Novel Psychoactive Treatment UK Network

NEPTUNE

Guidance on the Clinical Management of Acute and Chronic Harms of Club Drugs and Novel Psychoactive Substances

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Inspiring Improvement

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Chapter 11

Pipradrols and pipradrol derivatives

Pipradrols and pipradrol derivatives are a group of amphetamine-type substances (ATS) structurally related to methamphetamines. In recent years, 2-DPMP (desoxypipradrol, also known as 2-diphenylmethylpiperadine) and D2PM (diphenylprolinol) have appeared on the recreational drug market, initially as so-called legal highs.

2-DPMP was first sold as 'Ivory Wave', but there is some evidence that D2PM has since replaced 2-DPMP in Ivory Wave products. Brand names for these substances also included 'Head Candy' and it was also sold as a 'research chemical'. As with other 'legal highs', brand names can be misleading in identifying drug content and associated harms. Ivory Wave is a good example, inasmuch as it was shown have contained methylenedioxypyrovalerone (MDPV) and lidocaine,[1] in addition to 2-DPMP and D2PM.[2]

2-DPMP and related compounds D2PM and diphenylmethylpyrrolidine are Class B under the Misuse of Drugs Act.

11.1. Brief summary of pharmacology

Desoxypipradrol (2-DPMP) is a long-acting noradrenaline–dopamine reuptake inhibitor originally developed as a treatment for narcolepsy and attention deficit hyperactivity disorder (ADHD). 2-DPMP is thought to increase the release of dopamine and decrease dopamine reuptake, similar to the effects of cocaine.[3] There is some evidence that 2-DPMP is more potent than cocaine in stimulating dopamine release and in inhibiting its reuptake.[4] It is also comparable to amphetamine and methamphetamine in its potential to cause acute toxicity. 2-DPMP has particularly long-lasting effects and a longhalf-life.[2] The substance is capable of inducing agitation, which may last for several days after a single dose.[4]

D2PM is a pyrrolidine analogue and 2-DPMP is a desoxy analogue of pipradrol. It has been argued that, based on published evidence, that the binding and activity of D2PM at the dopamine reuptake transporter are similar to those of cocaine, although it appears that D2PM has less biological activity.[3] D2PM also has long-lasting effects, albeit shorter than those of 2-DPMP.

11.2. Patterns of use and routes of ingestion

Pipradols are typically part of a drug-using repertoire and their use has been reported among a minority of users. For example, in a survey of individuals attending gay-friendly nightclubs in south-east London (July 2011), 0.6% of 315 individuals reported that they had used a pipradrol: 1.0% had used within the last year and 0.6% had used or

were planning to use a pipradrol on the night of the survey.[5] Pipradrols were also detected in an analysis of anonymous pooled urine samples from stand-alone urinals.[6]

It is important to note that people who use 2DPM and D2PM do not necessarily know that they have consumed this drug. In a case series of five patients who presented to an emergency department (ED) in London, none of them knew that they had consumed it. They were sold it instead of the substance they had intended to buy.[7]

2-DPMP is sold as a hydrochloride salt or in free-base form. It is described by retail websites 'as a white crystal powder with not much smell' or 'a white coloured fine powder', with a purity of up to 99.9%.[2]

Oral ingestion is the most common route of administration of 2-DPM ('bombed' wrapped in a cigarette paper) or dissolved in water. However, the drug can also be insufflated, used rectally, smoked and intravenously injected.[2] Based on analysis of online fora, Corkery et al. reported that doses range from 1 mg to 10 mg according to mode of use, typical oral doses being 1–2 mg, but the optimum dose being thought of as 5–10 mg. The authors also reported that there is no information on whether the effects of 2-DPMP are dose-dependent or dependent on the mode of ingestion.[2] The elimination half-life is 16–20 hours.

The oral and insufflation of D2PM have been reported. The typical human active dose of D2PM is 2–5 mg, but reports on online drug user fora suggest that rectal doses range from 10 mg to 30 mg and oral doses from 35 mg to 50 mg.[2]

An analysis of user reports suggested that 2-DPMP effects are felt within 60 minutes of oral use, and may last up to 24 hours (or even 48 hours). The psychoactive effects of D2PM are similar to those of 2-DPMP but appear to occur 15 minutes after ingestion and may last up to 10 hours.[2]

Nasal irritation and epistaxis may occur after nasal insufflation. Analysis of user reports suggest that prolonged use of D2PM can cause craving and increased need to re-dose.[2]

11.3. Desired effects

Analysis of user reports of the desired psychoactive effects of 2-DPMP include prolonged euphoria, increased energy and alertness, sociability, and loquacity.[2] Other stimulant effects reported include sweating and bruxism.[3] The desired psychoactive effects of D2PM are, similar to those of 2-DPMP, but as mentioned earlier, occur sooner and last for less time.[2]

11.4. Mortality

2-DPMP has been detected in three fatalities in the UK,[2] its role in these deaths has not yet been established. There have been no reports of deaths directly attributed to either D2PM or 2-DPMP.

