NEW PSYCHOACTIVE SUBSTANCES:

HIGH INDEX OF SUSPICION NEEDED IN CLINICAL SERVICES

PROFILE

TEXT BY

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This article is an edited version of an article published on the NAMS website (http://goo.gl/WIQWJT).

New psychoactive substances (NPS), commonly marketed as "bath salts" or "plant food", are chemical compounds designed by chemists to circumvent the current legislation against drugs of abuse. They have been touted as "legal" highs, as many of these synthetic compounds do not fall under the scheduled controlled substances list in many nations. This has prompted many countries to take legislative action against these new substances. These drugs are synthetic derivatives from many drug classes, including phenethylamines, cannabinoids, cathinones and piperazines. However, they frequently escape detection from the immunoassay kits commonly used in routine laboratories. The Central Narcotics Bureau website reports that heroin and methamphetamine are the two most commonly abused drugs in Singapore, but little is known about the prevalence and problems associated with NPS use in the local context. *While NPS is currently not a problem in Singapore, given the growing incidences of abuse of these psychoactive substances in European countries, it is important for clinicians to be cognisant of these substances. Only when clinicians are aware of these substances would they have a high index of suspicion when they encounter patients presenting with specific clinical manifestations.*

Gamma-hydroxybutyric acid (GHB), a metabolite of gamma-aminobutyric acid that has its origins as early as the 1960s and later became notoriously known as a date-rape drug, was one of the first NPS to be synthesised. GHB has since been scheduled as a controlled drug in many countries, including Singapore. Thereafter, the market saw the emergence of other types of NPS such as synthetic cathinones, eg, mephredone and synthetic cannabinoids (also known as spice). Perhaps an inherent difficulty in classifying these substances as illegal based on class of drugs stems from the fact that some members in the same class may have already been used for their therapeutic properties, eg, the synthetic cathinone, bupropion, is commonly used as an anti-depressant and smoking cessation agent. Therefore, it is difficult, if not impossible, to have a blanket ban on whole classes of chemicals. This belies the fact that new NPS are hitting the market as the older ones get outlawed and enter the controlled drugs registry. Hence, it is difficult to ascertain whether a clinical syndrome is due to NPS or the myriad of such chemicals present. However, an index of suspicion based on certain recurring clinical patterns can possibly lead to an expedient diagnosis and treatment, after other acute medical conditions have been ruled out.

CLINICAL PRESENTATION

While there have been disturbing news reported in the *Sun*, of a man tearing off his scrotum after using "meow meow" (mephedrone) due to hallucinations, as well as other similar horrid news related to NPS, the presentation is often less conspicuous. Patients may not disclose their use of an NPS during history-taking, or they may not perceive NPS to be drugs, as these substances are marketed as supplements, "plant food" or "bath salts". In the absence of clinical tests, clinicians should have a high index of suspicion that patients

presenting with brief delirium with no other organic cause may in reality be labouring from the effects of an NPS. In particular, the Crime Survey of England and Wales (CSEW) 2013/14 found that young persons between 16 and 24 years old have about a three times greater propensity of using an NPS such as mephredone and salvia than the general adult population. The CSEW report also suggested that there may be a significant association between the nightlife economy and the use of NPS, with a greater frequency of use among those who visit nightclubs more frequently.

Synthetic cathinones such as mephredrone are stimulants that resemble amphetamines in their action. The clinical syndrome is, therefore, one of cardiovascular, central nervous system and sympathetic overdrive, manifested as agitation, tachycardia, raised arterial blood pressure, dilated pupils, hyperthermia, muscle clonus and sialorrhoea. As the syndrome worsens, confusion, seizures, arrhythmias and respiratory arrest may ensue. Biochemical abnormalities reported include renal impairment with elevated potassium and creatinine, as well as elevated liver enzymes and creatine kinase. The group of phenethylamine compounds produce sympathomimetic effects such as agitation, raised blood pressure, tachycardia, dilated pupils, clonus and seizures, as seen with synthetic cathinones. Hallucinations due to 5-HT2A agonism, however, are more prominent in this group of compounds. Biochemical abnormalities reported include elevated creatine kinase, deranged liver enzymes, and renal impairment with consequent increased creatinine and serum potassium.

Besides cathinones and phenethylamine compounds, which have stimulant properties, the piperazine family of drugs such as benzylpiperazine (BZP) and trifluoromethylphenylpiperazine (TFMPP), which have been branded as safer choices in lieu of ice and ecstasy, also produce stimulant effects. Caution must be exercised, as not all piperazine derivatives exhibit such stimulant properties. MT-45, an NPS from the same family that has recently appeared on the market, has demonstrated opioid-like symptoms such as respiratory depression and decreased levels of consciousness. Some of these patients have responded well with the competitive opioid receptor antagonist Naloxone. Patients who have taken synthetic cannabinoids such as spice/K2 have also been known to demonstrate symptoms of sympathetic overdrive such as elevated heart rate, agitation, excessive sweating, high blood pressure and muscle twitches. Confusion, hallucinations, paranoia and cognitive impairment can also follow.

MANAGEMENT OF NPS OVERDOSE AND TOXICITY

Having a high index of suspicion based on the pattern of common presenting complaints mentioned above would help clinicians to decide on the appropriate management. While many treatments involve supportive measures such as hydration and monitoring, there is at present no specific antidote for most of the NPS. Thus far, the evidence suggests that benzodiazepines may be helpful in ameliorating the sympathomimetic overdrive effects associated with the ingestion of NPS. Benzodiazepines can be given intravenously to counteract the sympathomimetic effects on the heart, reducing the chance of arrhythmias and heart attack, as well as preventing seizures. The use of antipsychotics is controversial, and some have suggested that drug interactions with NPS may render them unsafe.

Given that NPS usually come in various combinations of chemicals and the labelled preparation may not be the actual constituents, it is very important for clinicians to first focus more on immediate and supportive management.

The use of NPS is a new and emerging problem in the drug abuse landscape in Singapore. Clinicians need to be aware of the use of such substances in Singapore and to have a high index of suspicion of possible NPS abuse when young people present with agitation, psychosis or confused states. ◆

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