribed drug registry, regional health care services, municipal social services.

What are the symptoms and health risks of xylazine?

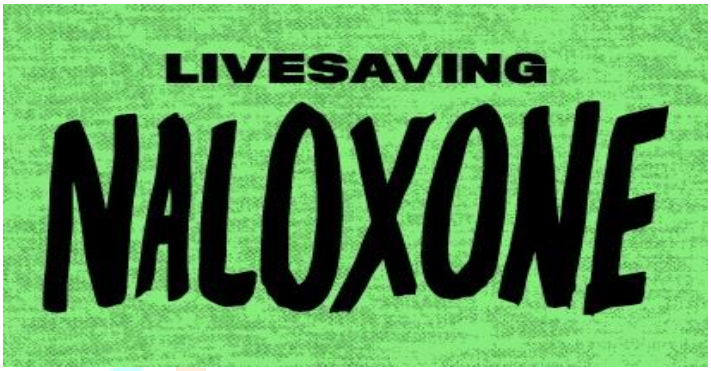
Xylazine can cause-

- sedation
- difficulty in breathing
- dangerously low blood pressure
- slowed heart rate
- wound that can become infected
- severe withdrawal symptoms
- death

How people are exposed to xylazine?

Illegal drugs such as cocaine, heroin, and fentanyl can be mixed with xylazine, either to enhance drug effects or increase street value by increasing their weight. People who use illegal drugs may not be aware of the presence of xylazine. DEA laboratory system reported that approximately 23% of fentanyl powder and 7% fentanyl pills seized by the DEA in 2022 which contained xylazine. Xylazine is usually injected, although it can be swallowed or sniffed.

What should be given as the antidot for opioid drugs and overdose of xylazine?



Naloxone should be given in response to any suspected drug overdose to reverse any possible opioid effects. Naloxone will not reverse the effect of xylazine. However, because xylazine is often used with opioids like fentanyl, naloxone should still be given, especially since the effect of xylazine may continue after naloxone is given.

This study is in line with prior studies that have identified social platform, as a potential conduit for supply and sale of illicit opioids, for the purpose of defecting, classifying, and reporting illicit online pharmacy selling controlled substances illegally in accordance with US Food and Drug Administration (FDA) and the US Drug Enforcement Agency (DEA). Further development of solutions based on these methods has the potential to proactively alert regulators and law enforcement agencies of illegal opioid sales, while also making the online environment safer for the public.

Drug prescriptions preceding opioid related deaths-a register study of forensic autopsy patients. Opioid overdose death have increased in many developed as well as developing countries in recent decades including America, Sweden, Australia, India etc, despite increased treatment efforts and harm-reduction interventions. Further knowledge in this field is needed if this trend is to b reversed. Previous research suggest that mental health and patterns of prescription of opioids and other prescription drugs are associated with increased opioid related mortality. The present study therefor aimed to investigate what drugs were prescribed during the last six months of life to individuals with history of illicit substances use who died with opioids present in their blood, the relationship between drugs found in blood at the time of death, and if prescription of specific drugs was temporally associated with death. Prescription of certain drugs, especially alprazolam and diazepam, should ne made with great caution to patients having history of illicit substance use or concurrent use of opioids.

Illicit use initiation of therapy and opioid use in combination with other psychoactive medications are context most clearly associated with impaired of daily activities. Clinicians should counsel patient on the risk of impairment when initiating therapy, when co-prescribing opioids and other psychoactive drugs, or when a patient is suspected of having an opioid use disorder.

What should be done for someone with signs and symptoms of a possible opioid overdose involving opioid and xylazine?

- Call the ambulance and stay with the person until responder arrive. Overdose is a medical emergency. First responders can assess the situation and provide treatment.
- Give naloxone as it can reverse the effect of any opioid and will not cause harm if opioids are not involved in overdose.

- Responders have reported that rescue breaths are especially helpful for people who have used xylazine because it causes breathing to slow down.
- To give rescue breaths to adults, make sure the person's chin, tilt the head back, and pinch the nose closed. Place your mouth over the person's mouth t make seal and give two slow breaths. Watch for the person' chest (but not the stomach) to rise and follow up with one breath every 5 second.

For people who use illegal drugs, the following strategies can help reduce the risk of overdose?