11.5. Acute harms

Information on the acute toxicity related to both D2PM and 2-DPMP is very limited. Reports suggest the development of sympathomimetic features similar to those seen with other recreational drugs and other amphetamines in particular, such as MDMA. They also suggest that these compounds may be associated with significant neuropsychiatric symptoms, which can be prolonged in nature, in which respect they are different to other sympathomimetic compounds.[3]

The limited experience of the UK National Poisons Information Service (NPIS) suggests that their acute clinical effects include tachycardia, palpitations, convulsions, raised levels of creatine kinase, acute renal failure and chest pain (sometimes with ECG abnormalities). There is also a reported risk of serotonin toxicity.[8] D2PM and 2-DPMP are related predominantly to neuropsychiatric symptoms.[4]

There is emerging evidence that they have sympathomimetic properties similar to cocaine.[3] The initial pattern of acute toxicity is similar to that of other sympathomimetic drugs, with users describing a 'rush'.[7] Prolonged and clinically significant neuropsychiatric symptoms have been reported following the use of the D2PM.[3,7] A high risk of central nervous and cardiovascular system toxicity has been suggested.[9] One case report of a presentation to a London emergency department associated with the use of D2PM (in addition to glaucine) described an individual who presented with acute onset of agitation and chest pain. The authors suggested that the D2PM was likely responsible for the ischaemic chest pain, as the acute toxicity of glaucine is more hallucinogenic in nature.[10]

There are two reports of acute harms associated with 2-DPMP (products sold as 'Ivory Wave' and 'Whack') from Scotland and Ireland,[1,11] although both studies lack robust analytical confirmation or have none at all ('Whack' also contained fluorotropacocaine).

An analysis of 37 consecutive patients attending the Royal Infirmary of Edinburgh emergency department in July and August 2010 with self-reported Ivory Wave use was carried out. Over a similar time frame, enquiries regarding Ivory Wave' to the NPIS, by telephone and via the internet-based TOXBASE®, were analysed. Analysis of both sets of data showed a toxidrome which lasted several days, and included tachycardia (65%), tachypnoea (76%), dystonia (18%), rhabdomyolysis (96%), leucocytosis (57%), agitation (62%), hallucinations (50%), insomnia (32%) and paranoia (21%).[1]

The use of D2PM and 2-DPMP is related to neuropsychiatric symptoms. There were 49 enquiries to the Irish National Poisons Information Centre relating to 'Whack'; these commonly described cardiovascular effects, including hypertension in 10 cases, and tachycardia. Neuropsychiatric effects were also reported, including agitation and psychosis, and these persisted for up to five days. However, this study was limited by the fact that fluorotropacocaine was also found in Whack and that there was no analysis of biological samples.[11]

Similarly, 96% had neuropsychiatric features in a case series of acute intoxication related to Ivory Wave. Cases presented up to a week after use, with tachycardia,

dystonia, rhabdomyolysis, agitation, hallucinations and paranoia. A similar Ivory Wave product contained 2-DPMP in another study, but that was limited by the fact that in the majority of cases biological samples were not analysed.[1]

A case series with analytical confirmation of D2PM in five individuals who presented to a London emergency department described patients showing the neuropsychiatric symptoms of agitation, anxiety and insomnia, lasting for 24–96 hours following the use of the D2PM.[7]

11.6. Chronic use

No information is available on the long-term effects of desoxypipradrol or of D2PM. Analysis of user reports suggest that, as with desoxypipradrol, prolonged use of D2PM leads to craving and a need to re-dose.[2]

11.7. Management of acute harms

The limited evidence on the acute toxic effects of 2-DPMP and D2PM suggests that the management of their harms is similar to the management of the harms from other stimulants and ATS.

Because of the particularly long-lasting effects of these drugs, the authors of a case series said that an important part of the management of presentations for acute intoxication was the reassurance of individuals that the prolonged neuropsychiatric symptoms will resolve.[7]

For up-to-date guidance on the management of pipradrol acute toxicity, it is recommended that information be sought from the National Poisons Information Service (NPIS), specifically the NPIS 24-hour telephone service and the poisons information database TOXBASE®:

http://www.toxbase.org/Poisons-Index-A-Z/2-Products/2-DPMP/

It is recommended that relevant clinicians and departments are registered to receive these facilities.

Non-UK readers should consult their local or national guidelines.

11. 8. Harm reduction

For more information on the reduction of the harms of ATS, see Chapter x, bearing in mind the fact that 2-DPMP and D-2PM are potent amphetamine-type stimulants. 2-DPMP in particular is a long-acting drug, capable of causing severe agitation, which can last for several days after a single dose

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