Novel Psychoactive Substances (NPS)

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Summary Writer: Theoni Haralabopoulos

Script Writer: Zeff Koutsogiannis

Editor: Venita Munir

Interviewer: James Edwards

Interviewee: Zeff Koutsogiannis

About Dr Zeff Koutsogiannis

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Introduction

In this podcast we hear from Dr Zeff Koutsogiannis, an Emergency Physician and Toxicologist. This podcast provides an overview of novel psychoactive substances (NPS), detailing their impact in the clinical setting, and focusing on the initial assessment and management of patients who have taken these designer drugs.

Case

A 19 year old male has been brought into the emergency department with police from a dance party. He is agitated and displaying bizarre behavior after taking what you think is ecstasy. He is one of three people taken to hospital with a similar presentation. Others at the scene were worried that there was a 'bad batch' of ecstasy out there, with novel psychoactive substances (NPS) called 'N-bomb' or 'Flakka'.

1. What are Novel Psychoactive Substances (NPS)? What is 'N-bomb' and 'Flakka'?

- NPSs are designer drugs that are produced to mimic traditional recreational drugs such as cannabis, ecstasy, or heroin.
- They are novel in the sense that they have been either newly produced, or that they are an old drug with a new quality.
- There are different legalities associated with them in various countries. N-bomb or Flakka may not be an NPS now because they are illegal.
- There has been an explosion in these substances in the last 10 to 15 years.
- The broad categories are stimulants, synthetic cannabinoids (designed to mimic cannabis), hallucinogens, and sedative agents (such as designer opioids or designer benzodiazepines).
- The stimulant group is the most common, particularly at the dance party scene, because they are designed to mimic the effects of the usual drugs people would take in this setting, such as amfetamines.
- The main receptors are for dopamine, noradrenaline, and serotonin. The effect of each of these neurotransmitters differs in every individual, depending on their release and reuptake.
- The common stimulants belong to the cathinone group. They are substituted amfetamines, possessing different chemical structures. Phenethylamine is the basic building block for neurotransmitters, with the addition of various chemical groups to achieve different effects.
- Bath salts, Flakka and N-bomb are street names to suggest certain cathinones, their chemical names are quite long. Their true effect may be quite different to that perceived on the street.

2. You have mentioned that NPSs have proliferated over the last 10 to15 years. Why is this?

- It began in the mid-2000s in the UK, and a variety of factors contributed. Ecstasy became a category A banned substance. You would get a criminal record if you were caught with this drug. People turned toward other drugs that were less illegal to use. The GFC contributed, as well as the billions of dollars' worth of safrole oil that was seized from China as part of border control (safrole oil is the main ingredient in MDMA). Cocaine was also less pure and more expensive at this time.
- Mephedrone was the first cathinone, and it wasn't illegal. It was marketed as plant food, and clearly labelled as 'not for human consumption'. This is how the law was bypassed. However, it was eventually banned.
- Subsequently, another substance was produced that wasn't illegal, and the cycle continued. A similar pattern occurred for the synthetic cannabinoids, such as K2 and spice. These were marketed as potpourri, not for human consumption, and would have the same effects of cannabis.
- As the years have passed, there are now hundreds of NPSs, and all available on the web.

3. How does your clinical approach to the new NPSs differ compared to traditional drugs?

- My management does not differ as you do not really know what a patient has taken and you treat the clinical scenario in front of you.
- Metamfetamine or ice can produce a variety of effects, and so do the NPSs. You don't need to know what the drug is to treat the patient.
- The presentation is dependent on the ratio of dopamine, serotonin and noradrenaline. For example, MDMA is primarily serotonergic, and makes you feel 'warm and fuzzy', and can elicit mild hallucinations. Flakka is a potent dopaminergic and noradrenergic agonist which causes marked agitation and neurotoxicity. The N-bomb is a substituted amfetamine with potent serotonin-2A agonism which is hallucinogenic, so patients can get quite agitated.
- The syndrome that you see clinically is a spectrum from mild to severe of sympathomimetic or serotonergic toxidrome behavioural disturbance. The hyperthermia that can occur is fatal.
- It is variable, some patients can present with mild agitation and settle down; others can present with an excited delirium which can become a mental health emergency.
- When it is a 'bad batch of ecstasy' it is not ecstasy. It is something else that is being sold as MDMA.

