CASE REPORT

A novel psychoactive substance poses a new challenge in the management of paranoid schizophrenia

Caroline Anderson,¹ Christopher Morrell,¹ David Marchevsky²

¹Milton Keynes Hospital,
Milton Keynes,
Buckinghamshire, UK
²Campbell Centre, Milton
Keynes, UK

Correspondence to

Dr Caroline Anderson,
c.anderson@doctors.org.uk

Accepted 8 April 2015

SUMMARY

Novel psychoactive substances (NPS), or 'legal highs' are becoming more commonly used as recreational substances in the UK. Their clinical effects are little known and vary considerably between substances. This case discusses a psychiatric inpatient who repeatedly used a stimulant NPS called 'el blanco' while on leave, precipitating relapses of his schizophrenia. The patient initially denied drug use, considering legal highs as different from drugs. The relationship between NPS use and mental state was eventually revealed on careful direct questioning. He recovered and was discharged following treatment with clozapine and education about NPS use. We suggest that specific questioning about NPS usage is added to routine psychiatric history taking and that patients using NPS should be educated about the substances' use.

BACKGROUND

Novel psychoactive substances (NPS) are a growing problem in the UK. Commonly known as 'legal highs', they are a heterogeneous group of synthetic compounds that are designed to mimic the effects of illegal drugs. Similar to illegal compounds, these novel substances can be classed broadly into the categories of stimulants, hallucinogens and sedatives with multiple subclasses which are described in detail elsewhere.¹

Stimulants include the synthetic cathinones and phenylethylamines, which are structurally similar to the amphetamines and methylphenidate derivatives.² Synthetic cocaine substitutes are also available and have a stimulant effect.¹ Piperazines mimic ecstasy with less intensity.¹ Hallucinogens are primarily methylenedioxymethamphetamine-like drugs, synthetic tryptamines and plant-derived tryptamine analogues, which bear similarities to lysergic acid 2,4-dimethylazetidine.² Phencyclidine-like dissociative drugs, in particular ketamine, are also gaining popularity for their dissociative effects.¹ Sedatives include γ -aminobutyric acid receptor agonists, such as γ -hydroxybutyric acid and synthetic cannabinoids, which resemble cannabis in their clinical effects³ as well as synthetic opioids. Herbs and plants are also commercially available and widely used for a range of psychological effects.¹ Prescribed drugs continue to be sold on the black market, and an increasing range of performance and image-enhancing drugs are available; however, these fall outside of the definition of NPS used here.

Clinical understanding of the effects of NPS is limited by their evolving nature and inconsistent formulation.⁴ To date, there is very little evidence about the clinical impact of NPS in the UK. There is no published UK research on the use and impact of these substances on patients under the care of mental health services. An Italian study compared NPS use in psychiatric patients with a random sample of healthy subjects and found that NPS use was significantly higher in psychiatric patients than in healthy individuals.⁵ This is in continuity with the increased prevalence of drug use in mental health service users compared with the general population.^{6,7}

In this case, we present a patient who had repeated relapses of schizophrenia while taking the NPS 'el blanco', a stimulant reported to contain ethylphenidate and benzocaine.⁸ It demonstrates the psychoactive effects of this drug and is illustrative of the problems of legal high use in psychiatric patients.

CASE PRESENTATION

A man, in his 30s, with a 9-year history of paranoid schizophrenia was transferred to our care under Section 2 of the Mental Health Act 1983, after having spent 3 weeks at an out-of-area hospital. On arrival to our centre, he presented as settled in mental state. He went out for 6 hours on section 17 leave, and on return, he was found to be severely thought disordered exhibiting a chaotic and bizarre behavioural pattern. Vital signs were normal except for a pulse rate of 124 bpm, which dropped to 85 bpm within an hour. He was unable to give any explanation about what had happened due to the severity of his thought disorder. The disturbance in mental state persisted for 4 weeks with very little improvement, and he was placed under section 3 for treatment. After 6 weeks of inpatient care, his presentation improved and unescorted leave was felt to be safe and appropriate. He denied substance misuse on leave. He returned from 4 h leave and again was observed to have a disturbance in mental state, almost identical to his previous presentation. Physical examination and vital signs were normal, and urine drug screen was negative for commonly tested compounds. He remained an inpatient for the following 2 weeks, improving after 10 days. He was able to engage in discussion about his activities on leave and on direct questioning revealed that he had purchased a legal high called 'el blanco', which he consumed as

CrossMark

To cite: Anderson C,
Morrell C, Marchevsky D.
BMJ Case Rep Published
online: [please include Day
Month Year] doi:10.1136/
bcr-2015-209573

a drink by mixing the powder with a cola drink. The substance had cost £20 for 1 g and he had taken all of it, with the belief that it helped him more than medication. He did not consider it to be a 'drug'. He had taken this on both sets of leave, suggesting a causal relationship between use of the substance and deterioration in mental state. Both times he had gone out on day leave and had monitored compliance with his medication prior to taking leave, which strengthens the probability that his deterioration was due to substance use. The patient had poor insight into his mental illness and the fact that substance use could cause deterioration.

