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EDITORIALS

Spice and all things nasty: the challenge of synthetic cannabinoids

An evolving problem that is difficult to detect and treat

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The Psychoactive Substances Act 2016, which came into force in May, signals a new approach to drug controls in the UK. For the first time, the basis for illegality is pharmacological action rather than chemical structure. The act made it illegal to produce or supply "spice" or synthetic cannabinoids and to possess them in a custodial setting.

Synthetic cannabinoids are a group of structurally unrelated compounds that act at the cannabinoid receptors CB1 and CB2. Spice is the commonest UK term, but there are more than 500 other street names, including black mamba and annihilation.[1] The chemicals are synthesised in a laboratory, dissolved in a solvent, then sprayed onto plant material, which is smoked or, less commonly, taken orally or injected. Previous attempts to ban synthetic cannabinoids failed because compounds with novel structures could be produced quickly. The clinical challenge of these substances mirrors the legislative challenge in that the severity of harms demands a substantial response while their chemical variety makes monitoring and treatment challenging.

Scale of the problem

Synthetic cannabinoids are the most commonly used novel psychoactive substances in Europe and the US.[2 3] Their use is more common in adolescents: 10% of American and 6% of European teenagers have used synthetic cannabinoids.[2 4] Teenagers use them because their previously unregulated status, availability, and marketing as "herbal" led to the misconception that they were innocuous.[5] In an internet survey 37% of users reported harmful synthetic cannabinoid use and 15% reported dependence.[6]

Up to a third of prisoners in the UK use synthetic cannabinoids,[7] possibly as a substitute for cannabis; positive tests for cannabis have fallen by 59% over the past decade while use of spice has increased.[8 9] Synthetic varieties are often more harmful than cannabis, and a report from nine English prisons recorded 54 serious incidents in which spice was implicated over three months in 2015; in 44% of these the prisoner required hospital admission for toxicity, 19% involved violence, and 9% self harm.[9] These substances have also been associated with psychosis characterised by aggression and requiring continuing antipsychotic treatment.[5]

Greater toxicity can be attributed to three pharmacological features.[10] Firstly, synthetic cannabinoids show a 50-300 times greater affinity for the CB1 receptor than tetrahydrocannabinol (THC), so a smaller amount occupies most receptors. Secondly, they are full agonists at CB1 receptors, whereas tetrahydrocannabinol is a partial agonist, so stimulate the receptor more. Thirdly, synthetic cannabinoids are also full agonists at the CB2 receptor, with downstream effects on other receptors including the 5HT2A receptor, implicated in tachycardia and seizures. Other pharmacological effects are less well described but include modulation of dopamine, noradrenaline, glutamate, and γ-aminobutyric acid transmission.[5]

Assessment and treatment

Guidelines produced by NEPTUNE, an expert group of addictions specialists, toxicologists, and emergency medicine physicians funded by the Health Foundation to respond to the challenge of novel psychoactive substances in the UK, provide an overview of the assessment and treatment of both acute toxicity and chronic use of synthetic cannabinoids as well as online educational resources.[11]Diagnosis of acute toxicity relies on clinical recognition because synthetic cannabinoids cannot be detected by routine urine tests.[6-12] Clinically, intoxication resembles cannabis intoxication: conjunctival injection, dry mouth, cold extremities, tachycardia, and hypertension.[13]

The NEPTUNE guidelines do not suggest investigations, but the following may detect reported complications: electrocardiography to detect arrhythmia and ischaemia; blood tests for urea and electrolytes, liver enzymes, and glucose; and blood gases to detect electrolyte disturbance, hepatotoxicity, renal toxicity, and acidosis.[13] Supportive measures, including intravenous fluids, antiemetics, and benzodiazepines, are the mainstay of treatment. Second generation antipsychotics are

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recommended for psychotic symptoms because they are 5HT2A antagonists.[11] Recommended support for abuse and dependence includes psychosocial interventions that are effective for all addictions, including brief intervention, structured psychosocial support, and signposting to mutual aid, delivered according the stepped care model prevalent in the UK.[11]

Synthetic cannabinoids are undoubtedly an increasing problem, albeit in circumscribed populations. Severe acute toxicity is common, and dependence is a risk in heavy users. Uncertainty exists about further spread and route of use, and prevalence in other vulnerable populations such as psychiatric patients. The effects of the ban are uncertain: while it may increase users' perception of harmfulness, there are also harms associated with illegality, such as criminalisation. The predominant chemical families of synthetic cannabinoids already in circulation are unknown, limiting the development of effective urine tests. Finally, the optimal treatment of toxicity is still unknown. Although an antidote, rimonabant, exists, it has severe side effects, and it is unclear how or if it should be used in practice. Research to identify best practice and best treatments is therefore a high priority.

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