4. What is your assessment when such patients present to the emergency department?

- Like any emergency department patient, you need to know what their vital signs are, including temperature. As previously mentioned, a higher temperature is associated with higher morbidity and mortality.
- Try to get a sense of whether the patient has a sympathomimetic or serotonergic toxidrome. Look for autonomic effects and CNS excitation, and the severity.
- There is a degree from mild to severe of agitation, tachycardia, hypertension, and hyperthermia. Patients can even have seizures, as their body systems are 'ramped up', including the central nervous system.

5. How is the patient's temperature assessed?

- Temperature can be taken as like any other emergency department patient. There is no need for a rectal temperature.
- Many patients in these cases run a high temperature like 37.5 or 38 degrees. Once it reaches 39 or above, you know the patient is getting hot. Some patients present

with temperatures up to 41, 42 or even 43 degrees, and you have limited time before this can become fatal.
- The combination of a hot day, movement from dancing and psychomotor agitation drives the temperature up.

6. What are the management priorities for this patient?

- The initial priority is to be respectful and nonjudgemental, and to treat the patient in front of you with the problem that they have.
- The management priority is to control the patient's behaviour and cool them if their temperature is high.
- Management is also dependent on severity. Benzodiazepines can be useful for the stimulant drugs. Tachycardia, hypertension and agitation respond well to benzodiazepines. If severe, dopamine antagonists like droperidol or ketamine can be used.
- Diazepam is the benzodiazepine of choice for toxicologists as it is longer acting and lipid soluble (has greater CNS accessibility). Midazolam is water soluble and faster acting.

7. What kind of cooling techniques are used?

- This depends on the severity of hyperthermia. Stripping the patient is one way. Fanning or misting is another way.
- If the hyperthermia is severe, patients may need to be intubated to be cooled down.

8. What are some of the complications associated with stimulant NPS intoxication?

- There is a spectrum of severity. At the severe end of the spectrum, patients can have multiorgan failure, extreme agitation, lactic acidosis, rhabdomyolysis, coagulopathy and acute kidney injury (AKI). These are all associated with severe hyperthermia.
- In the milder setting, patients may present with seizures, hyponatraemia from SIADH or water intoxication, as drinking water can be excessive at dance parties.
- There are acute and long-term psychiatric effects. Patients can present with an acute psychosis. This may settle, but sometimes it does not.
- The cardiovascular complications of these drugs, as well as the traditional ones, are often forgotten about. They cause vasospasm and thrombogenesis. We have seen 19- and 20-year olds with myocardial infarcts. We have seen a stroke in a 23-

year-old. Therefore, do not ignore chest pain or headache in a young person who has taken these drugs. Take it seriously.

9. Is the urine drug screen useful for NPSs?

- Urine drug screens are not helpful in the emergency department. They may be good for surveillance in the community.
- There are a lot of false positive and false negative urine drug screens in the emergency department. The urine can stay positive for, for example, amfetamines, for three to four days. Therefore, it does not tell us what the patient has taken on the day of presentation.
- It may be helpful in children who may have taken medications from their parents and are exhibiting bizarre behaviour.
- For the case above, a urine drug screen would not be helpful.

10. Take home messages

- NPSs are novel psychoactive substances designed to mimic the traditional recreational drugs that we are familiar with, such as MDMA and cannabis.
- The main syndromes that patients present with are a combination of the sympathomimetic and serotonergic toxidromes.
- Do not focus on the street names or what the patient may have taken. What is important is what's in front of you and how you will manage the patient, that is, how you will control the patient's agitation or behavioural disturbance, and cool them as required.
- Address severe hyperthermia early as it is life threatening. The deaths that occur at music festivals tend to be hyperthermia-related, others arrhythmia-related.
- Have an idea of how to pharmacologically manage a patient in an agitated state, whether it be due to an NPS or not, ranging from mild to severe. Every hospital usually has a guideline on how to pharmacologically manage a patient with behavioural disturbance, usually a combination of benzodiazepines and dopamine antagonists.

Reference

- See eTG: Toxicology and Toxinology Guidelines for information on Novel Psychoactive Substance poisoning, available to eTG complete subscribers. https://www.tg.org.au/news/its-time-to-pick-your-poison-toxicology-and-toxinology-guidelines-out-now/

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