INVESTIGATIONS

On each occasion, vital signs were close to normal by the time he returned from leave and urine drug screen showed no evidence of drug use. Routine blood tests were normal, but formal toxicology was not carried out.

DIFFERENTIAL DIAGNOSIS

The patient's symptoms were typical for him during a relapse of his paranoid schizophrenia. The obvious differential diagnosis is a drug-induced psychosis. However, given the duration of the psychosis, and its similarity to this patient's usual relapses, this was excluded.

TREATMENT

Acute behavioural disturbances and agitation were managed with clonazepam 0.5 mg four times per day with haloperidol and lorazepam on an as-required basis. Seclusion was used on one occasion due to his behavioural disturbance endangering himself. Antipsychotic treatment was olanzapine 10 mg two times per day at the time point when he was transferred to our care and he complied with this. This was changed to pipotiazine palmitate 50 mg every four weeks during the first relapse, with the aim of improving compliance after discharge.

Following the connection between 'el blanco' usage and mental state deterioration being made, the patient was placed on a leave programme of multiple 30 min blocks, which minimised his ability to travel to the shop where he purchased legal highs. Longer leave was permitted with an escort.

Clozapine was initiated as it was felt that his recovery was incomplete on the previous treatment regimens, with residual symptoms of mild thought disorder and poor insight. With clozapine, we aimed to improve symptoms as well as increase insight into the connection between NPS use and illness. We hoped that further recovery with increased insight would prevent further usage of NPS.

Once therapeutic levels of clozapine were reached, the patient stabilised enough to engage in discussion and education about NPS usage. He was then able to undertake longer periods of leave, which were successful in facilitating discharge, 6 months after admission.

OUTCOME AND FOLLOW-UP

The patient responded well to clozapine, and despite still admitting a temptation to return to legal drugs, was able to see the negative aspects of taking them—citing a lack of knowledge of the long-term effects as a major deterrent. This was sufficient to prevent him from taking them and he was successfully discharged from inpatient care. He is currently receiving support from community teams and doing well, 3 months after discharge.

DISCUSSION

NPS are an increasing challenge for clinicians. They tend to be sold as research chemicals, bath salts, spices or plant food, and

are generally labelled 'not for human consumption'. They are named in a variety of ways: some are named after the chemical they are purported to contain, after the plant they are extracted from, similarly to medicines they are related to, or are given names with no relation to the chemical content.⁹ The available drugs are constantly changing and inconsistency in formulation of the same or similarly named products makes it difficult to diagnose their usage or predict their effects on patients.⁴

Data on use of NPS has gradually been emerging over the last 5 years. It is clear that NPS are being more commonly used as recreational substances^{10 11} and that adverse effects from NPS use are increasing, evidenced by the increasing enquiries and reports of misuse to poisons services.¹² Much of the marketing of NPS and the transfer of knowledge about use and effects of the substances between users is internet based, which has allowed for thorough investigation into these topics.^{13–19}

However, data on the clinical effects of NPS has been slow to emerge. The majority of evidence on the clinical effects of NPS concentrates on patients who have become critically ill after having taken legal highs. There is very little available information on NPS use in psychiatric patients, although anecdotal evidence suggests that use is widespread among patients in the UK and occurs in patterns similar to those of patients who are addicted to illegal drugs. Two cases reporting NPS use in psychiatric patients exist to date. The first discusses a psychiatric inpatient admitted to intensive care following use of a substance named neuregulin 3 (NRG-3), which he had bought from an online company.²⁰ A second report tells of a schizophrenic patient, with comorbid polysubstance abuse, who became addicted to 'bath salts' as an alternative to methamphetamine. He relapsed after several weeks of daily use and he only recovered when the product he was taking was made illegal.²¹

There is little knowledge about the impact that one-off or intermittent NPS use can have on mental health, particularly in patients with pre-existing conditions. This case indicates that use of NPS can be a precipitant for relapse among patients with schizophrenia. The primary limitation is a lack of formal toxicology screening, but given that NPS are rarely picked up on routine toxicology this is of debatable significance. We suggest that specific enquiry about legal highs is added to the routine drug and alcohol screening questions on admission to hospital. Further research into the use of NPS among psychiatric patients and the correlation with clinical course is needed urgently to allow adaptation of services to the needs of their users.

Learning points

- ▶ Novel psychoactive substances (NPS) are a growing problem in clinical practice and may be under-recognised by clinicians.
- ▶ These are especially likely to be a problem in vulnerable groups, such as psychiatric patients, who may not consider them as 'drugs'.
- ▶ NPS may cause significant symptoms outside the critical care context and should be considered as a possible cause of psychiatric symptomatology.
- ▶ Questions about NPS use should be added to routine psychiatric history taking and formal toxicology should be included in the routine psychiatric assessment.
- ▶ More research should be conducted into the link between NPS use and psychiatric disease course.