- ✓ **Never use alone:** a trusted contact can help reduce overdose risk by giving naloxone or calling ambulance in case of an emergency. People who don't have a trusted contact nearby can take advantage of services that allow people to seek non-judgemental support over a phone or a video call when they are using drugs. Never use alone is a nationwide service that connects callers to trained volunteers who will gather basic information about the caller's location, stay on the line to use substances alone, and alert ambulance if the caller becomes unresponsive.
- ✓ **Carry naloxone and how to use it:** because xylazine is often mixed with opioids like fentanyl, cocaine, heroin, morphine, naloxone should be given in response to a suspected overdose a reverse any possible opioid effect. Importantly, naloxone will not reverse effects of xylazine. In the event for an overdose, call emergency health service providers for additional medical treatment.
- ✓ **Rescue breaths** are especially helpful for people who have used xylazine causes breathing to slow. Harm reduction experts also suggest rolling individuals on their, into the recovery position.
- ✓ **Know the risk of using illegal drugs with unknown ingredients:** Illegal drugs are unregulated-they don't come with an ingredients list. As a result, dosage and purity are difficult to determine. Heroin, fentanyl, and cocaine may be mixed with xylazine or other substances. Counterfeit pills that closely resemble prescription medications and contain illegal substances are increasingly common in the illegal

drug market.

- ✓ **Seek medical care for skin wounds:** Skin wounds may become infected and worsen quickly. When treated early wound can be managed with basic wound care techniques, if left intreated, wound can lead to amputation or become life threatening.

- ✓ **Reduce injection related risk:** According to the national harm reduction coalition, the risk of infection can reduced by using sterile injection equipment, rotating injection sites, allowing skin veins time to heal before another use, and taking drugs in other ways besides injection.

- ✓ **Test drugs before using:** there are commercially available test strips to test the presence of xylazine in drug sample.

- ✓ Fentanyl test strips can be used for the test of opioids, stimulants, or prescription medications for fentanyl18. When people have knowledge that their drugs contain fentanyl, they can take steps to reduce their risk of opioid overdose.
- ✓ Educate the public about the increasing presence of xylazine in the drug supply and how to respond to suspected xylazine- involved injuries and overdose.
- ✓ Raise awareness of the changing illegal drug market place and the common use of illegally made fentanyl with other drugs like xylazine.
- ✓ Provide messaging to community groups (particularly those providing services to people at higher risk), community leaders, school officials, faith-based leaders, parents, students and others about the changing illegal drug supply and risk for exposure to strong opioids like fentanyl or fentanyl mixed with xylazine.

Harm reduction organization:

- Call ambulance immediately after recognizing an overdose or resuscitating a patient. Naloxone available in the field may not be enough to reverse a fentanyl-involved overdose, and in the case of fentanyl mixed with xylazine, symptoms associated with xylazine may continue after naloxone is given.
- Provide test strips for people who use drugs as a part of community drug checking programs. These are key opportunities to educate people who use drugs about the increasing presence of xylazine. This also provides an opportunity to educate and encourage people who use drugs about how to use various harm reduction strategies.
- Link people who are a risk for overdose with care and track their retention in care programs, including wound care.
- Increase overdose prevention education and take-home naloxone to people who use drugs, their friends, and other likely to witness or experience an overdose.
- Partner with public safety and public health to obtain and disseminate the latest information o local drug supply and overdose trends.

First responders to overdoses:

- Consider xylazine as a contributor to overdose when naloxone administration is ineffective.
- Provide rescue breath. Rescue breaths are an especially helpful intervention for people who have used xylazine since it causes breathing to slow.

Healthcare providers:

- ✓ Talk to patients about the changing illegal drug supply and risk for overdose and exposure to highly potent opioids like fentanyl and fentanyl mixed with xylazine.
- ✓ Counsel patients to call emergency health care services and that naloxone will not reverse the effect of xylazine. In the event of an overdose involving fentanyl and xylazine, naloxone should be given, but its important to note that the effects of xylazine may continue after naloxone administration.
- ✓ Provide active referral to treatment and care options and recovery support services, including wound care.
- ✓ Implement post overdose response protocols that incorporate link between public health, treatment providers, community based service organizations, and healthcare providers. These protocols promote overdose education, treatment, linkage to care and medications for opioid use disorder and naloxone distribution.

CONCLUSION:

This study was carried out to find out the effects and the current status of opioid derivatives and other illegal drugs on forensic studies, their sales, their exposure to people, their general information, mechanism of action, pharmacological effects, overdose and their severe side effects including life threatening adverse drug reactions and most importantly their treatment and management of overdose and addictions.

This study also overlooked the relationship of the prescription drugs with opioids, their adverse drug reaction as well as drug-drug interaction which can lead to the severe life threatening events including rates of death i.e. mortality and their solutions as well.

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