ToxTalks:

A Bulletin for Healthcare Professionals Who Manage Poisoned Patients

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Source: U.S. Drug Enforcement Agency
www.dea.gov

Nitazenes

Over the past decade, there has been a surge in the prevalence of new psychoactive substances (NPS) worldwide. However, accurately gauging their societal impact remains challenging due to underreporting and limited detection methods. At the University of Virginia Health, within both the Division of Medical Toxicology's clinical practice and in association with the Blue Ridge Poison Center, we have observed a concerning rise in the encounter rates of NPS, including opioids. Among the emerging NPS opioids encountered nationally, nitazenes are contributing to the unprecedented epidemic of opioids.

Nitazenes constitute a novel class of synthetic opioids linked to recent overdose fatalities in the United States. This class encompasses over twenty distinct substances, including isotonitazine, protonitazene, metonitazene, and etonitazene. Nitazenes were initially explored as potential pain relievers in the 1950s by the Swiss chemical research laboratories CIBA Aktiengesellschaft, but were never approved for therapeutic use in humans in the United States. Interest in nitazenes waned outside specialized opioid research until their resurgence in the illicit drug market in recent years.

As regulatory bodies like the Drug Enforcement Administration (DEA) and the Food and Drug Administration (FDA) have enhanced their capability to identify and regulate fentanyl analogs, clandestine chemists have revisited historical pharmacology research, leading to the emergence of new nitazene analogs. Despite regulatory efforts, the detection and regulation of nitazenes remain challenging, contributing to their implication in numerous drug-related overdose deaths in Europe and the United States.

Nitazenes act as potent μ-opioid receptor agonists, similar to morphine and fentanyl, but there is limited human clinical data on their pharmacokinetics and pharmacodynamics due to the absence of clinical trials. Laboratory assessments indicate that some nitazene analogs surpass fentanyl in potency. Clinically, nitazene toxicity

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manifests as an opioid toxidrome, characterized by miosis (constricted pupils), central nervous system depression, and respiratory depression, and are increasingly associated with fatal outcomes as recently seen in Philadelphia[1]. Due to their high potency, rapid onset of clinical effects can occur following exposure, potentially resulting in death before administration of naloxone or seeking medical assistance. While naloxone has shown efficacy in reversing nitazene-induced opioid overdoses, larger and multiple doses may be necessary to counteract severe respiratory depression.

Despite their increasing presence in numerous countries, awareness of nitazenes among medical providers remains limited, compounding the challenges in identifying and managing cases of nitazene overdose. In addition, standard urine drug screens will not detect nitazenes, subsequently resulting in underreporting. As nitazenes and other NPS increase in prevalence in society, clinicians need to have a heightened awareness for public health surveillance and consider advanced testing at laboratories that can detect such emerging substances. The clinicians at the UVA Health's Blue Ridge Poison Center can assist. Please call 1-800-451-1428 (direct clinician line) if questions arise or if substances such as the nitazenes are suspected as we work collaboratively with the Virginia Department of Health to perform surveillance for emerging novel substances.

[1] Nitazenes found in 5 overdose deaths in Philly – here's what they are and why they're so deadly (theconversation.com)

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