Contributors CA drafted the article and conducted the literature search. CM revised the article and aided with the literature search. DM advised on content and supervised the writing of the article.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- Schifano F, Orsolini L, Duccio Papanti G, *et al.* Novel psychoactive substances of interest for psychiatry. *World Psychiatry* 2015;14:15–26.
- Gibbons S. "Legal highs"—novel and emerging psychoactive drugs: a chemical overview for the toxicologist. *J Am Acad Clin Toxicol* 2012;50:15–24.
- Seely KA, Lapoint J, Moran JH, *et al.* Spice drugs are more than harmless herbal blends: a review of the pharmacology and toxicology of synthetic cannabinoids. *Prog Neuropsychopharmacol Biol Psychiatry* 2012;39:234–43.
- Baron M, Elie M, Elie L. An analysis of legal highs: do they contain what it says on the tin? *Drug Test Anal* 2011;3:576–81.
- Martinotti G, Lupi M, Acciavatti T, *et al.* Novel psychoactive substances in young adults with and without psychiatric comorbidities. *BioMed Res Int* 2014;2014:1–7.
- Ringin PA, Melle I, Birkenæs AB, *et al.* Illicit drug use in patients with psychotic disorders compared with that in the general population: a cross-sectional study. *Acta Psychiatr Scand* 2008;117:133–8.
- McCREADIE RG. Use of drugs, alcohol and tobacco by people with schizophrenia: case-control study. *Br J Psychiatry* 2002;181:321–5.
- Revealed: The cocktail of chemicals in legal highs sold on Britain's high streets [Internet]. Mirror. (cited 20 Jan 2015). <http://www.mirror.co.uk/news/uk-news/revealed-cocktail-chemicals-legal-highs-2472206>
- Novel psychoactive substances report (2011)—Publications—GOV.UK [Internet]. (cited 20 Nov 2014). <https://www.gov.uk/government/publications/novel-psychoactive-substances-report-2011>
- Wood DM, Hunter L, Measham F, *et al.* Limited use of novel psychoactive substances in South London nightclubs. *QJM* 2012;105:959–64.
- Dargan PI, Albert S, Wood DM. Mephedrone use and associated adverse effects in school and college/university students before the UK legislation change. *QJM Int J Med* 2010;103:875–9.
- Wood DM, Hill SL, Thomas SHL, *et al.* Using poisons information service data to assess the acute harms associated with novel psychoactive substances: poisons information services and NPS. *Drug Test Anal* 2014;6:850–60.
- Schmidt MM, Sharma A, Schifano F, *et al.* "Legal highs" on the net—evaluation of UK-based Websites, products and product information. *Forensic Sci Int* 2011;206:92–7.
- Davey Z, Schifano F, Corazza O, *et al.* E-psychonauts: conducting research in online drug forum communities. *J Ment Health* 2012;21:386–94.
- Bruneel CA, Lakhdar CB, Vaillant NG. Are "legal highs" users satisfied? Evidence from online customer comments. *Subst Use Misuse* 2013;49:364–73.
- Corazza O, Valeriani G, Bersani FS, *et al.* Spice, Kryptonite, Black Mamba: an overview of brand names and marketing strategies of novel psychoactive substances on the web. *J Psychoactive Drugs* 2014;46:287–94.
- Corazza O, Simonato P, Corkery J, *et al.* Legal highs: safe and legal heavens? A study on the diffusion, knowledge and risk awareness of novel psychoactive drugs among students in the UK. *Riv Psichiatr* 2014;49:89–94.
- Hohmann N, Mikus G, Czock D. Effects and risks associated with novel psychoactive substances: mislabeling and sale as bath salts, spice, and research chemicals. *Dtsch Arzteblatt Int* 2014;111:139–47.
- Soussan C, Kjellgren A. Harm reduction and knowledge exchange—a qualitative analysis of drug-related Internet discussion forums. *Harm Reduct J* 2014 (cited 1 Nov 2014). <http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=prem&AN=25200686>.
- Smith C, Williams M, Shaikh M. Novel psychoactive substances: a novel clinical challenge. *BMJ Case Rep* 2013 (cited 1 Nov 2014). <http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medl&AN=23964049>.
- McClean JM, Anspikian A, Tsuang JW. Bath salt use: a case report and review of the literature. *J Dual Diagn* 2012;8:250–6.

Copyright 2015 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit

<http://group.bmj.com/group/rights-licensing/permissions>.

BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- Submit as many cases as you like
- Enjoy fast sympathetic peer review and rapid publication of accepted articles
- Access all the published articles
- Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow