South Western Sydney
Local Health District

NSW GOVERNMENT

MANAGING NOVEL SHORT ACTING (NITAZENE) WITHDRAWAL SYNDROME: A CASE SERIES FROM AUSTRALIA

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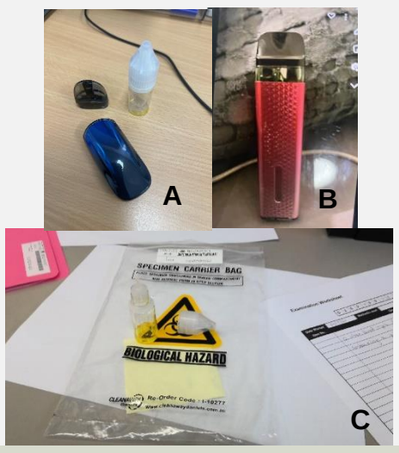
1. Introduction

Nitazenes, a class of synthetic opioids (2-benzyl-benzimadazoles), have higher potency and toxicity than other opioids (1). They are used orally, inhaled, and intravenously (2). Protonitazene, a nitazene subtype, has been detected in Australian poisoning cases via e-cigarettes (3). Toxicity mimics opioid overdose, affecting the μ-opioid receptor (MOR) with symptoms like reduced consciousness and respiratory depression (4). Higher or repeated naloxone doses are needed for reversal (5). Nitazenes are undetectable by standard urine drug tests or fentanyl strips (2).

This ***case series*** follows three patients with nitazene dependence admitted to Fairfield Hospital's In-patient Withdrawal Unit, Drug Health Services in SWSLHD. Two patients, previously opioid-naïve, mistakenly believed they were using a vaporized marijuana product, while the third intentionally acquired nitazenes. Three distinct withdrawal management approaches are presented. This is the first recorded case of nitazene dependence in NSW.

Case 1

A 22-year-old man presented to a Sydney metropolitan hospital after prolonged use of a vaporized e-cigarette product, with his last use occurring the night before. His only prior substance use involved recreational cannabis and cigarettes, with no significant medical or mental health history.



Images A) Refillable re-chargable e-cigarette with liquid (confirmed protonitazene) B) Different refillable re-chargeable e-cigarette device used by Case 1 C) Yellow liquid for vaporisaton confirmed as protonitazene (separate to Image A)

Upon admission, he exhibited symptoms of tremor, anxiety, restlessness, diaphoresis, rhinorrhoea, new onset back pain, arthralgia, piloerection, and diarrhoea. Suspected of polysubstance withdrawal, novel opioid withdrawal was also considered due to the vaporized method of administration. He was initially given 2mg sublingual buprenorphine/ naloxone with no adverse reaction and gradually increased to 32mg daily by the third day. Despite this, his symptoms persisted, prompting the use of a subcutaneous 160mg buprenorphine injection and adjunctive diazepam to manage anxiety and agitation. His symptoms continued to worsen, requiring additional buprenorphine injections and increased diazepam doses.

Opioid Withdrawal Scale*

Anxiety
Agitation/ Restlessness
Diarrhoea
Stomach Cramps
Muscle Cramps
Bone Pain
Lower Back Pain
Nausea/ Vomiting
Lacrimation
Rhinorrhoea
Sweats
Goose Bumps
Yawning
Dilated Pupils

* Score 1 for symptom being present

Over the course of his **15-day admission**, he received a total of four top-up buprenorphine injections before being discharged into the care of his parents with follow-up planned at an opioid treatment clinic.

Protonitazene was detected in both the e-cigarette product and his blood and urine samples.

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Case 2

A 25-year-old man with a history of high opioid dependence, including daily use of 200-300mg tapentadol, was referred for opioid maintenance treatment. He had been intentionally sourcing and importing nitazenes for personal recreational use, while also being prescribed medicinal cannabis, dexamphetamine, and clonazepam.

The nitazene, obtained in powder form (image D), was consumed through smoking, ingesting, and snorting. Despite microdosing, he experienced multiple overdose episodes, one of which resulted in third-degree burns.

Given his high opioid tolerance and need for surgery, he was started on 20mg daily methadone with slow increase and monitoring at an outpatient clinic.

Future plans included transitioning him to injectable buprenorphine. Urine test was negative for nitazenes, though one powder sample detected metonitazene, while another contained only paracetamol.

Case 3

A 32-year-old man self-referred to an inpatient withdrawal assistance unit for dependence on the same vaporized e-cigarette product as Case 1. He had previously used tramadol for chronic lower back pain.

The patient was treated with a rapid subcutaneous buprenorphine induction, starting with 28mg of sublingual buprenorphine/naloxone on the first day, followed by 12mg of buprenorphine/naloxone and a 300mg subcutaneous buprenorphine injection (Sublocade®) on the second day. His symptoms progressed similarly to Case 1.

He was discharged on the **fourth day** and will continue follow-up at an outpatient opioid treatment clinic for ongoing buprenorphine injections. Both his urine and blood tests were positive for protonitazene.

Discussion & Conclusion

The three cases demonstrate the complexity of managing nitazene dependence, with protonitazene identified as the primary substance in two patients. All individuals experienced severe withdrawal symptoms requiring high-dose buprenorphine or methadone, with symptom persistence despite aggressive treatment. Rapid subcutaneous buprenorphine induction was utilized in two cases, while methadone was chosen for a patient with complex needs. All patients required ongoing outpatient care for long-term management.

These cases highlight the emerging threat of nitazenes, the need for specialized withdrawal protocols, and the challenge of treating novel synthetic opioid dependence.

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