THE NORTHERN HOSPITAL

ALPHA - PVP

"Tango", India ink crayon and watercolour, 1984, René Gruau

Sometimes a waltz is being played and, against the green background, the black profiles whirl obstinately like those cut-out silhouettes that are attached to a phonograph's turntable. Night comes rapidly after this and with it the lights. But I am unable to relate the thrill and secrecy that subtle instant holds for me. I recall at least a magnificent tall girl who had danced all the afternoon. She was wearing a jasmine garland on her tight blue dress, wet with perspiration from the small of her back to her legs. She was laughing as she danced and throwing back her head. As she passed the tables, she left behind her a mingled scent of flowers and flesh. When evening came, I could no longer see her body pressed tight to her partner, but against the sky whirled alternating spots of white jasmine and black hair and when she would throw back her swelling breast, I could hear her laugh and see her partner's profile suddenly plunge forward. I owe to such evenings the idea I have of innocence. In any case I learn not to separate these creatures bursting with violent energy from the sky where their desires whirl.

Albert Camus, "Summer in Algiers", 1938

In the 21st these creatures may burst with an energy more violent than Albert Camus, could have ever imagined. The term "flakka" apparently derives from the Spanish word "flaco" for thin. South Americans also use "la flaca" as a "clubbing" term for a good looking (and desirably thin) girl.

Alpha - PVP is typically presented as a white or pinkish crystal, (i.e like a "bath salt") or as a more finely powdered form, (DEA, USA)

ALPHA - PVP

Introduction

Alpha-PVP (alpha-Pyrrolidinopentiophenone, or alpha-pyrrolidinovalerophenone) is one of an emerging group of illicit **synthetic cathinone** psychostimulants

This drug is *cheap* to procure and it is *more toxic* than many other synthetic recreational drugs, making it a potentially very serious public health risk.

It can induce a severe "excited delirium", i.e an agitated psychosis. Frequently this behavior is aggressive and violent and is associated with a high risk of harm to self and/ or others.

Alpha - PVP can induce a severe "excited delirium", i.e. an agitated psychosis. Frequently this behaviour is aggressive and violent and is associated with a high risk of harm to self and/ or others with consequent morbidity and mortality by "misadventure".

Extremely bizarre behaviour can be observed.

It can also have lethal medical complications

These factors make this agent an extremely dangerous one and sets up the potential to create a major emerging public health problem.

It appeared initially in the USA in 2014. A death from IV use has also been recorded in Australia in 2014. [1]

History

Alpha - PVP emerged in the USA, in particular, Florida, in 2014.

A death from IV use has also been recorded in Australia in 2014. [1]

Illicit use

Alpha - PVP is readily procurable and is cheap, making this agent an extremely dangerous agent and an emerging public health risk.

"Street" names are legion, and vary according to both place and time, but the currently most popular names for alpha - PVP include:

1. **Flakka**:

   - This name apparently comes from the Spanish word "flaco" for thin. South Americans also use "la flaca" as a "clubbing" term for a good looking (and desirably thin) girl.

2. Gravel:

- Derived from its crystalline appearance.

3. Bath Salts:

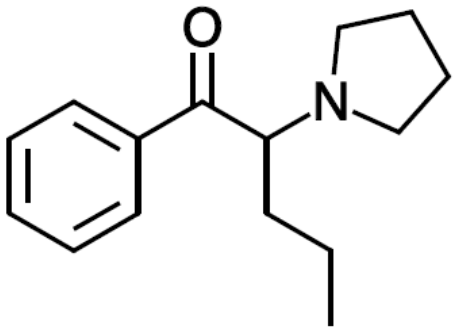
- This name derives from instances in which certain synthetic designer drugs with white powder, granule, or crystalline form were sold disguised as true bath salts, (such as Epsom salts).

  More specifically it refers to an emerging family of drugs containing one or more synthetic chemicals related to **cathinone**.

4. Monkey Dust

It should be noted however that using a slang term /abbreviation to try and identify a drug of abuse is potentially dangerous since there are many regional variations and the terms change over time.

Chemistry



The basic chemical structure of alpha - PVP

Chemically alpha - PVP is a **synthetic cathinone** and is related to **MDPV** (both of which are **pyrovalerones**).

The commonest **synthetic cathinones** include:

- 3,4-methylenedioxypyrovalerone (**MDPV**)
- **Mephedrone**
- Methylone

There are however many others.

Much is still unknown about how these substances affect the human brain, and each one may have somewhat different properties.

Chemically, they are similar to amphetamines (such as methamphetamine) as well as to MDMA (ecstasy).

Synthetic cathinones are structural analogues of cathinone, the naturally occurring β-ketone amphetamine analogue found in the *Catha edulis* (the **Khat plant**). [1]

As structural analogues of β-ketone amphetamines, cathinones are expected to have amphetamine-like effects.

Many cathinones have been shown to be inhibitors of monoamine transporters, but selectivity of cathinones for serotonin, noradrenaline and dopamine transporters varies considerably in vitro.

Pyrovalerone-cathinones (e.g., MDPV) are potent and selective dopamine and noradrenaline uptake blockers, but are not effective releasers of monoamines.

The potency of these drugs on the noradrenaline and dopamine transporters is associated with their stimulant and psychoactive effects.

Pathophysiology

The exact mechanism(s) of action of alpha - PVP are unknown, but currently are thought to involve:

1. Monoamine re-uptake inhibition of **noradrenaline** and **dopamine** within the CNS

2. Serotonergic activity.

    - The hallucinatory effects often reported in users of alpha - PVP are consistent with other drugs such as MDMA or LSD that raise levels of a third neurotransmitter, serotonin.

Pharmacokinetics

Little is known about this agent's pharmacology.

Absorption

- Alpha - PVP can be ingested, injected, insufflated, taken sublingually, and vaporized and inhaled.

Distribution

- Penetrates the blood-brain barrier

Further details are unknown

Metabolism and excretion:

- Known metabolites include:
  - ♥ Hydroxyalkyl-PVP
  - ♥ Hydroxyphenyl-PVP
  - ♥ Di-hydroxyphenyl-PVP.

Risk Assessment

Three cases of drug related deaths are reported by Richards-Waugh et al, (2013), with concentrations of 0.1, 0.5 and 0.29 mg/L in three deaths where the drug was found to be the cause or a significant contributory cause. [4]

The dangers of these agents are compounded by the fact that these products may contain other, unknown ingredients that may have their own harmful effects.

Also, drug users who believe they are purchasing other drugs such as ecstasy may be in danger of receiving synthetic **cathinones** instead. For example, mephedrone has been found commonly substituted for MDMA in pills sold as "ecstasy" in the Netherlands.

The single biggest factor influencing death from an alpha - PVP intoxication is the route of exposure to the drug - **intravenous injection.**

Clinical Features

The effects of synthetic cathinones (as a group) are said to begin to occur within 15 - 45 minutes of exposure and the desired effects last from 2 - 7 hours.

However, the undesirable effects can last from hours to days.

Alpha - PVP can induce a severe "excited delirium", i.e. an agitated psychosis. Frequently this behaviour is aggressive and violent and is associated with a high risk of harm to self and/ or others with consequent morbidity and mortality by "misadventure".

Desirable effects of cathinones reported by users include:

- Increases in energy
- Euphoria
- Increased libido.

Alpha - PVP toxicity is essentially characterized by:

1. **Hallucinations**, **acute behavioural disturbances, or frank psychosis.**

    - Extremely bizarre behaviour can be observed

      Frequently this behavior is aggressive and violent and is associated with a high risk of harm to self and/ or others.

2. **Adrenergic stimulation**

3. **Serotonergic features:**

    - Essentially a serotonin syndrome.

Toxic effects can be **severe and life-threatening,** and can include

1. Self harm and/or harm to others whilst in an agitated / psychotic state

2. Autonomic effects:

    - Tachycardia
    - Hypertension/ hypotension
    - Tachypnea
    - Facial flushing/ diaphoresis
    - Mydriasis
    - **Hyperthermia**

3. Coma

4. Seizures

5. Rhabdomyolysis

7. Acute kidney injury.

These features have been described as "**excited delirium syndrome**".

Dependence:

Early indications are that synthetic cathinones have a high abuse and addiction potential.

Withdrawal:

Frequent consumption may induce tolerance, dependence, and strong withdrawal symptoms when not taking the drug.

Investigations

There are no readily available specific tests available making a diagnosis of alpha-PVP intoxication in the ED.

Investigations are therefore directed at ruling out alterative diagnoses and diagnosing secondary complications.

The following may be *considered*.

Blood tests:

1. FBE
2. CRP
3. U&Es/ glucose
4. LFTs
5. CK/ myoglobin.
6. Coagulation profile
7. Blood alcohol.
8. VBGs/ lactate

Liquid chromatography mass spectrophotometry can be used in specialized laboratories to reveal the qualitative presence of α-pyrrolidinopentiophenone (α-PVP) in forensic / coroners cases. [1]

ECG

Where possible.

Look for arrhythmias, ischemic changes.

CT Scan:

This will be impossible for agitated patients, unless intubated or heavily sedated.

CT scan may not be required, consider risk versus benefit.

Management

Currently, no specific antidote exists for cathinone exposure.

Management therefore is supportive for both the **behavioural disturbances** and the **medical complications**.

For hallucinations and acute behavioural disturbances:

Management is supportive, including:

1. Repeated verbal reassurance:

    - This is very important in those who are orientated or aware enough of their real environment.

2. Physical Restraint:

    - Physical restraint, as for any extremely agitated and psychotic patient may be required for **patient and/ or staff safety**.

3. Emergency chemical sedation:

    - **Benzodiazepines** titrated to clinical effect

    - **Antipsychotics** titrated to clinical effect:

      Options include: [3]

      ♥ Droperidol

      ♥ Olanzapine

      ♥ Haloperidol

    - **Ketamine sedation may ultimately be required for very severe agitation.**

For medical complications:

Management is supportive, including:

1. Intubation and ventilation as required

2. Activated charcoal:

    - The efficacy of gastrointestinal decontamination is not proven.

As these compounds are rapidly absorbed and patients usually present late in established toxicity, the risks of activated charcoal (e.g. seizures/ excited delirium) outweigh any (theoretical) benefit.

Activated charcoal is not recommended.

It may be *considered* in intubated patients (for possible coingestions)

3. Control of seizures

- IV benzodiazepines

4. Control hyperthermia:

- Cooling ice packs (or similar)
- IV cooled fluids
- May require paralysis and ventilation.

5. IV fluids as required

In particular for:

- Dehydration
- Acute kidney injury
- Rhabdomyolysis

6. Hypertension:

- Sinus tachycardia and hypertension can initially be controlled with IV titrated benzodiazepines.

If refractory to the above, further options include:

- Phentolamine 1 mg IV repeated every 5 minutes, as required.
- GTN infusion
- Nitroprusside infusion

Note that beta blockers are contraindicated in sympathomimetic toxicity, (they will result in unopposed alpha stimulation - by the blockade of beta -2 receptors).

7. Correct electrolyte disturbance as required:

- e.g. hyperkalemia in rhabdomyolysis.

Disposition:

The cathinones are a novel and potentially life-threatening group of synthetic recreational psychostimulant drugs.

The optimum period of observation for these patients is not established.

Suspected cases should be discussed with a **Clinical Toxicologist**.

Appropriate psychiatric assessment may be necessary following resolution of toxicity depending on the circumstances of the exposure.

References

1. Kate Sellers et al. Death due to intravenous use of α-pyrrolidinopentiophenone. MJA 201 (10) 17 November 2014.

2. Alpha-PVP in Toxbase Website, November 2018

3. Alpha-PVP in TOXINZ Website, Accessed January 2019.

4. Alpha - PVP in EROWID Website, Accessed November 2018.

   - https://www.erowid.org/

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