



Review on :- Xylazine Drug

1*Rutuja Deepak Patil ,2* Mr. Pramod B. Chikkodi

1*B Pharmacy Student , Nootan College of Pharmacy , Sangli

2*HOD, Department of Pharmacy, Nootan College of Pharmacy, Sangli

Abstract:-

Xylazine is a alpha -2-agonist analgesic sedative drug. It is a non-opioid drug. It belongs to tranquilizer. It is called flesh eating or zombie drug . It is veterinary drug approved for animal but it's use has been increased with illicit drug as it is not clinically approved for human use .The overdose death rates are increased due to people unaware of presence of xylazine with fentanyl, heroin, street drug. Xylazine is poisoning drug which has increased death rates in recent years. The objective of this review is to overcome the xylazine drug risk factor by understanding its pharmacology, Adverse effect, treatment and management . It showed adverse effects like rotting of skin , scars on skin and holes in legs . This review study about the structure and some case report of xylazine showing adverse effects.

Keywords:- Xylazine, overdose, street drug, traq, withdrawal

Introduction and Background:-

Xylazine is an non-narcotic sedative drug used for analgesia and muscle relaxation exclusively in veterinary medicine.(1) It is not approved for human use according to FDA(2) It was investigated as sedative hypnotic, analgesic and anaesthetic drug in human but it discontinued for the use of human due to central nervous system depression and severe hypotension adverse effect shown to a human. It is a dangerous poisoning drug because it depress breathing, blood pressure, heart rate and body temperature critical level.(3) It is a tranquilizer, sedative drug , it also refers to as tranq or tranq dope which is recently found to be use as an adulterant in drug of an abuse sold on the streets with cocaine, heroin, and fentanyl, speedball.(4,5) Xylazine has gained popularity as it is use with adulterant drug . It was first identified in Puerto Rico as a prevalent additive in street drugs in the early 2000s.(6,7) The State Unintentional Drug Overdose Reporting System (SUDORS) has identified xylazine as an emerging adulterant in illicit drug mixtures. Xylazine is found as a primary constituents in retail street samples, but also found in trace quantities. As per the reports there is use of xylazine as it increase the effect from fentanyl and delays the withdrawal duration of symptoms.(8)

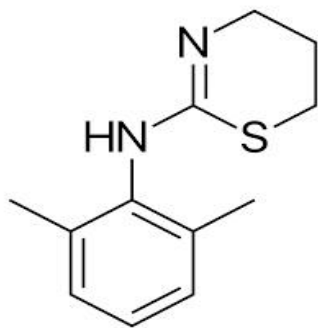


Fig.1 Structure of Xylazine

It was first developed by Farbenfabriken Bayer in the Federal Republic of Germany as a medicinal drug . It is reported to misused in several cities and countries across United States and Canada. The presence of xylazine in drugs tested in labs has increased in every region of the United States and the region of South from 2020 to 2021. In studies it showed that Xylazine was involved less than 1% of drug overdose deaths in 2015 and nearly 7% till 2020, but it showed 80% of overdose death in 2021 and 2022. In Philadelphia reported 90% of xylazine in the lab-tested dope which has increase the risk of overdose when combine with other drug. According to New York City department of health , around 2,668 people died due to Xylazine overdose in 2021. In coming years the Xylazine overdose is going to become worse (9,10) According to Drug enforcement administration over 48 to 50 states are seized with the mixture of xylazine fentanyl.(11) Us-FDA has cited awareness against xylazine misuse which shows the zombie like symptoms to the human.(12)

It was figured out that first quarter of 2022 in Vermont Xylazine was found to be 30% fatal opioid overdose, the percentage went higher in specific months 50% in Feb 2020, 41% June 2022, 32% in November 2022. In second quarter of 2022 overdose increased to 643 deaths.(13) US FDA has taken action to restrict the entry of xylazine into illicit street drug to overcome with the overdose deaths rates and stop the use of xylazine for human to prohibit it's adverse effects.(14)

Pharmacology and MOA:-

Xylazine is pharmacologically similar to clonidine. It belongs to thiazine group. Xylazine is a α -2-adrenergic agonist effective against α -2-receptors in central nervous system. Due to the α -2-agonist effects it shows the inhibitory effect on brain stem vasomotor center . It acts as an α -2-receptor agonist in both central and peripheral nervous systems, causing a strong sympatholytic effect by activating central presynaptic α -2 receptors. It inhibit the release of noradrenaline and dopamine synapse in the central nervous system . As xylazine is veterinary drug so there is limited information available on pharmacological activities on humans. It is quickly absorbed into the body. It metabolized in the kidney 70% in excreted through the kidney and 30% in the bile only 8% remain unchanged total excretion occurs within 10-15 hours. Half life of xylazine elimination is 23-50 minutes.(2,3)

Sign and Symptoms:- As Xylazine is dangerous it shows symptoms like CNS and respiratory depression, hypotension, bradycardia , hypothermia, miosis, or high blood glucose level. Repeated exposure result in dependence and withdrawal. Withdrawal symptoms are like it can cause severe anxiety or agitation when there is increase or decrease of usual drug dose. It also shows the symptoms like necrotic skin ulceration which are different from soft tissue infection . If ulcers are left untreated it can cause eschar.(3,12)

Xylazine Adverse effect on Humans :-

As is dangerous to human. It causes adverse effects on human as overdose deaths, Respiratory depression (slowed breathing), drowsiness and amnesia, hypotension (dramatic drop in blood pressure), nausea and vomiting, slowed or stopped heart rate. The most dangerous side effects is an irreversible condition in which body tissues dies) the necrotic skin ulcers.(15) It also triggers the Hypotension and respiratory depression. (16) The untreated wounds of skin ulcer may increase the risk of bacteremia, endocarditis, sepsis, limbs amputation, and death (17)

There is one case which belongs to skin ulcer. The female patient of 37 year old in Philadelphia with a known history of opiate use disorder cause leg skin ulcers, cellulitis and osteomyelitis due to inject of xylazine drug. At her clinic visit she was diagnosis with ulcer on her lower extremities. Her ulcer was smelling like foul, had copious purulent drainage, and were present on both the anterior aspects of her legs, extending from just below the knee to above the ankle. They were extending into the bone at some places. She was admitted for eight weeks for the treatment. She was discharged after few weeks.(1)

The another effect of xylazine is overdose deaths there is a case related to it 41 year old male patient was admitted at poisoning department of Quilo hospital on June 2022 . He had a history of depression, he was found with Xylazine injected. He was admitted for 3 days , on the last day at afternoon he died due to respiratory and cardiac arrest. He was also diagnosed with multiple ulcerated scars on right arm and anterior and medial skin on both legs.(18)

Treatment and Diagnosis of Xylazine:-

Treatment:- No approved antidote is there for a xylazine overdose in humans. There is a ability of naloxone to reverse the effects of a xylazine overdose.

Naloxone does not completely treat the overdose of xylazine. It is essential that any person suspected with overdose should call to the emergency number so it can save the life of a suspected patient. The number of xylazine in the drug samples has been increased , it is found in Los Angeles, Sa Francisco and San Diego in 2023.

Till now there is no any accurate treatment for xylazine overdose is available .(2)(19)

Diagnosis:- Xylazine is detected or diagnosis by using the xylazine test strip. It is rapid lateral flow immunoassay for the detection of xylazine in liquid or powder samples of a drug . It is a rapid detection strip. The strip are safer consumption sites. Toxicology testing is the another potential source of information about the xylazine trends. Due to the half-life of 23-50 min xylazine get eliminated it is sometimes difficult to detect it.(8,20)

Management of Acute Xylazine:- (21)

There should be proper “recovery position ” by treating the suspected patient by administered with naloxone.

Use the following steps to place a person in the recovery positions :-

- Kneel beside the patient.
- Extend the patient's arm that is closest to you above their head.
- Fold their other arm across their body, placing the back of their hand against the cheek closest to you.
- Bend the knee farthest from you and place the foot flat on the ground.
- Roll the patient toward you onto their side.
- Tilt their head back to open the airway: check for airway obstruction; clear any obstruction present if possible.
- Adjust their top leg so the hip and knee are bent at right angles.

Managing the Xylazine withdrawal Symptoms:- By treating with benzodiazepine and or alpha-2-adrenergic agonist, clonidine, dexmedetomidine tizanidine , guanfacine.

Managing xylazine for wounds:- (22)

- Clean the wounds.
- Avoid alcohol and hydrogen peroxide.
- Manage the pain.

Conclusion:- Xylazine is dangerous to human use because it is not approved for human . The use of Xylazine should be prohibited. There should be proper knowledge provided to the citizens about Xylazine Adverse effect and to overcome with its overdose deaths. It is the responsibility of all citizens to be aware of use of Xylazine as a speedball drug. Xylazine has no permanent antidote it is treated by naloxone and by management of withdrawal Symptoms. There are strips for detecting the xylazine drug. Xylazine overdose deaths can be decrease by taking precautions and having proper knowledge of Xylazine drug. If there will no proper use of Xylazine then there will be increase in the number of deaths and skin wounds in future.

References:-

- 1.Srikrishna V Malayala et al., “Xylazine-Induced Skin Ulcers in a Person Who Injects Drugs in Philadelphia, Pennsylvania, USA,” *Cureus*, August 19, 2022, <https://doi.org/10.7759/cureus.28160>.
2. Sandeep Singh et al.,AN EMERGENCE DRUG ABUSE: XYLAZINE, https://www.researchgate.net/publication/370340372_AN_EMERGENCE_DRUG_ABUSE_XYLAZINE.
3. Jewell Johnson et al., “Increasing Presence of Xylazine in Heroin and/or Fentanyl Deaths, Philadelphia, Pennsylvania, 2010–2019,” *Injury Prevention* 27, no. 4 (August 2021): 395–98, <https://doi.org/10.1136/injuryprev-2020-043968>.
4. Leigh Ann Anderson, Xylazine(Tranq Dope), May 5, 2023. <https://www.drugs.com/illicit/xylazine.html>.
5. Xylazine: US witnesses 'zombie drug' attack across states. Economic Times, Feb 27, 2023, https://m.economictimes.com/news/international/us/xylazine-us-witnesses-zombie-drug-attack-across-states-details-here/amp_articleshow/98189433.cms.
- 6.Elmosry Khaled and Hassan Hendawy, “Novel Xylazine Voltammetric Sensors Based on Zinc Oxide Nanostructure,” *Egyptian Journal of Chemistry* 0, no. 0 (September 4, 2023): 0–0, <https://doi.org/10.21608/ejchem.2023.228115.8398>.
7. Thomas Quijano et al., “Xylazine in the Drug Supply: Emerging Threats and Lessons Learned in Areas with High Levels of Adulteration,” *International Journal of Drug Policy* 120 (October 2023): 104154, <https://doi.org/10.1016/j.drugpo.2023.104154>.
8. Claire M. Zagorski et al., “Reducing the Harms of Xylazine: Clinical Approaches, Research Deficits, and Public Health Context,” *Harm Reduction Journal* 20, no. 1 (September 30, 2023): 141, <https://doi.org/10.1186/s12954-023-00879-7>.
9. What You Should Know About Xylazine., Drug Overdose, CDC Injury Center., July 17, 2023, https://www.cdc.gov/drugoverdose/deaths/other-drugs/xylazine/faq.html?s_cid=qr2022.
10. What is the ‘Zombie drug’ Xylazine? Here are some symptoms of the drug which created havoc in the US., Economic Times., Feb 24, 2023, https://m.economictimes.com/news/new-updates/what-is-the-zombie-drug-xylazine-here-are-the-symptoms-of-the-drug-which-created-havoc-in-the-us/amp_articleshow/98207144.cms.

11. DEA Reports Widespread Threat of Fentanyl Mixed with Xylazine., <https://www.dea.gov/alert/dea-reports-widespread-threat-fentanyl-mixed-xylazine>.
12. LeeKee Choon et al., “A Case Series of Accidental Xylazine Intoxication in Humans; Is There a Role of Naloxone as an Antidote?,” *Turkish Journal of Emergency Medicine* 23, no. 2 (2023): 119, https://doi.org/10.4103/tjem.tjem_198_22.
13. Shahana Ayub et al., “Xylazine in the Opioid Epidemic: A Systematic Review of Case Reports and Clinical Implications,” *Cureus*, March 29, 2023, <https://doi.org/10.7759/cureus.36864>.
14. FDA NEWS RELEASE. FDA Takes Action to Restrict Unlawful Import of Xylazine, February 28, 2023, <https://www.fda.gov/news-events/press-announcements/fda-takes-action-restrict-unlawful-import-xylazine>.
15. J. Deva Anban et al., “Molecular Structure, Electronic Properties and Drug-Likeness of Xylazine by Quantum Methods and Qsar Analysis,” *SN Applied Sciences* 2, no. 10 (September 12, 2020): 1685, <https://doi.org/10.1007/s42452-020-03493-5>.
16. Pyramid Healthcare., Xylazine: What It is and How It Affects Humans., March 10, 2023, <https://www.pyramid-healthcare.com/xylazine-what-it-is-and-how-it-affects-humans/>.
17. Ping Dai et al., “Hyperpyrexia and Skin Lesions Caused by Xylazine: A Case Report,” preprint (In Review, September 12, 2023), <https://doi.org/10.21203/rs.3.rs-3312754/v1>.
18. Dai et al. Xylazine Intoxication, A Case report Bayramoglu A, Saritemur M, Kocak AO*, Omeroglu M and Akbas Department of Emergency Medicine, Faculty of Medicine, University of Ataturk, Erzurum, Turkey
19. XylazineLACounty., <http://publichealth.lacounty.gov/sapc/docs/public/overdose-prevention/XylazineLACounty.pdf>.
20. Authors, Sarah Jones, and Sharon Bailey, *Xylazine Test Strips for Drug Checking: CADTH Horizon Scan*, CADTH Horizon Scans (Ottawa (ON): Canadian Agency for Drugs and Technologies in Health, 2023), <http://www.ncbi.nlm.nih.gov/books/NBK595122/>.
21. Bhavani Nagendra Papudesi, Srikrishna Varun Malayala, and Angela C. Regina, “Xylazine Toxicity,” in *StatPearls* (Treasure Island (FL): StatPearls Publishing, 2023), <http://www.ncbi.nlm.nih.gov/books/NBK594271/>.
22. NEW YORK STATE Department of Health., Xylazine: What Clinicians Need to Know., <https://www.health.ny.gov/publications/12044.pdf>

